نهمین سمینار کشوری

ایران - اصفهان ۲۵ آبان ۱۴۰۲

ژنتیک پزشکی

(تشخیصی_تحقیقی)

دانشگاه علوم پزشکی اصفهان برگزار می کند

سمینار کشوری ژنتیک پزشکی (تشخیصی_تحقیقی)

دارای امتیاز بازآموزی

دومین

گروه هدف:

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ژنتیک مولکولی و پزشکی مولکولی

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محورها:

ژنتیک بالینی و مشاوره ژنتیک

نازایی و سقط های مکرر غربالگری

و تشخیص قبل از تولد

ژنتیک سرطان

ژنتیک بیماری‌های ارثی

ژن درمانی و ویرایش ژنی

۲۵ آبان ماه

۱۴۰۲

ساعت ۸ صبح تا ۶ بعد از ظهر

مکان برگزاری:
دانشگاه علوم پزشکی اصفهان

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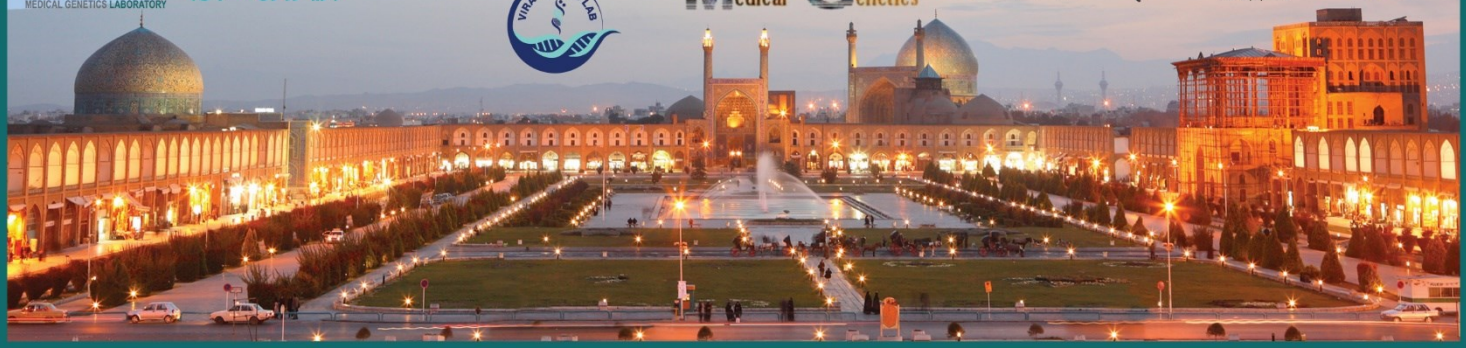

حامیان
نهمین سمپنار کشوری ژنتیک پزشکی
(تشخیصی_تحقیقی)

برگزار کننده:

دانشگاه علوم پزشکی اصفهان

حامیان:

آزمایشگاه ژنتیک پزشکی هارمونیک

شرکت تریتا ژن

درمان نگار آیندگان-لیان آزمای بهار

آزمایشگاه ژنتیک پزشکی ویرا

شرکت کاراژن تشخیص

هلدینگ بوعلی و آکا

آزمایشگاه هارمونیک

کلینیک چند تخصصی نوژن

آزمایشگاه اریترون

پیام رئیس سمینار

بسم الله الرحمن الرحیم

سمینارهای ژنتیک پزشکی (تشخیصی- تحقیقی) که هر ساله به عنوان یکی از ارزشمند ترین سمینار ژنتیک پزشکی در کشور برگزار می‌شود، فرصتی عظیم برای به اشتراک گذاری دانش، تجارب و پیشرفت‌های اخیر در زمینه تشخیص و تحقیقات ژنتیکی را فراهم می کند. ما افتخار برگزاری نهمین دوره این سمینار در شهر اصفهان داریم.

این سمینار فرصتی مناسب برای ارتقاء همکاری‌های علمی و تبادل اطلاعات بین اعضای ارجمند جوامع پزشکی و ژنتیکی می‌باشد. موضوعات متنوع ارائه‌شده در این سمینار از تشخیص تا تحقیقات پایه و بالینی را پوشش می‌دهد و امیدوارم که ما بتوانیم از این فرصت برای بهبود بهترین روش‌های تشخیصی و درمانی در حوزه ژنتیک پزشکی بهره بریم.

بر خود لازم می دانم، از تمامی اعضای کادر اجرایی و علمی، مدیران، سخنرانان و شرکت‌کنندگان عزیز این سمینار تشکر کنم.. امیدوارم که این سمینار بتواند یک فرصت مناسب برای یادگیری، تبادل افکار و آشنایی با همکاران عزیز باشد.

دکتر محمد امین طباطبائی فر

دبیر علمی نهمین سمینار کشوری ژنتیک پزشکی (تشخیصی-تحقیقی)

ایران- اصفهان- آبان ماه ۱۴۰۲

سازمان سمینار

رئیس سمینار/وبینار:

دکتر محمد امین طباطبائی فر (استاد تمام و متخصص ژنتیک پزشکی)

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- دکتر فرخنده بهجتی- استاد تمام و متخصص ژنتیک پزشکی
- دکتر جواد کریم زاد حق- متخصص ژنتیک پزشکی
- دکتر امید ایروانی- متخصص ژنتیک پزشکی
- دکتر آرش پولادی- پزشک و متخصص ژنتیک پزشکی
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- موسی رضا شیری- کارشناسی ارشد ژنتیک پزشکی
- مهسا زمانی- کارشناسی ژنتیک

عنوان پنل		اعضا پنل	عنوان سخنرانی
افتتاحیه و سخنرانی دبیر علمی	۸:۰۵–۸:۱۵	دکتر محمد امین طباطبائی فر استاد تمام گروه ژنتیک دانشکده پزشکی، دانشگاه علوم پزشکی اصفهان ، رئیس آزمایشگاه هارمونیک	دبیر علمی سمینار
پانل ژنتیک بالینی و مشاوره ژنتیک	۸:۱۵–۸:۳۰	دکتر محمد رضا نوری دلویی استاد تمام دانشکده پزشکی، دانشگاه علوم پزشکی تهران	تاریخچه ژنتیک پزشکی
	۸:۳۰–۸:۴۵	دکتر سید محمد اکرمی استاد تمام دانشکده پزشکی، دانشگاه علوم پزشکی تهران ،رئیس انجمن ژنتیک ایران	وضعیت ژنتیک پزشکی ایران: فرصت‌ها و تهدیدها
	۸:۴۵–۹:۰۰	دکتر حسین نجم آبادی استاد تمام دانشگاه علوم توانبخشی و خدمات اجتماعی، موسس مرکز تحقیقات ژنتیک	کاربرد توالی یابی نسل جدید برای تشخیص اختلالات مندلی در جمعیتی با نسبت خویشاوندی بالا: نتایج بیش از ۱۴۰۰ خانواده ایرانی
	۹:۰۰–۹:۱۵	دکتر صادق ولیان استاد تمام ژنتیک دانشگاه اصفهان از سال ۱۳۹۰ و موسس اولین آزمایشگاه تشخیص قبل از تولد بیماری های ژنتیک در اصفهان	Exome sequencing identifies novel variants associated with non-syndromic hearing loss in the Iranian population
	۹:۱۵–۹:۳۰	دکتر مجید حسین زاده دکترای تخصصی ژنتیک پزشکی و استادیار دانشکده پزشکی ، دانشگاه علوم پزشکی اصفهان	نقش متخصصین ژنتیک بالینی در شناسایی ، تشخیص و مدیریت بیماریهای نادر
	۹:۳۰–۹:۴۵	دکتر بتول آزاده متخصص بیماری های کودکان، اصفهان	ژنتیک بالینی و مشاوره ژنتیک
	۹:۴۵–۱۰:۰۰	دکتر محمد جواد ملک نیا دکترای حرفه ای پزشکی، مشاور ژنتیک و بیماری های ارثی	مشاوره ژنتیک در بیماریهای شایع عصب شناختی
	۱۰:۰۰–۱۰:۲۵	پذیرایی و استراحت و بازدید از پوسترها	
	۱۰:۲۵–۱۰:۳۰	بزرگداشت زحمات پروفسور فقید محمد حسن کریمی نژاد	

پانل نازایی و سقط های مکرر & غربالگری و تشخیص قبل از تولد	۱۰:۳۰–۱۰:٤٥	دکتر رکسانا کریمی نژاد دکترای تخصصی ژنتیک پزشکی، مرکز پاتولوژی و ژنتیک کریمی نژاد-نجم آبادی	کاربرد میکرو آرایه های کروموزومی در تشخیص قبل از تولد و تجربه ۵۹۰۰ مورد انجام شده در مرکز پاتولوژی و ژنتیک کریمی نژاد نجم آبادی
	۱۰:٤٥–۱۱:۰۰	دکتر محمد امین طباطبایی فر استاد تمام و عضو هیات علمی گروه ژنتیک دانشکده پزشکی، دانشگاه علوم پزشکی اصفهان ، رئیس آزمایشگاه هارمونیک	Harmony Prenatal Test: Application and Implementation for the First Time in Iran
	۱۱:۰۰– ۱۱:۱۵	دکتر سمیه خانجانی متخصص زنان و زایمان، فلوشیپ پریناتولوژی اصفهان	When Is Non-Invasive Prenatal Testing Reliable in Pregnancies with Vanishing Twin? - A Systematic Review of Case Reports
	۱۱:۱۵–۱۱:۳۰	دکتر جواد کریمزاد حق متخصص ژنتیک پزشکی دوسلدورف – المان ، موسس آزمایشگاه ژنتیک واتسون	Perry syndrome combined with 22q11.2-microduplication-syndrome in a large Dutch family: the challenge of ethical dilemmas and PGD
	۱۱:۳۰–۱۱:٤٥	دکتر فرخنده بهجتی استاد تمام ژنتیک پزشکی، دانشگاه علوم توانبخشی و خدمات اجتماعی و بیمارستان فوق تخصصی صارم	Prenatal karyotype analysis of 8245 amniotic fluid samples of Iranian women and report of their chromosomal abnormalities based on maternal age of above and less than 35 years: A 15-year single-center study
	۱۱:٤٥–۱۲:۰۰	دکتر سید محمد سید حسنی استاد ژنتیک پزشکی ، موسس مرکز ژنتیک پزشکی، یزد	مشاوره ژنتیک در ارزیابی سلامت جنین
	۱۲:۰۰–۱۲:۱۵	دکتر پرهام مردی دکترای حرفه ای پزشکی، بیمارستان فوق تخصصی صارم	Identifying Screening Cut-Off for Amniocentesis in Down Syndrome Patients
	۱۲:۱۵–۱۲:۳۰	دکتر منصور صالحی استاد تمام و عضو هیئت علمی گروه ژنتیک و بیولوژی مولکولی دانشکده پزشکی علوم پزشکی اصفهان، مدیر آزمایشگاه ژنتیک پزشکی ژنوم اصفهان	Genetic Factors Associated with Recurrent Pregnancy Loss
	۱۲:۳۰–۱۲:٤٥	دکتر رسول صالحی استاد تمام و عضو هیئت علمی گروه ژنتیک و بیولوژی مولکولی دانشکده پزشکی علوم پزشکی اصفهان، رییس مرکز تحقیقات	Preimplantation Genetic Diagnosis/Testing (PGD/PGT): A multi-potential technology

		بیماری های ارثی کودکان، استاد و عضو هیئت علمی گروه ژنتیک و بیولوژی مولکولی دانشکده علوم پزشکی اصفهان	
	۱۲:٤٥–۱۳	**دکتر امید ایروانی** متخصص ژنتیک پزشکی، موسس کلینیک چند تخصصی خدمات ژنتیک نوژن	Clinical importance of fetal examination in abortion, stillbirth and perinatal deaths
	۱۳:۰۰–۱۳:۱۵	**دکتر آسیه جعفری** متخصص پزشکی قانونی و مسمومیتها, سازمان پزشکی قانونی کشور, تهران	**به روز رسانی دستورالعمل اجرایی ماده ٥٦ قانونی حمایت از خانواده و جوانی جمعیت**
	۱۳:۱۵–۱٤:۱۵	**ناهار و نماز**	
پانل بیماری های ارثی و ژنتیکی	۱٤:۱۵–۱٤:۳۰	**دکتر احسان غیور** متخصص ژنتیک پزشکی ، مدیر عامل کلینیک و رئیس تیم تخصصی ژنتیک کلینیک نسل فردا	Leveraging consanguinity in neuromuscular inherited diseases
	۱٤:۳۰–۱٤:٤٥	**دکتر مجید مجرد** دانشیار گروه ژنتیک و مدیر گروه ژنتیک‌پزشکی و پزشکی‌مولکولی دانشگاه علوم پزشکی مشهد، مدیرعامل شرکت پارس سیمرغ دارو دماوند	New advancements in CRISPR based gene therapy of Duchenne muscular dystrophy
	۱٤:٤٥– ۱٥:۰۰	**دکتر سید مهدی کلانتر** استاد تمام دانشگاه علوم پزشکی شهید صدوقی یزد	Heterozygous ANKRD17 loss-of-function variants cause neurodevelopmental delay, learning difficulties, seizures, microcephaly, and poor speech
	۱٥:۰۰–۱٥:۱٥	**دکتر فرزانه پویا** متخصص ژنتیک پزشکی، مرکز ژنتیک کریمی نژاد–نجم آبادی	The Eighth Case with Mucolipidosis II/III Result from Mutation in TMEM251 in the World
	۱٥:۱٥–۱٥:۳۰	**دکتر ناصر عجمی** متخصص ژنتیک پزشکی ، دانشگاه علوم پزشکی مشهد	Expanding the phenotypic, genotypic, and functional spectrum of *CNPY3* - associated DEE
	۱٥:۳۰–۱٦:۰۰	**پذیرایی و استراحت و بازدید از پوسترها**	
پانل ژنتیک سرطان	۱٦:۰۰–۱٦:۱٥	**دکتر محمد کاظمی** استادیار پزشکی مولکولی، گروه ژنتیک و بیولوژی مولکولی، دانشگاه علوم پزشکی اصفهان	Knockdown of lncRNA FLVCR1-AS1 and evaluation of its inhibitory effects on

proliferation and induction effects on apoptosis of Colorectal Cancer cell line			
Low risk and high risk CLL patients by genetic feature: prognosis, future plan and response to therapy	**دکتر مرجان یغمایی** دکترای تخصصی ژنتیک پزشکی و موسس آزمایشگاه ژنتیک پزشکی دکتر یغمایی، دانشیار گروه ژنتیک، دانشگاه تهران	۱۶:۱۵–۱۶:۳۰	
Developing a Gene Delivery System as a vehicle in Gene Therapy: MCM-Co-Polymerized based Nanosystem Functionalized with MUC-1 Aptamer against Breast Cancer	**دکتر لاله شریعتی** استادیار پزشکی مولکولی گروه بیومواد، نانوتکنولوژی و مهندسی‌بافت، دانشکده فناوری‌های نوین علوم پزشکی مرکز تحقیقات بیوسنسور دانشگاه علوم پزشکی اصفهان	۱۶:۳۰–۱۶:۴۵	
Two Distinct Cancer-Causing Variants in a Family with Multiple Affected Members	**دکتر مهرداد زینلیان** استادیار دانشکده علوم پزشکی ، دانشگاه علوم پزشکی اصفهان	۱۶:۴۵–۱۷:۰۰	
Cytogenetically Balanced Translocation in a Newborn Diagnosed with VACTERL Association	**دکتر احمدرضا صالحی** دکترای تخصصی ژنتیک پزشکی، مرکز ژنتیک مام	۱۷:۰۰–۱۷:۱۵	
Complex hypodiploidy karyotype in acute myeloid leukemia at diagnosis	**دکتر رضا صدریا** دکتری تخصصی ژنتیک پزشکی، سوپروایزر آزمایشگاه پیوند	۱۷:۱۵–۱۷:۳۰	
اختتامیه و اهداء تندیس و جوائز		۱۷:۳۰–۱۸	

سخنران: **دکتر سید محمد اکرمی**

وضعیت ژنتیک پزشکی ایران: فرصت‌ها و تهدیدها

دکتر سید محمد اکرمی

استاد دانشگاه علوم پزشکی تهران، رئیس انجمن ژنتیک پزشکی ایران

چکیده

ژنتیک پزشکی پل ارتباطی بین مطالعات پایه و یافته‌های بالینی است. پیشرفت‌های چند برابری در مدت کوتاه، این علم را منحصر به فرد در میان علوم سلامت قرار داده است. ژنتیک پزشکی به عکس سایر تک رشته‌های آزمایشگاهی به مدیریت بیماری شامل تشخیص، درمان، پیشگیری، غربالگری، پیگیری و پیش آگهی می پردازد. خودکفایی ایران در تربیت نیروی انسانی در مقاطع دکتری ژنتیک پزشکی و کارشناسی ارشد ژنتیک انسانی در دانشگاه‌های علوم پزشکی در این ارائه بیان خواهند شد.

با توجه به افزایش سن ازدواج و بارداری در کشورمان خطر افزایش ناهنجاری‌های مادرزادی و تریزومی‌های شایع کروموزومی ۱۳ و ۱۸ و ۲۱ را محتمل می‌نماید. از سوی دیگر با توجه به افزایش ازدواج فامیلی بیماری‌های اتوزومال مغلوب در حال افزایش‌اند.

فرصت‌ها و تهدیدها با رویکرد ژنتیک اجتماعی در همایش تبیین خواهند شد.

سخنران: **دکتر حسین نجم آبادی**

کاربرد توالی یابی نسل جدید برای تشخیص اختلالات مندلی در جمعیتی با نسبت خویشاوندی بالا: نتایج بیش از ۱۴۰۰ خانواده ایرانی

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چکیده

توالی یابی نسل جدید (NGS) به عنوان یکی از قدرتمند ترین روشها برای تشخیص اختلالات مندلی نادر، بویژه بیماریهای دارای منشا ژنتیکی متنوع، شناخته شده است. درحالی که نرخ تشخیصی تست های مبتنی بر NGS درکوهورت های بیماران انتخاب نشده در حال حاضر بین ۲۵ تا ۳۴ درصد گزارش شده است، مطالعات در چندین جمعیت خاور میانه ای بیانگر بازده بالاتر تا ۴۸ درصد برای اینگونه تست ها میباشد، که با میزان بالای ازدواج خویشاوندی و شیوع بیماریهای اتوزوم مغلوب در این جمعیت ها مطابقت دارد. ما در این مطالعه برای اولین بار به ارزیابی عملکرد تست NGS در تشخیص طیف گسترده ای از بیماری های مندلی در جمعیت ایران با نسبت خویشاوندی بالا پرداخته ایم. در این گزارش نتایج تست تشخیصی NGS در ۱۴۳۶ خانواده که طی هشت سال به یک آزمایشگاه ژنتیک پزشکی در تهران مراجعه کرده اند مورد بررسی قرار گرفته است. در مجموع ۱۰۷۵ بیمار به روش توالی یابی کل اگزوم (WES) و ۳۶۱ بیمار توسط توالی یابی پنل ژنی و اکثرا به صورت فقط پروباند (٪۹۱.۶) مورد آزمایش گرفته اند. نرخ کلی تشخیص ٪۴۶.۶ ارزیابی شد که از ٪۲۴ در بیماران با ناهنجاریهای قبل از تولد تا بیشتر از ٪۶۷ در بیماران با ناهنجاری های پوست متغیر بود. این مطالعه منجر به شناسایی ۶۵۹ واریانت بیماری زا یا احتمالاً بیماری زا مرتبط با بیش از ۳۴۱ اختلال شناخته شده ژنتیکی شد که ازاین بین ۲۴۱ واریانت جدید بوده و تا کنون در مقالات علمی گزارش نشده اند. با توجه به درصد بالای ازدواج خویشاوندی در این کوهورت، اکثریت موارد تشخیص قطعی مربوط به بیماریهای اتوزوم مغلوب بودند. این ویژگی همچنین منجر به شناسایی وضعیت ناقلی مشترک در زوجینی شد که جهت تشخیص بیماری مشکوک به اتوزوم مغلوب در فرزندان متوفی خود مراجعه کرده بودند و نمونه ی بیمار جهت تست مستقیم در دسترس نبود. همچنین در این مطالعه چندین نمونه از وراثت مغلوب در ژن هایی که تا به قبل تنها با بیماریهای اتوزوم غالب مرتبط شده بودند، از جمله *DCTN1* ، *KCNC3*، *BICC1*، *GLI3*، *MITF*، *HARS1* و *UFSP2* مشاهده گردید. و در نهایت، ۹۴ واریانت بیماری زای مغلوب با احتمال اثر بنیانگذار در جمعیت ایران شناسایی شد. این جامع ترین گزارش از طیف جهش های مرتبط با بیماریهای مندلی شناخته شده در جمعیت ایران است که می تواند به عنوان منبعی منحصر به فرد برای مطالعات ژنومیک بالینی در سطح محلی و فراتر از آن قرار گیرد.

سخنران: دکتر صادق ولیان

Exome sequencing identifies novel variants associated with non-syndromic hearing loss in the Iranian population

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Autosomal recessive non-syndromic hearing loss (ARNSHL) is a public health concern in the Iranian population, with an incidence of 1 in 166 live births. In the present study, the whole exome sequencing (WES) method was applied to identify the mutation spectrum of NSHL patients negative for GJB2 gene mutations. First, using ARMS PCR followed by Sanger sequencing of the GJB2 gene, 63.15% of mutations in patients with NSHL were identified. Among the identified mutations in GJB2:p.Val43Met and p.Gly21Arg were novels. The remaining patients were subjected to WES, which identified novel mutations including MYO15A:p.Gly39LeufsTer188, ADGRV1:p.Ser5918ValfsTer23, OTOF:p.Asp661GlyfsTer2, MYO7A: c.5856+2T>c (splicing mutation), FGF3:p.Ser156Cys. The present study emphasized the application of WES as an effective method for molecular diagnosis of NSHL patients negative for GJB2 gene mutations.

Keywords: Non-syndromic hearing loss; GJB2; Iranian population; Whole exome sequencing; Molecular diagnosis

سخنران: **دکتر مجید حسین زاده**

نقش متخصصین ژنتیک بالینی در شناسایی ، تشخیص و مدیریت بیماریهای نادر

مجید حسین زاده

استادیار گروه ژنتیک و بیولوژی مولکولی دانشگاه علوم پزشکی اصفهان

چکیده

اخیرا تلاشهای متعددی در جهت جمع آوری داده های مرتبط بابیماریهای نادربه منظور اشتراک آنها برای گروههای مختلف از بیماران گرفته تا تولید کنندگان دارو وارایه کنندگان خدمات کلینیکی و پارا کلینیکی صورت پذیرفته است یکی از کاملترین پایگاهها کنسرسیوم RARE-Xم میباشد که اطلاعات چندین پایگاه داده بیماری‌های نادر را به اشتراک میگذارد، این پایگاه تخمین زده که تاکنون حدود ۱۰۸۶۷ بیماری نادر ژنتیکی وجود دارد که بسیار بیشتر از تخمین‌های قبلی(۵۰۰۰ تا ۸۰۰۰) است. درمان کمتر از ۱۰ درصد این بیماری ها، با استفاده از داروهایی است که پیامدها ومشکلات ناشی از اختلالات ژنتیکی غیرطبیعی را کاهش می‌دهند، هرچند بهبودی کامل بوجود نمی آورند. در حالی که۹۰ درصد باقی مانده گزینه های درمانی قابل قبولی ندارند

ژنتیک بالینی ، یک تخصص در زمینه مدیریت بیماران وکمک به خانواده هایی است که دارای یک بیماری ژنتیکی داشته یا در معرض خطر ابتلا به آن هستند. متخصصین این رشته از نزدیک با مشاوران ژنتیک برای حمایت از بیماران، خانواده ها و تیم های بالینی همکاری میکنند. ارزیابی علایم بالینی،یافته های پاراکلینیکی و سابقه پزشکی بیمار، جمع‌آوری و تجزیه و تحلیل سابقه خانوادگی ،شناسایی الگوهای وراثت و محاسبه خطر تکرار بیماری ، به شناسایی خانواده‌هایی که در معرض خطر احتمالی یک بیماری ژنتیکی هستند، کمک می‌کنند. این متخصصین با ارایه اطلاعاتی در مورد آزمایش ژنتیک،تفسیر ونتیجه گیری از این تستها به سایر کارکنان بخش سلامت برای تشخیص بیمارانی که ممکن است بدونه این جمع بندی اطلاعات قادر به تشخیص آن نبوده اند کمک میکنند.متخصصان ژنتیک بالینی اغلب در تحقیقات پزشکی مشارکت می کنند .برگزاری برنامه های آموزشی ترکیبی ژنتیک پزشکی و ژنومیک با گروههای تخصصی نظیر اطفال، طب داخلی، نورولوژی جنین شناسی و زنان و زایمان ،نقص ایمنی و غدد درون ریز ،باروری و ناباروری و جراحی اطفال از مواردی است که علاوه بر کمک به تصمیم گیری صحیح در مورد بیماران، باعث میگردد مهارت ایشان در این رشته ها نیزافزایش یابد

در کشور های برخوردار از این رشته اکثر متخصصین ژنتیک بالینی در سیستم بهداشت به صورت دولتی یا خصوصی کار می کنند و بخشی از یک تیم ماهر در خدمات تشخیصی هستند. متخصصین ژنتیک بالینی برای ارائه مشاوره و ارزیابی در موارد زیر فعالیت دارند : انکولوژی، بارداری و ناباروری و مراقبتهای دوران بارداری، قلب و عروق، نورولوژی و عصب شناسی، اطفال، غدد و اختلالات متابولیک، ناهنجاریهای مادرزادی و اختلالات یادگیری، نقص ایمنی و غیره

متخصص ژنتیک بالینی با شناسایی فنوتیپ بیماری و ارزیابی اطلاعات موجود، تشخیص افتراقی های ممکن را مطرح ساخته و بر اساس آن آزمایش و اقدامات تشخیصی مناسب را توصیه میکند: به عنوان مثال، اندازه‌گیری متابولیتها و/یا فعالیت آنزیم ها برای خطاهای مادرزادی متابولیسم، آزمایش مولکولی یا سیتوژنتیک برای بررسی فنوتیپ های پیچیده نظیر ناتوانی ذهنی و/یا ناهنجاری های مادرزادی . سپس هر آزمایش بر اساس یافته های بیمار و سابقه خانوادگی بیمار تفسیر می شود. گاه نتایج یک آزمایش با استفاده از آزمایش دیگری تأیید می شود. تفسیر نتایج نامشخص باید با ظرافت ودقت ویژه ای صورت پذیرد. آزمایش‌های جدیدتری که حساسیت و دقت را بهبود می‌بخشد (توانایی آزمایش برای تشخیص یک فرد با یک بیماری خاص) مدنظرقرار داده می شوند. که میتواند احتمالاً با معرفی پانل‌های چند ژنی، توالی‌یابی کل اگزوم و توالی‌یابی کل ژنوم همراه گردد. پانل‌های چند ژنی که چندین ژن را در یک زمان مورد بررسی قرار می‌دهند (مانند ناشنوایی و کاردیومیوپاتی) و آزمایش‌هایی که کل ژنوم را مورد توجه قرار می‌دهند، امروزه الگوی بررسی را به «اول ژنوم» (و دوم فنوتیپ) تغییر داده است.

سخنران : دکتر بتول آزاده

ژنتیک بالینی و مشاوره ژنتیک

بتول آزاده

مشاوره ژنتیک همان گونه که عنوان آن نشان می دهد با دو رشته از دانش بشری ،علم ژنتیک و مشاوره ، در ارتباط است. بنا براین مشاور ژنتیک باید هم با اصول و مبانی ژنتیک آشنا باشد تا بتواند اختلالات ژنتیکی را تشخیص دهد و هم باروش های بر قراری ارتباط و شیوه های کمک رسانی به افراد آشنایی داشته باشد تا بتواند به حل مشکل یاری رساند.

تعریف مشاوره: از مشاوره تعریف های متفاوتی با توجه به دیدگاه های مختلف ارائه شده است . اما بر اساس جنبه های مشترک این تعاریف می توان گفت:مشاوره ارتباطی یاورانه و رویاروی بین دو فرد است ،یکی مراجع که مشکلی دارد و دیگری مشاور که با توجه به دانش و مهارت خود می تواند در حل مشکل و تصمیم گیری درست مراجع را یاری رساند.

مشاوره ی ژنتیک همانند همه مشاوره های پزشکی یک فرآیند ارتباطی شامل:

تشخیص؛ توضیح؛ راهنمایی: برای انتخاب بهترین گزینه است. با این تفاوت که نتیجه مشاوره ممکن است به جز شخص مشورت جو بر سلامت سایر افراد خانواده نیز تاثیر بگذارد.

این فرآیند به بیمار و خانواده اش کمک می کند تا:

۱ -واقعیت های پزشکی (مربوط به خود) را درک نماید.

۲ -سهم توارث را در بیماری خود و احتمال بروز مکرر آن را در خویشاوندان خود بداند.

۳ -راه های موجود برای رویارویی با مشکل را بشناسد(روش های تشخیص قبل از تولد، روش های جایگزینی باروری ،...).

۴-بتواند راهی را که با اهداف ،ا رزش ها و اعتقادات وی سازگار است انتخاب نماید.

۵ -بتواند در حد امکان با بیماری خود کنار بیاید و تبعات آن را تحمل نماید.

اندیکاسیون های مشاوره ژنتیک: به طور کلی در هر عارضه ای که احتمال ژنتیکی بودن آن وجود داشته باشد، مشاوره ژنتیک ضروری است.

هم چنین با مشاوره ی دقیق می توان معلوم کرد که آیا بیماری مورد نظر ارثی هست یا خیر.

در صورت ارثی بودن بیماری میزان بروز آن در فرزند بعدی نیز اهمیت دارد.

اندیکاسیون های انجام مشاوره ژنتیک

- نگرانی از خطر بروزمکرر یک بیماری فا میلی
- نقایص متعدد مادرزادی
- عقب ماندگی های ذهنی
- بیماری های عصبی مزمن و پیشرونده
- اختلالات عصبی – عضلانی
- کوتولگی و اختلالات رشد
- اختلالات متابولیک
- شکل و قیافه غیر طبیعی
- ابهام تناسلی ،اختلال بلوغ
- رویارویی با مواد تراتوژن و مو تاژن
- نازایی ،عقیمی و سقط های مکرر
- حاملگی در سنین بالا
- ازدواج با خویشاوندان
- کسب اطمینان از ناقل نبودن برای یک بیماری ژنتیکی شایع در جمعیت (تالاسمی، هموفیلی،و ...)
- سرطان ،دیابت،بیماری های قلب

سخنران: **دکتر رکسانا کریمی نژاد**

کاربرد میکرو آرایه های کروموزومی در تشخیص قبل از تولد و تجربه ۵۹۰۰ مورد انجام شده در مرکز پاتولوژی و ژنتیک کریمی نژاد نجم آبادی

رکسانا کریمی نژاد[۱]

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چکیده

از سال های ۱۹۹۰ که استفاده از میکرو آرایه ها برای تشخیص بیماری ها کاربرد روتین پیدا کرده در بسیاری از موارد از جمله تشخیص علل ژنومیک در افراد با تاخیر رشد ذهنی و جسمی، با طیف اوتیسم، و اختلالات متعدد مادرزادی توان و قدرت تشخیصی بیشترش اثبات شده وجایگزین کاریوتایپ روتین شده. سال ۲۰۰۵ اولین گزارش استفاده از این تکنیک برای تشخیص قبل از تولد منتشر شد و از آن پس در مراکز بیشتری به این منظور کاربرد پیدا کرد.

مطالعات چند مرکزی متعددی با توجه به نتایج بدست آمده جایگزینی استفاده از کاریوتایپ روتین با استفاده از میکرو آرایه ها را توجیه میکنند. بخصوص درمواردی که اختلالات ساختاری در سونوگرافی جنین مشاهده میشود و یا اینکه برای مواردی که افزایش قابل ملاحظه ای داشته باشد.

از سال ۱۳۹۳ هم ما در مرکز پاتولوژی و ژنتیک کریمی نژاد نجم آبادی از این تکنیک برای تشخیص قبل از تولد استفاده کرده ایم. از آن تاریخ مجموعا ۵۰۷۰ مورد انجام شده که علل مراجعه و نتایج بدست آمده بررسی میشوند.

با توجه به تجربه ما انجام تشخیص قبل از تولد با استفاده از میکروآرایه های کروموزومی به طور قابل توجهی امکان تشخیص اختلالات ژنومیک را افزایش میدهد و میتواند جایگزین مناسبی برای کاریوتایپ روتین باشد.

Oral presentation: **Dr Mohammad Amin Tabatabaiefar**

Harmony Prenatal Test: Application and Implementation for the First Time in Iran

Mohammad Amin Tabatabaiefar[1,2], Atefe Yadollahi Khales [2]

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2.Harmonic medical genetic lab, Isfahan, Iran.

The Harmony Test is the most well-known brand of non-invasive prenatal testing (NIPT), and it works through detecting the fatal DNA that circulating in the mother's blood. Investigation of this type of DNA (Cell-free DNA), results in more accurate assessment of genetic abnormalities such as, Down's, Edward's or Patau syndrome.

Harmony Prenatal Test is able utilize microarray technology due to its proprietary targeted approach. Microarray technology further enhances performance, speed, and efficiency.

The Harmony NIPT is particularly recommended for those who are over 35, parents who have had a high probability result in their current or previous pregnancy, or a confirmed such chromosomal condition in a previous pregnancy and those who wish to avoid unnecessary invasive testing, which carries a risk of miscarriage.

The test can be used in singleton, twin, and egg-donor pregnancies. It can be performed as early as 10 weeks of gestation.

The results of this test determine if there is a high probability or low probability of the baby having one of the chromosomal conditions; Trisomies 21, 18, and 13 , Sex chromosome aneuploidy, Monosomy X and Fetal sex.

The Harmony test is being used in more than 100 countries around the world. Harmonic Medical Genetics Laboratory in Isfahan started to perform the test for the first time in Iran..

Oral presentation: **Dr Somayeh Khanjani**

When Is Non-Invasive Prenatal Testing Reliable in Pregnancies with Vanishing Twin? - A Systematic Review of Case Reports

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Background: Fetal demise can complicate aneuploidy screening in a multi fetal pregnancy. The cell-free DNA (CF-DNA) from a non-viable conception may lead to be discordant with the viable fetuses. The Aim of the study was to evaluate a safe waiting period, follow-on single fetal demise in a twin gestation before performing NIPT.

Materials and Methods: We searched through online database including: CINAHL, Cochrane Library, Database of Abstracts of Reviews of Effects (DARE), Current Contents, Google Scholar, PubMed, PsycINFO, Thomson Reuters, Scientific Information Database (SID) and Medical Library (MedLib). The search keywords were as follow: ((NIPT) OR (non-invasive prenatal screening testing) OR (cell-free DNA)) AND ((vanishing twin) OR (co-twin demise)). 201 studies across the eight scientific web sites were detected. 178 excluded for duplication or being irrelevant. 29 studies were fully read. 4 case series, met the criteria for systematic review.

Results: The finding suggested the NIPT screening test can be falsely-positive several weeks after vanishing twins although live fetus is normal. Therefore, duration in which placenta can release CF-DNA of vanished twin is unknown. In addition, several weeks after reduction the fetal CF-DNA increases and then decreases, thus CF-DNA analyzing in multi-fetal pregnancies with reduction can be challenging as well.

Conclusion: In pregnancies with vanishing twin or reduction, evaluating NIPT results is more complex than single fetal pregnancy. According to studies, after a fetal demise, the cytotrophoblast continues to release to the CF-DNA in the maternal circulation for a variable time, which may cause a false-positive result if the demised twin is aneuploidy.

Keywords: Cell-free DNA, non - invasive prenatal testing, fetal demise, vanishing twin, multifetal pregnancy.

Oral presentation: **Dr Javad Karimzad Hagh**

Perry syndrome combined with 22q11.2-microduplication-syndrome in a large Dutch family: the challenge of ethical dilemmas and PGD

Javad Karimzad Hagh

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Background :Perry syndrome is very rare and a neuropsychiatric disease with autosomal dominant inheritance. About 50 patients worldwide have been reported. Perry syndrome (the most common phenotype associated with DCTN1 gene) is characterized by parkinsonism, psychiatric symptoms, unexpected weight loss, central hypoventilation. The average age of disease onset in patients with Perry's syndrome is 49 years (range: 35-70 years; manifestation variability) and the average duration of the disease is five years (range: 2-14 years. A mutation in the DCTN1 gene changes the structure of dynactin-1 and makes it less able to bind to microtubules and transport intracellular substances. This abnormality causes dysfunction of neurons and eventually death. 22q11.2 duplication syndrome is a condition caused by an extra copy of a small piece of chromosome 22q11 that contains about 30 to 40 genes. The characteristics of this disease are very different even among members of the same family (variability within the family). Affected individuals may have mental or learning, developmental delay, cardiovascular abnormalitie, slow growth resulting in short stature, and weak muscle tone (hypotonia), but generally mild. Many people with this condition have no apparent physical or mental disability. Microarray testing of apparently normal parents of an affected child results in a 22q11.2 duplications, suggesting that many individuals can carry this duplication without phenotypic effect. The etiology of phenotypic variation is unclear, but proposed explanations include penetrance, epigenetic factors, modifier genes, and environmental factors.

Case Presentation: We report part of results of a large Dutch family with 16 siblings in which two pathogenetic mutations are distributed in whole family:

1. A pathogenetic mutation in the DCTN1 gene (c. 94-2A>G).
2. A photogenetic chromosomal mutation (microduplication at 22q11.2 (arr[hg38] 22q11.2 (23324770_24670517)x3)).

Within these large four-generation families we found a variety of clinical symptoms such as heart disease, hypotonia, clinodactyly, intellectual disability, developmental delay, Learning Disability, dyslexia, depression, autism spectrum disorder (ASD), aggressive behavior, hearing impaired, parkinsonism, hypospadias and bronchitis. The different age-related-expression and severity of the symptoms are very widely. In addition, there is a major challenge in genetic counseling for ethical issue, including different symptoms and legal options when carrying out PGD in pregnant women.

Key Words: Perry syndrome, DCTN1 gene, 22q11.2 microduplication syndrome, aCGH, PGD, WES, express variability, LCR regions

Oral presentation: **Dr Farkhondeh Behjati**

Prenatal karyotype analysis of 8245 amniotic fluid samples of Iranian women and report of their chromosomal abnormalities based on maternal age of above and less than 35 years: A 15-year single-center study

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Aims: The aim of this study was to assess the prevalence of different chromosomal abnormalities in amniotic fluid samples of Iranian women referred to Sarem Women's hospital. Besides, to identify different indications of referral and the prevalence of abnormalities in each category, and assigning the abnormality rate to mothers' age, of 35 years and above and less than 35.

Material and Methods: 8245 amniotic fluid samples of women were referred to Sarem women's hospital from March 2006 to March 2022. After receiving genetic counseling, they were referred for cytogenetics investigation.

Findings: 4.8% of samples had chromosomal abnormalities of which 70.45% were numerical and 29.55% were structural. The most common numerical abnormality was trisomy 21 accounting for 36.11% of all abnormal cases and 51.25% of numerically abnormal cases. Abnormal Maternal Serum Screening Test (AMSST) was found to be the major indication of referral with 76.5% of all referrals. 46.71 % and 53.29% belonged to the <35 and ≥35 age groups, respectively with trisomy 21 responsible for 45.02% of abnormalities in women of ≥35 age and structural abnormalities of 29.18 % of women <35.

Conclusion: This study emphasizes prenatal screening and cytogenetic testing for chromosomal abnormalities. Furthermore, the high level of both numerical and structural chromosomal abnormalities in women of both age groups highlights the significance of cytogenetic testing for all pregnant women regardless of their age.

Keywords: Iranian Women; Prenatal Diagnosis; Chromosome Abnormalities; Maternal Age; Maternal Serum Screening Test; Down syndrome

سخنران: **دکتر سید محمد سید حسنی**

مشاوره ژنتیک در ارزیابی سلامت جنین

سید محمد سید حسنی

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مقدمه: ناهنجاریهای جنینی در ۲.۵ درصد از تولدها دیده می شود که بخش قابل توجهی از آنها بدلیل اختلالات ژنتیک بروز می نمایند. آزمایشات ژنتیک قبل از تولد که به دو دسته تست های غربالگری و تستهای تشخیصی تقسیم می شوند ، اطلاعات ارزشمندی را در خصوص سلامت ژنتیک جنین ارائه می دهند. در این راستا مشاوره ژنتیک نقش مهمی در ارزیابی فامیلی و تعیین ریسکهای بروز بیماری و پیشنهاد تست مناسب غربالگری برای مراجع و تفسیر و جمع بندی نتایج و نهایتا ارائه مشاوره اطلاعاتی به خانواده ها و پزشکان ارجاع دهنده را خواهد داشت.

مواد و روشها: روشهای متعددی برای غربالگری استفاده می شود که در جریان آن از مارکرهای بیوشیمیایی ، سونوگرافیک، ژنتیک و غیره استفاده می شود. که هر کدام حساسیت (Sensitivity) و دامنه ی شناسایی (Detection rate) خاص خود را دارد و بر این اساس و با توجه به نتایج حاصل از فرآیند مشاوره ژنتیک (تاریخچه بیماری، شجره فامیلی و تشخیصهای مطرح) راهکار مناسب پیشنهاد می گردد. بر اساس نتایج تست غربالگری ،زنان باردار با ریسک بالا مشخص شده و برای آنها تست تشخیصی درخواست گردید و در موارد با ریسک بینابینی اقدامات تکمیلی شامل سونوگرافی سافت مارکر درخواست شد و بر اساس نتایج آن و Likelihood ratio مربوط به سافت مارکرها ، ریسک اصلاح شده غربالگری(Adjusted risk) محاسبه و در خصوص بیمار تصمیم گیری شد .

نتایج: در بررسی بر روی ۵۴۲۶ مورد غربالگری انجام شده به روش بیوشیمیایی ، First Trimester Screening (FTS) برای ۳۷۹۹ نفر ، Quad Screening Test (QST) برای ۷۷۸ نفر و Sequential Screening Test (SST) برای ۸۴۹ نفر انجام شده بود که مجموعا ۴۲۱ نفر (۷.۷۶درصد) در گروه پرخطر(ریسک $\leq\frac{1}{250}$) و ۶۵۹ نفر (۱۲.۱۴ درصد) در گروه با خطر بینابینی($\frac{1}{1500}\leq$ریسک $\leq\frac{1}{250}$) و ۴۳۴۶ نفر (۸۰.۰۹ درصد) در گروه کم خطر(ریسک $\geq\frac{1}{1500}$) قرار گرفتند . حاملیگی های پرخطر بر اساس نتایج FTS در ۳.۹۲ درصد موارد و بر اساس QST در ۲۲.۵۸ درصد موارد و براساس SST در ۱۱.۴۲ درصد موارد گزارش شده بود.

از طرف دیگر، از بین ۴۲۵۹ مورد آمنیوسنتز انجام شده بیشترین فراوانی نسبی اتیولوژیک مربوط به خطر تریزومی ۲۱ با فراوانی ۵۸.۳ درصد بوده است، درحالیکه موارد پرخطر برای تریزومی ۱۸ و تریزومی ۱۳ به ترتیب ۲.۸ و ۰.۲ درصد را به خود اختصاص می دادند. ۱۲.۳ درصد از جنینها نیز دارای سافت مارکر مثبت در سونوگرافی بودند. نهایتا از بین نمونه های آمنیوسنتز مورد بررسی ۱۸۶ جنین با فراوانی نسبی ۴.۳۶ درصد جهت سقط درمانی به پزشکی قانونی معرفی شده بودند .

بحث: این بررسی بخوبی نقش مشاوره ژنتیک در ارزیابی ریسک پایه بر اساس شجره فامیلی و بکارگیری مارکرهای مختلف در غربالگری و تشخیص اختلالات ژنتیک وتوصیف ریسکهای بینابینی را نشان میدهد که نهایتا نقش قابل توجهی در کاهش موارد مثبت کاذب و همچنین افزایش حساسیت آزمایشات غربالگری دارد.

*در ارائه این مقاله راهکارها و چالش های مربوط به ارزیابی سلامت جنین و همچنین شیوه نامه کشوری فعلی به بحث گذاشته می شود .

Oral presentation: **Dr Parham Mardi**

Identifying Screening Cut-Off for Amniocentesis in Down Syndrome Patients

Parham Mardi

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Down Syndrome (DS) is a prevalent chromosomal condition that imposes a significant burden on affected individuals, families, and healthcare systems. While there is no cure for DS, efforts have focused on preventing its occurrence through gestational screening, such as combined tests or noninvasive prenatal testing (NIPT), followed by amniocentesis for high-risk pregnancies. Disability-Adjusted Life Years (DALY) for DS in Iran were calculated at 30.38 DALYs per 100,000, indicating 26,126 years were lost due to DS in 2019. The prevalence of DS in Iran in 2019 was 29.32 cases per 100,000 live births, equivalent to approximately 25,215 prevalent cases in the country. Each DS case is responsible for 1.036 DALYs in Iran, with an incidence of 1.44 new cases per 100,000 live births. First-trimester screening involves a combination of ultrasound measurements and maternal serum markers to assess the risk of chromosomal abnormalities. In Iran, this is the most common screening method for DS. The study provides data on screening probabilities based on a study conducted in Southeast Asian populations. The crude birth rate in Iran was 15.12 per 1000 inhabitants in 2019, resulting in 1,209,600 neonates born that year. The study estimates a 1% incidence of spontaneous abortion following amniocentesis in Iran, potentially leading to around 12,906 abortions if amniocentesis were conducted for all pregnant women. Three scenarios are examined: amniocentesis for all, amniocentesis for no one, and amniocentesis for mothers at risk. The study calculates DALY burdens for each scenario, showing that a 1:100 cut-off for amniocentesis offers the optimal balance between reducing the DS burden and minimizing invasive procedures. This study addresses the ethical complexities of prenatal testing and amniocentesis, considering the fear of abortion and potential risks associated with these procedures. It emphasizes the need for well-informed, patient-centered guidelines that consider both medical accuracy and individual values and preferences. The study's findings have significant implications for healthcare policies and practices in Iran, potentially leading to improved public health outcomes and resource allocation. In conclusion, this research provides valuable insights into the optimal cut-off value for amniocentesis in DS screening, taking into account the DS burden and the risks of invasive procedures. The study contributes to the ongoing discourse on personalized medicine, healthcare policies, and patient-centered decision-making in prenatal care. Future research could explore broader social and cultural dynamics influencing the adoption of DS screening protocols and acceptance of amniocentesis in different countries.

Oral presentation: **Dr Mansoor Salehi**

Genetic Factors Associated with Recurrent Pregnancy Loss

Dr. Mansoor Salehi

Professor of Human Genetics, Isfahan University of Medical Sciences, Cellular, Molecular and Genetics Research Center

Recurrent pregnancy loss (RPL) refers to the experience of two or more clinical pregnancy losses before 20 weeks of gestation. This obstetric complication affects approximately 2.5% of couples. The most common causes of RPL are genetic abnormalities, including chromosomal and single-gene defects. Currently, there is a lack of a dependable diagnostic or prognostic biomarker for RPL. Studies have identified genes such as factor V Leiden (FVL), factor II (F2), and methylenetetrahydrofolate reductase (MTHFR) to be associated with RPL, although this still needs to be confirmed, and researchers continue to discover other genes that play role in this distressing pregnancy disorder. Besides, recent studies have identified circulating microRNAs and long non-coding RNAs (lncRNAs) as potential biomarkers for RPL.

To clarify the role of genetic factors in RPL, we refer to the two couples who had a consanguineous marriage and experienced recurrent miscarriages. The first couple had a history of successful pregnancy after nine years of infertility. After the second episode of infertility, they had five abortions at 12, 5,5, 14, and 12 weeks of gestation. In the fourth abortion, NT sonography (a month before abortion) and first-trimester screening were normal, but there was no fetal heartbeat in the last sonography. The CGH-Array on this aborted fetus was normal. For the fifth abortion, the ultrasound result at 9-week age was normal, but at 12-week age, it revealed intrauterine fetal demise (IUFD). The whole exome sequencing (WES) analysis in this product of abortion identified mutations located in 1) SLC7A9, 2) EXT1, and 3) MYH9 genes, which are associated with 1) Cystinuria, 2) Exostoses, multiple, type 1, and 3) Deafness, autosomal dominant 17 respectively. The second couple had a history of one successful pregnancy and three abortions at 16, 14, and 15 weeks of gestation due to heart failure. In the last miscarriage, Thrombophilia was diagnosed at the 12th week of pregnancy, and aspirin and heparin were taken from weeks 12 to 15. However, despite taking medicine, the fetus was aborted. The CGH-Array on the second aborted fetus was also normal. WES analysis on the last aborted fetus identified a mutation in the *LAMA4* gene, an important gene associated with Cardiomyopathy, Dilated, 1JJ.
Genetic testing of the products of conception from couples experiencing RPL may aid in defining the underlying etiology and counsel patients about prognosis in a subsequent pregnancy.

Oral presentation: **Dr Rasoul Salehi**

Preimplantation Genetic Diagnosis/Testing (PGD/PGT): A multi-potential technology

Rasoul Salehi, Sharifeh Khosravi, Sima Jafarpour

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The development and improvement of Assisted Reproductive Technologies (ART) and Preimplantation Genetic Testing (PGT) have been aimed at providing a solution for infertility and genetic diseases by facilitating a healthy live birth. Both technologies, ART and PGT, have been progressing in parallel, and the success of one is greatly dependent on the success of the other.

PGT can be performed for the detection of monogenic disorders/single gene defects (PGT-M), chromosomal structural rearrangements (PGT-SR), or aneuploidy (PGT-A) in preimplantation embryos. PGT-M and PGT-SR aim to establish a pregnancy unaffected by the familial disorder or by a chromosome imbalance, respectively, by diagnosing and selecting genetically suitable (unaffected) embryos for transfer to the womb. The aim of PGT-A is to improve the success rate of ART, i.e., to increase implantation, ongoing pregnancy, and live birth rates and to reduce the miscarriage rate. This is attempted by assessing the chromosomal complement in embryos before implantation to exclude the aneuploid embryos from the transfer.

Overall, subsequent to oocyte collection and fertilization, embryos are cultured in the laboratory, and cells from embryos are removed (biopsied) and used for genetic analysis. The stage of embryo development, at which biopsy is performed (polar body, blastomere, or trophectoderm biopsy), is determined by the indication tested for, the patient's reproductive potential and history, the requirements of the diagnostic protocol and the embryo-transfer policy of the assisted reproduction center.

HLA typing of preimplantation embryos can be performed as a sole indication when the affected child requires transplantation to treat an acquired disease, or in combination with PGT-M to support parents to concurrently avoid the risk of having another affected child. The HLA super locus located on the short arm of chromosome 6 represents an extremely polymorphic locus with different regions and more than 4,000 alleles. Moreover, recombination through HLA genes has been observed indicating that HLA alleles exhibit a high degree of genetic diversity among the populations. Thus, the chance of finding individuals with the same HLA alleles on all loci is very unlikely. PGD as an alternative technique offers the possibility of pre-selecting not only disease-free embryos but also HLA compatible with the expected affected sibling that will be an appropriate donor of cord blood at birth or future bone marrow stem cells.

Here I am presenting our experience on beta-thalassemia as a most prevalent single gene disorder in Iran as well as many other countries located on the thalassemia belt in specific geographical places on the earth. Combination of beta-thalassemia with HLA selection and, if required embryos' gender would provide not only a disease-free healthy baby for the family but also provide adequate means of HLA-match stem cell therapy using the cord blood stem cell for her/his affected sibling.

Oral presentation: **Dr Omid Iravani**

Clinical importance of fetal examination in abortion, stillbirth and perinatal deaths

Omid IRAVANI*, MD PhD, Mojtaba Baktashian*, MD PhD

**NewGene Multidisciplinary Genetic Clinic, Isfahan Healthcare City*

Diagnosing and managing pregnancy problems, especially those that lead to miscarriage or stillbirth is a sensitive and complex issue. In most cases, pregnancy products are buried immediately after abortion. Meanwhile, without examining pregnancy products, it is impossible to determine the type of disorders leading to abortion or stillbirth. In some cases, the embryo is genotyped without matching with the phenotype and is subjected to unnecessary or inappropriate genetic tests. In both cases, access to the cause of abortion or stillbirth is not possible, and in this case, decision-making for subsequent pregnancies is faced with serious challenges and ambiguity. This vicious cycle is inevitably continued by conducting expensive genetic tests on healthy couples, which result in confusion, ambiguity, and imposing unnecessary costs. In cases where the fetus is subjected to legal abortion with radiological findings, diagnostic examinations of the fetus are also necessary because many radiological findings are not specific for the definitive diagnosis of genetic, hereditary, or congenital abnormalities. The only exception is in cases where the genetic diagnosis of the type of disorder has been confirmed or ruled out by sampling placental villi or amniocentesis. In some cases, the findings of the examination of the fetus and fetal appendages indicate the occurrence of intrauterine infections, thrombophilia, or autoimmune factors in the mother, in such cases, appropriate treatments and preventive measures are taken for subsequent pregnancies by conducting more Para-clinical examinations. After genetic counseling and diagnostic examination of the fetus and fetal appendages, if necessary, the best and most accurate genetic test is selected and prescribed based on clinical findings. Diagnostic examination of the fetus and products of pregnancy is highly recommended in spontaneous abortions, recurrent abortions, missed abortion, stillbirths, legal abortions without a molecular diagnosis, prenatal deaths, and cases associated with retardation of fetal growth and development. In general, accurate diagnosis of the causes of miscarriage or stillbirth is complex and requires genetic counseling, detailed analysis of medical history, examination of pregnancy products, and sometimes additional tests. This issue is an important step for parents, which not only helps them make better decisions for the next pregnancy but also prevents the imposition of unnecessary and expensive tests.

Keywords: Abortion, stillbirth, perinatal deaths, fetal diagnostic examination, genetics

Oral presentation: **Dr Ehsan Ghayoor Karimiani**

Leveraging consanguinity in neuromuscular inherited diseases

Ehsan Ghayoor Karimiani

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Background: Consanguineous marriages are common in the Middle East and associated with an increased burden of autosomal recessive genetic conditions. We have characterised more than one thousand individuals with a variety of conditions such as inherited neurogenetic disorders including neuromuscular disease. The variant frequency data, enriched for homozygous variants, and particularly homozygous loss of function variants, provides an invaluable opportunity to gain scientific and clinical insights into gene function, as well as providing support for candidate disease gene identification and variant interpretation.

Methods: A complete clinical and paraclinical examination has been done by expert specialists and clinical geneticists. The team contributed to the discovery or identifies the mutated genes using the Exome Sequencing technique followed by comprehensive bioinformatics analysis.

Results: Likely pathogenic/pathogenic variants were detected in different disease-causing genes, including novel genes first identified in the population.

Conclusions: Our results provide novel insights into genotype-phenotype relationships and identify high frequency disease variants in this unique population, suggesting the utility of population specific sequencing efforts.

Oral presentation: **Dr Majid Mojarrad**

Identifying Screening Cut-Off for Amniocentesis in Down Syndrome Patients

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Duchenne muscular dystrophy (DMD) is caused by the dystrophin gene mutations and is one of the most common and lethal human hereditary disorders. A novel therapeutic approach using CRISPR technology has gained attention in the treatment of DMD. Gene replacement strategies are being proposed as a promising therapeutic option to compensate the loss of function mutations. Although, the large size of the dystrophin gene and the limitations of the existing gene replacement approach, could mean the gene delivery of shortened versions of dystrophin such as midystrophin and microdystrophins. There are also other approaches: including Targeted removal of dystrophin exons to restore the reading-frame; Dual sgRNA-directed DMD exon deletion, CRISPR-SKIP strategy; reframing of dystrophin using Prime Editing technology; exon removal using twin prime technology; TransCRISTI technology to targeted exon integration into dystrophin gene. Here we provide an overview of recent progresses in dystrophin gene editing using updated versions of CRISPR to introduce novel opportunities in DMD gene therapy.

Overall, the novel CRISPR based technologies are improving and expanding to allow the application of more precise gene editing for the treatment of DMD.

Oral presentation: **Dr SM Kalantar**

Heterozygous ANKRD17 loss-of-function variants cause neurodevelopmental delay, learning difficulties, seizures, microcephaly, and poor speech

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ANKRD17 is an ankyrin repeat-containing protein thought to play a role in cell cycle progression, whose ortholog in Drosophila functions in the Hippo pathway as a co-factor of Yorkie. Here, we delineate a neurodevelopmental disorder caused by de novo heterozygous *ANKRD17* variants data indicate that loss of *ANKRD17* is likely the main cause of phenotypes previously associated with large multi-gene chromosomal aberrations of the 4q13.3 region. Protein modeling suggests that most of the missense variants disrupt the stability of the ankyrin repeats through alteration of core structural residues. The major phenotypic characteristic of our finding is a variable degree of developmental delay/intellectual disability, particularly affecting speech. Pathogenic variants in *ANKRD17* have been reported in fewer than 35 patients worldwide, in only one paper. The patient is a 6-year-old female from consanguineous parents. She has neurodevelopmental delay, learning difficulties, seizures, microcephaly, and poor speech. In the first stage of investigation her karyotype was normal as well for parents. WES evaluation was requested the result was VUS for Deletions of the region containing *ANKRD17* on chromosome 4q13.3. Among the disease-associated OMIM genes in the interval which was confirmed by sanger sequencing.

Our study confirmed the wide spectrum of behavioral and neurological and psychiatric features of this rare condition, according of our finding this is the first case from Iran.

Key Words: neurodevelopmental delay, *ANKRD17* variants, WES, Sanger sequencing

Oral presentation**: Dr Farzaneh Pouya**

Xq28 Duplication Syndrome in a large family with X-linked mental retardation

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Abstract:

Duplications leading to functional disomy of chromosome Xq28 are an X-linked intellectual disability syndrome characterized by broad range of intellectual disability, absent speech, infantile hypotonia, and facial dysmorphism. This combination of symptoms is known as the Xq28 microduplication syndrome or Lubs syndrome. Here we present clinical and molecular data in a large family with an Xq28 duplication including the MECP2, GDI1, genes. Proband is an 8-year-boy clinically diagnosed with severe mental retardation, hypotonia and hypotelorism. Fragile X syndrome was excluded by molecular testing. Whole exome sequencing revealed no pathogenic variant. Oa-CGH was finally performed and a homozygote pathogenic gain of 656 Kb of Xq28 from nucleotide 153127628 to 153783184 was identified. Oa-CGH was then performed for the parents and the asymptomatic mother carried the gain. Our patient was compared with previously reported cases with Xq28. In X-linked mental retardation, Fragile X syndrome and single gene disorders first come to mind, but here we show that CNVs can be the cause of X-linked mental retardation and undermine the importance of oa-CGH in the workup of patients with X-linked mental retardation.

Keywords: oligo array comparative genomic hybridization (oa-CGH), X-linked mental retardation, duplicaton, Lubs syndrome, Xq28

Oral presentation: **Dr Naser Ajami**

Expanding the phenotypic, genotypic, and functional spectrum of CNPY3 - associated DEE

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Objective: Developmental and epileptic encephalopathy-60 (DEE60) is an autosomal recessive neurologic disorder characterized by the onset of infantile spasms, seizures, or myoclonus in the first months of life. EEG typically shows hypsarrhythmia, consistent with a clinical diagnosis of West syndrome. Affected individuals have severe global developmental delay with inability to sit, walk, or speak. Brain imaging may show brain atrophy and hippocampal malrotation. An important gene associated with DEE60 is *CNPY3* (Canopy FGF Signaling Regulator 3) on chromosome 6p21.1 which encodes a protein known as Canopy3 or PRAT4A (protein associated with TLR4A. It is localized in the endoplasmic reticulum (ER) and functions as a co-chaperone with the general chaperone gp96 to regulate the subcellular distribution and responses of multiple Toll-like receptors (TLRs). Recently, recessive *CNPY3* variants have been linked to DEE60 (MIM # 617929, PubMed: 29394991). With this study, we sought to expand the genotypic and phenotypic spectrum of *CNPY3* -associated DEE60 and aimed at establishing a functional read-out for identified variants.

Methods: Using GeneMatcher, we queried for additional patient cases with variants in *CNPY3*. An in-vitro functional assay is currently under development to help understand the pathophysiology and unravel the functional impact of detected variants on *CNPY3*.

Results: We identified seven additional family including 10 additional patients harboring biallelic and monoallelic variants in *CNPY3* (Table 1).

Conclusion: Our results suggest that *CNPY3* defects are a yet underdiagnosed cause of syndromic DEE60. Establishment of a functional read-out will help distinguishing benign from pathogenic variants in this gene.

Oral presentation: **Dr Mohammad Kazemi**

Knockdown of lncRNA FLVCR1-AS1 and evaluation of its inhibitory effects on proliferation and induction effects on apoptosis of Colorectal Cancer cell line

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Introduction: Colorectal cancer (CRC) is the third most common cancer and one of the most significant causes of death in the world. The Wnt signaling is the most important pathway which plays a role in progression of CRC and knowing and interfering in the expression of factors that change the expression of these proteins can help CRC treatment. MicroRNAs and long non-coding RNAs can interact with each other to regulate genes expression. The aim of the present study was to compare the expression of lncRNA *FLVCR1-AS1* in tumor and adjacent normal tissues of CRC patients and evaluate the effects of its inhibition on the expression of genes involved in the Wnt pathway and the rate of apoptosis and proliferation in colorectal cancer cell lines, through interaction with hsa-miR-381-3p.

Materials and methods: *FLVCR1-AS1* expression level was evaluated and compared with Real-Time PCR in tumor and adjacent non-tumor samples obtained from CRC patients and also was compared in different CRC cell lines. Then, a cell line with the high level of expression of *FLVCR1-AS1* was selected and divided into three groups: control, Negative control and case. Case and negative control group cells were transfected with sh*FLVCR1-AS1* and shNC, respectively, and then the expression level of *CTNNB1*, *LRP6* and *FZD3* genes as well as miR-381-3p, the proliferation, apoptosis and necrosis rates were compared between 3 groups by Real-Time PCR, MTT test and apoptosis assay (Annexin V/ PI double-staining), respectively.

Results: *FLVCR1-AS1* expression in tumor tissues increased more than 6 times compared to adjacent normal tissues. FLVCR-AS1 expression in cell lines HT29, HCT116 and SW480 was 50.74, 38.85 and 18 times more than its expression in CACO2, respectively. inhibiting *FLVCR1-AS1* with sh*FLVCR1-AS1* resulted in reduction of expression of *FLVCR1-AS1* compared to the control group by 70, 60 and 40 percent 24, 48 and 72 hours after transfection (p<0.001). Suppression of *FLVCR1-AS1* made increased expression of miR-381-3p by 4, 3 and 2 times 24, 48 and 72 hours after transfection (p<0.001). Also, 80% decrease in *CTNNB1* gene expression was observed 24 hours after transfection (p<0.001), but there was no significant difference 48 and 72 hours after transfection. In addition, 90% (p<0.001) and 60% (p<0.01) decrease in *LRP6* gene expression was seen 24 and 46 hours after transfection, while no significant decrease was observed after 72 hours. 90%, 85% and 75% (p<0.0001) reduction of expression of *FZD3* gene was reported at 24, 48 and 72 hours after transfection. The MTT results showed that the cell proliferation rate was 40%, 50% and 45% (p<0.001) decreased after transfection. Flow cytometry results indicated increase of 23 to 30 percent of apoptosis from 24 to 72 hours after transfection (p<0.0001).

Conclusion: FLVCR1-AS1 may act as a tumor promoter in CRC and targeting competitive endogenous RNA (ceRNA) network *FLVCR1-AS1*/miR-381-3p/*CTNNB1-FZD3-LRP6* may be a beneficial and appropriate approach in designing treatments for CRC patients.

Oral presentation: **Dr Marjan Yaghmaie**

Low risk and high risk CLL patients by genetic feature: prognosis, future plan and response to therapy

Marjan Yaghmaie

Associate Professor of Medical Genetics at Oncology, Hematology and Cell therapy Research Institute, Tehran University of Medical Sciences, Tehran, Iran

We will present two cases of low and high risk CLL. The first case, a 72-years old male presented with CLL 5 years ago that recently developed progressive anemia and lymphadenopathy and the FISH result showed del 13q and IGHV mutation is positive in this patient. We would like to see how the genetic information help to treatment decision and how he will be survived by these genetic hallmarks. The second case is a high risk 68-years old CLL patient who presented 3 years ago after discovering an asymptomatic lymphocytosis and confirmation of CLL diagnosis with flow cytometry. Over the past few months he had fatigue, splenomegaly and lymphadenopathy. We will discuss about the genetic tests we should order for this patient and since the patient had un-mutated IGHV and P53 mutation we will discuss about the future plan, response to therapy and prognosis of this patient.

Oral presentation: **Dr Laleh Shariati**

Developing a Gene Delivery System as a vehicle in Gene Therapy: MCM-Co-Polymerized based Nanosystem Functionalized with MUC-1 Aptamer against Breast Cancer

Yasaman Esmaeili[1], Arezou Dabiri[2], Fariba Mashayekhi[3], Ilnaz Rahimmanesh[2], Elham Bidram[1,3], Saeed Karbasi[3], Mohammad Rafienia[1,3], Shaghayegh Haghjooy Javanmard[2], Laleh Shariati[2,3*]

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This study introduces an innovative delivery approach employing the MCM-co-polymerized nanosystem, incorporating chitosan and polyethylene glycol, and targeted by the MUC-1 aptamer (MCM@CS@PEG-APT). This system enables delivery of the GFP plasmid. The synthesis of the nanosystem was thoroughly characterized at each step, including FTIR, XRD, BET, DLS, FE-SEM, and HRTEM analyses. The influence of individual polymers (chitosan and PEG) on payload retention was compared to the co-polymerized MCM@CS@PEG configuration. The nanosystem's potential for delivering GFP plasmid was assessed through fluorescence microscopy and flow cytometry. The co-polymerized nanosystem exhibited superior payload entrapment compared to separately polymer-coated counterparts. The presence of pH-sensitive chitosan contributed to efficient GFP plasmid delivery into target cells. Biocompatibility assessments indicated compatibility with living cells, positioning it as a promising candidate for targeted cancer therapy. Cellular uptake findings demonstrated the nanosystem's ability to deliver GFP plasmid into MCF-7 cells, with rates of 31%. Overall, our study explores the co-delivery potential of the MCM@CS@PEG-APT nanosystem in breast cancer therapy. This system's ability to co-deliver multiple agents precisely, combined with real-time gene expression monitoring, opens new avenues for targeted therapeutic strategies.

Oral presentation**: Dr Mehrdad Zeinalian**

Two Distinct Cancer-Causing Variants in a Family with Multiple Affected Members

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Introduction: Hereditary cancers account for 5-10% of all cancers, but they are extremely significant due to the fact that they can be passed down from one generation to the next and put family members at an increased risk. In spite of the fact that screening methods are one of the most important approaches to dealing with hereditary cancers, they lack high specificity and sensitivity. The advent of whole-exome sequencing (WES) has resulted in a substantial rise in the detection of pathogenic variants in high-risk families.

Methods: To identify a potential causative variant, we performed WES on a high-quality DNA sample of the proband from an Iranian family with several cancer-affected members suffering from ovary, colon, ductal breast, and brain cancer. The pathogenicity and the impact of the candidate variants on the structure and function of the protein were assessed with multiple in silico tools. Additionally, Sanger sequencing was used to segregate the candidate variants in this family.

Results: The WES data analysis revealed two pathogenic variants (NM_007194.4: c.538C>T, p.Arg180Cys and NM_000249.4, c.844G>A, p.Ala282Thr) in the CHEK2 and MLH1 genes, respectively. Sanger sequencing showed that neither of the two variants alone segregated with the symptoms in this family, but together, they explain the patients' phenotype. According to the structural analysis, arginine 180 and glutamic acid 149 lost their salt bridges due to the variant (c.538C>T).

Conclusion: Herein, we interestingly identify two pathogenic causative variants (CHEK2: NM_007194.4: c.538C>T, p.Arg180Cys and MLH1: NM_000249.4, c.844G>A, p.Ala282Thr) in a family with several cancer-affected members which can indicate the harmful effects of consanguineous marriages on cancer incidence. Additionally, the results of this study demonstrate the utility of WES in cancer diagnostics.

Keywords: hereditary cancer syndrome, CHEK2, MLH1, whole-exome sequencing

Oral presentation: **Dr Ahmad Reza Salehi**

Cytogenetically Balanced Translocation in a Newborn Diagnosed with VACTERL Association

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Objective: The VACTERL association is a very serious and rare condition that includes at least three of the following congenital anomalies: vertebral, anorectal, cardiac, tracheoesophageal fistula with or without esophageal atresia, renal, and limb anomalies. Approximately 90% of VACTERL association cases occur sporadically, whereas 10% of cases involve familial inheritance. The incidence estimated approximately 1 in 10000 to 1 in 40000 live births. Genetic or maternal risk factors have role in the etiology of the VACTERL association. Genetic risk factors include different gene mutation(s) or chromosomal aberrations.

Aim: Here we report a seven months old female newborn with differential diagnosis of VACTERL association whom diagnosed with a balanced translocation.

Materials and Methods: High resolution GTG banding and cytogenetic analysis performed for this patient on peripheral blood after antecubital blood drain and stimulation of white blood cells.

Results: After careful clinical examination, we diagnosed this patient with severe cardiac defect, imperforate anus, hearing loss, and bilateral thumb hypoplasia. Unfortunately, and due to severity of the cardiac disease, the patient passed away few days after our evaluation. Through cytogenetic analysis we identified the patient as a carrier of a balanced reciprocal translocation 46,XX,t(9;16)(q21.12;q21) between long arms of chromosomes 9 and 16.

Conclusion: Conventional cytogenetic analysis is the first-tier approach when encountering to congenital malformations and syndromic features. However, fine tuning and unraveling the exact breakpoints through more sophisticated techniques is strongly recommended for future research.

Keywords: VACTERL, Chromosomal Aberration, Cardiac Defect, Limb Anomalies

Oral presentation: **Dr Reza Sadria**

Complex hypodiploidy karyotype in acute myeloid leukemia at diagnosis

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In acute myeloid leukemia (AML) patients, chromosomal abnormalities are critical diagnostic and prognostic markers since they are at the core of risk classification algorithms. It is uncommon to identify hypodiploidy in AML, a rare cytogenetic abnormality that is frequently present in older male patients with the disease. Here we report a case of 69-year-old male, diagnosed with MDS transformation to AML according to WHO classification and a complex hypodiploidy karyotype at diagnosis. Prior to the initial diagnosis, he had a history of lymphoma for 8 years. The blast cell increased from 4% to 78% following the transformation event. An unusual complex but still close to diploid karyotype with eleven chromosomes was discovered by cytogenetic, and molecular cytogenetic (FISH) investigations. Chromosome analysis revealed three lineage. Abnormal male chromosome complement with the stem line clone as multiple rearrangements including of: 43,XY,del(5)(q31),der(7)t(7;?),-11,-12,add(13)(q10),-15,del(17)(p12),add(19)(p13),rob(15;21)(q10;q10). Two additional abnormal sub clones are identified; one sub clone with 42 chromosomes has all the abnormalities seen in the stem line, plus loss of Y chromosome and another sub clone had doubled with same changes. FISH assay for deletion of 17p confirmed 17p12 deletion (TP53) in 77% of cells scored. According to ELN 2022, the result of Gene alterations, along with translocations and inversion mentioned was negative. Elder AML's biological and clinical aspects of hypodiploidy are still little understood, but they could provide information for stratifying treatments in the future.

Keywords: Acute Myeloid Leukemia, hypodiploidy, Complex karyotype, TP53

Oral presentation: **Dr Majid Kheirollahi**

Simultaneous Preimplantation Genetic Diagnosis for spinal muscular atrophy and sex determination

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Abstract:

Proximal spinal muscular atrophy (SMA) is a common autosomal recessive disorder of childhood characterized by degeneration and loss of the anterior horn α-motor neurons of the spinal cord and the brain stem nuclei, leading to resulting in symmetrical proximal muscle weakness, wasting of voluntary muscle, and atrophy. In order to reduce SMA diseases, prenatal diagnosis (PND) testing is a routine test for diagnose fetuses, that are which is sampled by invasive procedures such as chorionic villus sampling (CVS) and amniocentesis (AF), followed by termination pregnancy of affected pregnancies fetus with legal abortion. Preimplantation genetic diagnosis (PGD) is an alternative to test PND that offers couples at risk for transmitting an inherited SMA disorder the possibility which eliminates the need for abortion during pregnancy.to avoid the termination of affected pregnancies and it allows the selection of unaffected intracytoplasmic sperm injection (ICSI) embryos for transfer to the mother's uterus. PGD accomplished by blastomere biopsy from cleavage stage embryo and followed by polymerase chain reaction (PCR)-based DNA analysis. In the present study, development of a PGD protocol for SMA using NESTED multiplex PCR for the combination of informative polymorphic linked short tandem repeat (STR) marker with deletions of exons 7 and 8 in SMN1 gene and deletions of exons 4 and 5 of NAIP gene. Additional multiplexing was performed with SRY and DAZ genes for determining sex. We optimized method following by PCR combined with restriction fragment length polymorphism (RFLP) and fragment analysis for informative STR markers for 52 single lymphocyte cells (SLC; 16, 30, 6 SLCs, for normal, heterozygote and affected samples, respectively). The technique was employed for 18 blastomeres during 4 stages of PGDs. For three of them, sexing was simultaneously performed by real-time PCR. Allele dropout, contamination, and PCR efficiency rate were examination in the SLCs and embryos. The PCR efficiency of for exons 7, 8 (SMN1) in the SLCs (6/52) and embryos (1/18) were 90%, and for 4, and 5 (of NAIP) evaluated 82%. The PCR carry-over contamination was 98% and 95% in the SLCs and embryos, respectively. The 95% of embryos were diagnosed, five of them were affected and eleven of them were unaffected. Our result suggests that our NESTED multiplex PCR protocol is an efficient method and an accurate protocol for PGD-SMA.

Keywords: Spinal muscular atrophy, Preimplantation genetic diagnosis, polymorphic markers, nested multiplex polymerase chain reaction, single human blastomere**.**

Poster presentation: **Ata Bushehri**

Genetic diseases and other unusual disorders presented in art paintings

Ata Bushehri, MD, PhD of Medical Genetics

Genetic disorders are diseases caused by abnormalities in an individual's genetic material. A good source providing purported evidence of the existence of genetic diseases in the past, before their identification by medicine, are European artists' paintings. Such paintings quite frequently depicted human anomalies and disorders.

The attention paid to Trisomy 21, a genetic condition described by Langdon Down in 1866, is due to concerns about establishing the age of this pathology during evolution. Due to the synergy between medicine and art history, it is possible to reconstruct the diseases that have characterized the most a certain historical period, as well as the perception of the population towards them. Using iconodiagnosis, namely studying works of art through medical imaging, it was found that in Europe, during the Renaissance, many different genetic disorders like Trisomy 21 was represented by Italian and Flemish painters in religiously inspired paintings.

Here in this work I present the examples of paintings depicting people suffering from diseases such as Down Syndrome, spondyloepiphyseal dysplasia congenita, Marfan syndrome, myotonic dystrophy, Paget's disease and tetralogy of Fallot.

Key words: genetic diseases, art paintings, Down syndrome, spondyloepiphyseal dysplasia congenita, Marfan syndrome, myotonic dystrophy, Paget's disease, tetralogy of Fallot.

Poster presentation: **Zahra Jafari**

An analysis of correlation networks identified new hub genes associated with papillary thyroid carcinoma

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Introduction: Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer and one of four types of endocrine cancer. Thyroid cancer's exact genetic causes remain unknown. Dipeptidyl Peptidase 4 (DPP4) encoded adenosine deaminase complexing protein-2 and T-cell activation antigen CD26 .Glucose and insulin metabolism, as well as immune regulation, are regulated by dipeptidyl peptidase 4. PTC patients are assessed for DPP4 gene expression in the current study. Additionally, it investigates its potential correlation with cancer incidence.

Methods: An analysis of weighted gene co-expression networks (WGCNA) was conducted to identify hub genes. The differential expression of hub genes was evaluated through a microarray meta-analysis of 149 PTCs and adjacent healthy tissue. Normalizing the metadata, performing principal component analysis (PCA), and analyzing Limma differential expression were performed. RT-qPCR was utilized to measure mRNA expression following RNA extraction and cDNA synthesis in 10 normal tissues and 10 PTC tissues.

Result: Our thorough bioinformatics study verified that DPP4 exhibited the most notable overexpression pattern in PTC patients (logFC=5.002, adj.p.val = 3.67E-63), which was one of the hub genes identified by WGCNA. DPP4 expression is significantly upregulated in the PTC and nearby normal tissues by RT-qPCR.

Discussion & Conclusion: The DPP4 gene expresses itself more prominently in PTC tissues, and its expression is correlated with the occurrence of PTC.

Keywords: papillary thyroid cancer (PTC), DPP4, WGCNA

Poster presentation: **Mohammad Zed Rahimi**

A prenatal CNV Characterization with familial history

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Background and Objectives: Intellectual disabilities (ID) originate during the developmental period and are characterized by significantly below-average intellectual functioning and adaptive behavior. The occurrence of seizure is higher in cases with intellectual disabilities (>25%) than in the general population (1%), which mostly manifest in the form of multiple seizure types. Based on the clinical guidelines, CGH-array method in patients with ID & seizure is in the first steps of investigation and the clinical interpretation of the results are very important that directly affect further physician's decision-making.

Case: This case presentation is about the 15 years old male patient with Intellectual Disability (ID) and seizure which his pregnant sister referred to our clinic for pregnancy consultation (G. A= 26 weeks) (Fig.1). Considering the patient's symptoms, array CGH and Fragile X tests were suggested for the affected male. Fragile X test was normal. The array CGH test conducted SurePrint G3 ISCA V2 8X60K whole genome Oligo-Array version 2. A microduplication of the 16P13.11P23 region, arr[GRCh38] 16p13.11p12.3(16,539,504-18,062,494)x3 (1.5 Mb), was detected in this patient, which included one OMIM gene; *XYLT1* (Fig.2). Initially, this variant was reported as likely pathogenic. Due to the time limit for making a decision on the fetus and also the cost limit of the patient's family, it was decided to directly test the fetus by CGH-array. Array CGH test result for the fetus, showed the same variant, which means the sister has also the same microduplication without any symptoms, indication of a familial benign CNV. Karyotype test was normal in the pregnant patient's sister. Furthermore, there is no report for pathogenicity of *XYLT1* gene duplication or dosage in the literature. The matching process on the Decipher is discussed in this report. In this case, finally based on whole Exome Sequencing (WES) for the affected person, we find a likely pathogenic variant in the X-linked Phosphoglycerate kinase 1 (PGK1) gene, (NM_000291.4: c.319G>C (p.Ala107Pro), rs1557247186(, with significant phenotype-genotype correlation and confirmed by sanger sequencing and segregated in the family. Fortunately, the resulted male newborn is normal and didn't have the causative variant.

Discussion & Conclusion: In the family reported here, we encountered such situation in which members of the family had the same finding with completely different manifestations. It is not completely clear for us that if possibly the mentioned symptoms and phenotype is a cumulative effect of both microduplication and the PGK1 gene variations or not. This needs further functional studies in future.

Keywords: 16p13-12 microduplication, a-CGH, WES, XYLT1 gene, CNV, PGK1 gene

Poster presentation: **Gholamreza Mesbah**

"Evaluation of apoptosis induced by bipSUR gene construct in metastatic breast cancer cells overexpressing cyclins D1 and E genes"S

Gholamreza Mesbah[1,3], Majid Shahbazi[2], Fatemeh Tash Shamsabadi[2], Fatemeh Namazi[1], Armaghan Davoudi[3,4], Mehrab Nasirikenari[5]

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Abstract:

Breast cancer is one of the most important diseases that affect human societies today. The occurrence of this disease is more common among women than men. Genetic change in the cellular DNA is one of the causes of this deadly disease. Today, with the progress of knowledge, several treatment methods are known to treat this disease, one of which is gene therapy and target therapy. Based on the results of using the bidirectional human breast tumor recombinant vector (bipSUR) in the ex vivo phase, the present study has designed an animal model to investigate the amount of apoptosis induction in the target cells. Considering that the genes of phase one of the cell cycle are highly expressed in human metastatic breast cancer cells, one of the ways to prevent the division and proliferation of cancer cells is to destroy them specifically by preventing the expression of the mentioned genes. By inducing apoptosis specifically in human breast cancer cells, bipSUR prevents the overexpression of cyclin D1 and E genes and thus can prevent tumor mass growth. Therefore, this genetic structure can be considered as a promising candidate for the treatment of human breast cancer.

Poster presentation: **Mahla Towhidifar**

The Role of miR-214-5p and miR-548-5p in Endometriosis

Fariba Dehghan, Mahla Towhidifar, Nasrin Ghasemi

Shahid Sadoughi University of Medical Sciences

Background: Endometriosis is a benign gynecological condition that affects approximately 1% of all women and up to 15% of females of reproductive age. To date, none of the suggested theories exhaustively explains the pathophysiology of the disease or its related clinical manifestations. As part of efforts to introduce new procedures for the early and non-invasive diagnosis of endometriosis, we investigated the alterations in miR-214-5p and miR-548-5p expression in both ectopic and eutopic tissues compared to normal endometrial tissue.

Materials and Methods: A total of 45 samples (15 eutopic, 15 ectopic, and 15 healthy controls) were collected from women referred to the Shahid Sadoughi Hospital (Yazd, Iran). RNA extraction was performed using an RNA extraction kit provided by the Yekta Tajhiz Azma. cDNA synthesis was performed using a Bon Stem miRNA 1st Strand cDNA Synthesis Kit. Specific primers were provided by Stem Cell Technology Company. Two-step qRT-PCR was performed according to the manufacturer's instructions. GraphPad Prism 8 software and the Two-Way ANOVA test were used to compare fold-change expression.

Results: The results suggest a downregulation in the expression levels of miR-214-5p (P-Value < 0.05) and an increase in miR-548-5p expression levels (P-Value < 0.05) in endometriosis samples compared to those in the control tissue.

Conclusion: miR-214-5p and miR-548-5p are critical regulators of endometriosis pathogenesis. The downregulation of miR-214-5p in people with endometriosis compared to healthy people implies its suppressive role. The upregulation of miR-548-5p confirms the oncogenic role of this microRNA in endometriosis conditions. Developing novel therapeutic strategies targeting these miRNAs can be promising in managing this disease.

Keywords: Endometriosis; miR-214; miR-548; Eutopic; Ectopic

Poster presentation: **Ashkan Pourtavakoli**

Expression assay of calcium signaling related lncRNAs in autism

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Abstract

Calcium signaling has essential roles in the neurodevelopmental processes and pathophysiology of related disorders such as autism spectrum disorder (ASD). We compared expression levels of SLC1A1, SLC25A12, RYR2 and ATP2B2, as well as related long non-coding RNAs, namely LINC01231, lnc-SLC25A12, lnc-MTR-1 and LINC00606 in the peripheral blood of patients with ASD with healthy children. Expression of SLC1A1 was lower in ASD samples compared with control samples (Expression ratio (95% CI)= 0.24 (0.08-0.77), adjusted P value=0.01). Contrary, expression of LINC01231 was higher in cases compared with control samples (Expression ratio (95% CI)= 25.52 (4.19-154), adjusted P value=0.0006) and in male cases compared with healthy males (Expression ratio (95% CI)= 28.24 (1.91-418), adjusted P value=0.0009). RYR2 was significantly over-expressed in ASD children compared with control samples (Expression ratio (95% CI) = 4.5 (1.16-17.4), adjusted P value=0.029). Then, we depicted ROC curves for SLC1A1, LINC01231, RYR2 and lnc-SLC25A12 transcripts showing diagnostic power of 0.68, 0.75, 0.67 and 0.59, respectively. To sum up, the current study displays possible role of calcium related genes and lncRNAs in the development of ASD.

Key words: autism spectrum disorder, SLC1A1, SLC25A12, RYR2, ATP2B2, LINC01231, lnc-SLC25A12, lnc-MTR-1, LINC00606, lncRNA

Poster presentation: **Elahe Hosseini**

Frequencies of two CYP3A5 defective alleles (CYP3A5*2, and *3) among normal population from north of Iran

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Background: Cytochrome p450 3A (CYP3A) group are considered as the main drug-metabolizing enzyme in human and *CYP3A5* is one of the core subfamily of the *CYP3A* group. This enzyme plays an important role in the metabolism of up to 60% of all prescribed drugs like midazolam, cyclosporine, alprazolam, triazolam, diltiazem, benzothiazepine, and tamoxifen. Previous investigations showed the polymorphisms CYP3A5*2 (rs28365083; g.27289C > A; T398N) and rs776746 (entitled *3) associated with gene function and expression. This study designed to evaluate the frequency of Cyp3A5*2 and Cyp3A5*3C alleles in Mazani ethnic population located in Mazandaran province, northern Iran.

Methods: 294 healthy individuals were selected from Mazandaran province. DNA was extracted from peripheral blood followed by genotype analysis using PCR-RFLP methods.

Result: The prevalence of two variants, *2 in *Cyp3A5* was 100% wild type (CC), and none for genotype *2 (AA) minor variant. The frequency of *3* allele was 35.72% normal AA, 13.94% heterozygous AG, and 50.34% mutant GG (*3/*3) genotype respectively. The Cyp3A5*3C allele frequency was 42.69% for A and 57.31% for the G allele.

Conclusion: Frequency of CYP3A5*2 in this study was similar to the most populations that were reported previously. A low frequency between zero to 1% was reported in different populations. Frequency of *3/*3 in Mazani ethnic population showed 50.34% in this study, lower than the average ranges in European (about 86%), and in the middle compared to the different Asian countries with 40% to 99% respectively.

Keywords: *Cytochrome P-450 CYP3A5, drug metabolism, Genotype, Gene Frequency, Mazandaran, Iran,*

Poster presentation: **AmirArsalan Aghabozorgizadeh**

Potential of GIHCG lncRNA as a diagnostic biomarker and prognostic factor in liver hepatocellular carcinoma

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Background and Objectives: Liver hepatocellular carcinoma is the third most common digestive cancer and the fourth cause of death worldwide (1). More than 85% of hepatocellular carcinoma cases occur in developing countries (2). Long non-coding RNAs, due to their ability to regulate gene expression at the epigenetic, transcriptional and post-transcriptional levels, can be closely related to tumor development and progression. Also, many studies have been conducted to investigate the function and clinical value of lncRNAs in various tumors, including hepatocellular carcinoma (HCC). However, the effects and functions of existing lncRNAs for the purpose of prognosis and diagnosis of liver hepatocellular carcinoma need to be optimized and updated (3). The purpose of this study was to investigate the expression changes of GIHCG long non-coding RNA in liver hepatocellular carcinoma and introduce it as a diagnostic biomarker and prognostic factor.

Material and methods: In order to investigate the changes of GIHCG expression in HCC, TCGA data provided by Oncodb database was used. Also, based on the clinical data of TCGA, the relationship between the expression of this gene and the mortality rate of patients and clinical characteristics was evaluated. The Kaplan-Meier curve was used to examine GIHCG expression changes and survival rate. Also, ROC curve was used to investigate the biomarker potency of GIHCG in HCC.

Results: The results of our investigations showed that the expression level of GIHCG in cancer samples increases significantly compared to normal samples (log FC = 2.09, p-value = 4.6e-50, FDR ≤ 0.001). Also, the results of this study showed that the expression level of GIHCG in cancer samples in stages 2 and 3 significantly increased compared to stages 1 and 4 (p-value = 2.7e-02). In addition, it was found that the expression level of GIHCG significantly increased in tumor samples that were histologically at G4 level (p-value = 1.1e-02). The results of this study showed that the expression level of GIHCG in samples with TNM status T4 significantly increases compared to T1 and T2 (p-value = 1.9e-07). Also, The Kaplan-Meier curve showed that increased expression of GIHCG is associated with poor prognosis of patients (logrank p: 1.0e-03). According to the ROC curve analysis, it was found that GIHCG lncRNA can be considered as an appropriate biomarker for the diagnosis of liver hepatocellular carcinoma (AUC = 0.94, p-value < 0.0001).

Discussion & Conclusion: The results of our study showed that the expression level of GIHCG increases in HCC and is associated with poor prognosis of patients. Also, we showed that GIHCG expression level in HCC can be considered as a diagnostic and prognostic biomarker.

Keywords: Liver hepatocellular carcinoma, GIHCG, lncRNA, Biomarker

Poster presentation: **Parniya Khosravi**

Identification of Genes Involved in Drug Resistance in Breast Cancer in Response to Treatment with Tamoxifen

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Introduction: Breast cancer is a disease that primarily originates in the breast glands. While it predominantly affects women, it can also occur in men. Various factors, including genetics, environmental elements, family history, and age, can contribute to the development of this type of cancer. One significant challenge in treating breast cancer is the resistance of certain cancer cells to drugs. This issue makes the treatment of some cases particularly difficult, requiring advanced and alternative therapeutic approaches. Therefore, further research and studies in the field of breast cancer treatment and prevention are of utmost importance in order to provide the best strategies for managing and treating this disease.

Materials and Methods: In this study, for the identification of genes and interaction networks associated with drug resistance in breast cancer, data related to resistance to the drug Tamoxifen were obtained from the GEO database. The series related to resistance to this drug were then identified. Subsequently, these series were analyzed using the GEO2R tool, and genes with differential expression associated with drug resistance were identified. Finally, the common DEGs among these series were determined, and the signaling pathways associated with them were identified using the KEGG database.

Results: Examination of the GEO database revealed that the series GSE 21618and GSE 26459 are associated with drug resistance in breast cancer to the drug Tamoxifen Analysis of these series showed that the gene gper1 with a logFC of -3.44 and an *adj. p-value* of 0.01616 is significantly downregulated in all drug-resistant breast cancer samples. Investigation of gper1 in the keg database indicated that this gene is effective in estrogen signaling. The identification of this gene in breast cancer is effective for drug design and also for overcoming drug resistance against this disease. It can help alter metabolic pathways and target gene expression activators to work towards treating this disease.

Keywords: GEO database, breast cancer, drug resistance, gene downregulation.

Poster presentation: **Hosna Niayesh**

The key signaling pathways implicated in endometriosis

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Endometriosis is a complex gynecological disorder characterized by the presence of endometrial-like tissue outside the uterus, leading to chronic pelvic pain and infertility in affected women. Endometriosis pathogenesis involves dysregulation of various regulatory pathways that contribute to the survival, proliferation, and invasion of endometrial cells in ectopic locations. This abstract provides an overview of the key signaling pathways implicated in endometriosis. One of the prominent signaling pathways involved in endometriosis is the PI3K/AKT/mTOR pathway. Activation of this pathway has been observed in endometriotic lesions and contributes to cell survival, proliferation, and angiogenesis. Dysregulation of this pathway may promote endometrial cell growth and survival outside the uterus. The estrogen receptor pathway is also critical to endometriosis pathogenesis. Estrogen promotes endometrial tissue growth and survival, and dysregulated estrogen signaling is implicated in endometriosis development. The estrogen receptor (ER) pathway, particularly ERα and ERβ, plays a key role in mediating estrogen effects on endometrial cells and contributing to endometriosis progression. The transforming growth factor-β (TGF-β) signaling pathway has been associated with endometriosis-related fibrosis and inflammation. TGF-β induces tissue fibrosis and modulates the immune response to endometriotic lesions. Dysregulation of TGF-β signaling may contribute to fibrotic adhesions and chronic inflammation associated with endometrios in addition, the Wnt/β-catenin signaling pathway has emerged as a critical player in endometriosis. Dysregulation of Wnt signaling can promote aberrant cell proliferation, migration, and invasion in endometrial cells. The activation of this pathway has been observed in endometriotic lesions and may contribute to the invasive and adhesive properties of endometriosis. Furthermore, the Notch signaling pathway has been implicated in endometriosis-related angiogenesis and cell fate determination. Dysregulated Notch signaling can promote blood vessel formation in endometriotic lesions and influence cell differentiation processes. In conclusion, dysregulation of multiple signaling pathways contributes to endometriosis pathogenesis. Understanding the intricate interplay between these pathways can provide valuable insights into the molecular mechanisms underlying endometriosis. This can potentially lead to targeted therapeutic interventions.

Keywords: Endometriosis, PI3K/AKT/mTOR, TGF-β, Notch

Poster presentation: **Dorsa Rostampour**

Whole-exome sequencing identified a novel mutation in *PLA2G6* gene of an Iranian family

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Background: Infantile neuroaxonal dystrophy (INAD) is a rare inherited neurological disorder that primarily affects infants and young children. Children with INAD Typically show normal development during the first few months of life, but symptoms begin to appear between the ages of 6 months and 2 years. Individuals with infantile neuroaxonal dystrophy experience progressive loss of vision, muscular control and mental skills, and other variable clinical signs. INAD is caused by mutations in the PLA2G6 gene, which is involved in the maintenance of nerve cells. This gene was mapped on chromosome 22q13.1. Studies of INAD in Iran are extremely rare, so, this study aimed to detect pathogenic variant in a consanguine Iranian family with infantile neuroaxonal dystrophy.

Materials and methods: Genomic DNA from 6ml peripheral blood was extracted from all participants using the salting out method. One µg of gDNA from patients was sheared, and exome capture was done using Sure Select Human All Exon V7r2. The enriched libraries were sequenced by NovaSeq 6000 platform with the coverage of target region about 100%. The sequencing data alignment, variant calling, annotation, variant prioritization, and prediction were performed as mentioned previously. To validate whole exome sequence results and segregation analysis we performed Sanger sequencing for the candidate variants for the patient and parents using the ABI3730 sequencer (Applied Biosystems).

Results: The proband (IV-3), a 2.5-year-old female, originating from Turkmen ethnicity from a consanguineous marriage who has shown signs of progressive hypotonia since 17 months of age (Figure 1). At the moment, she has signs such as developmental regression, destruction in the anterior horn neurons, nystagmus, feeding difficulty, speech delay, swallowing problems, and inability to walk. Brain MRI showed brief brainstorm involvement. Also, EMG-NCS revealed evidence of anterior horn cell involvement. Her elder sibling deceased at the age of 7 years with related symptoms. We discovered a novel homozygote pathogenic insertion variation NM_003560: c.1548_1549insCG (p.G517Rfs*29) in our patient (IV-3). Both parents (III5 & III6) and healthy brothers (IV-2) were identified as heterozygote carriers for this mutation. This variant, located in exon 10, causes a frameshift (p.G517Rfs*29) likely leading to premature termination of translation of PLA2G6 mRNA and truncation of the protein. Based on this evidence and following the latest American College of Medical Genetics (ACMG) guidelines, this PLA2G6 variation is categorized as a pathogenic variant.

Conclusion: Because of the clinical heterogeneity and rarity of infantile neuroaxonal dystrophy, whole exome sequencing is critical to confirm the diagnosis and is an excellent tool for INAD management. This mutation and associated clinical features expand the spectrum and phenotypes of PLA2G6-related disorders including neurodegenerative diseases.

Poster presentation: **Razieh Fatehi**

The Comprehensive Investigation of High-Grade Serous Ovarian Cancer Transcriptomics Data

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Introduction: Ovarian cancer is the main cause of mortality from neoplasm in women. Although ovarian cancer is a rare cancer it has the worst prognosis and the highest mortality rate. Ovarian cancer is a heterogeneous disease with different clinical and molecular characteristics. The most common type of ovarian cancer is High-Grade Serous Ovarian Cancer (HGSOC), which is the most lethal type and is responsible for 90% of deaths due to the high rate of recurrence and resistance to chemotherapy. In general, genetics is an important risk factor. Approximately 23% of cases are hereditary. The germ-line and somatic mutations in BRCA1 and BRCA2 genes involved with high penetrance. The genes involved in the Homologous Recombination Repair (HRR) pathway are other reasons responsible for susceptibility to this disease. The mutation in the TP53 gene is an early and common somatic mutation and an important molecular event in the pathogenesis of this disease. HGSOC is also associated with a lower prevalence of somatic mutations in the NF1, RB1, and CDK12 genes. Moreover, the role of signaling pathways, including the PI3K-AKT-mTOR pathway and the MYC pathway have been identified in HGSOC. In this study, by using the bioinformatics approaches a comprehensive investigation of HGSOC was performed.
Methods: The search strategy was based on "high grade serous ovarian cancer" term and Series Entry type, Expression profiling by array Study type, tissue samples, and Homo sapiens Organism filters. We focused on the datasets with enough samples, with healthy control samples, without treatment, and with acceptable quality. The differentially expressed genes (DEGs) were identified by considering the |log fold change|>2 and adjusted P value < 0.05 the cut-off. Using the TIMER2.0 database, the immune features related to differentially expressed genes were assayed to assess the tumor microenvironment. The DEGs interaction was retrieved based on the STRING database with a cut-off of 0.9. Using miRTarBase and lncHUB lncRNA Co-Expression libraries of the Enrichr database, the micro-RNA (miRNA) and long non-coding RNA (lncRNA) enrichment analysis were performed. The adjusted P value < 0.05 is considered a significant cut-off. By the DIANA-LncBase v3.0 database, miRNA-lncRNA interactions were retrieved. Finally, the combined mRNA-miRNA-lncRNA network was constructed. Using the cytoHubba plugin of Cytoscape software, the topology analysis of the network was performed. The pathway analysis based on KEGG and mirPathv3 databases was done. The mutation analysis of the candidate hub genes was carried out based on COSMIC, ICGC, and cbioportal databases. The survival analysis related to genes was investigated with the KM plotter online database. Finally, the expression levels of the genes were approved by TNMplot and HPA databases.
Results: We selected the GSE40595 dataset with 32 tumors epithelial and 6 healthy epithelium samples as control. 1602 genes were determined as significant differentially expressed genes with the |log fold change| >2 and adjusted P value < 0.05. The result of the immune infiltration investigation related to DEGs indicates the infiltration of Macrophage M2, Endothelial cell, T cell, NK cell, and Cancer-associated fibroblast. In the non-coding RNA enrichment analysis step, 110 miRNA and 405 lncRNAs were enriched with DEGs. Finally, we reached an integrated mRNA-miRNA-lncRNA network with 1895 nodes and 17832 edges. In the topological network analysis stage, we considered the 10 top nodes with the highest MNC, Degree, Betweenness, and Closeness parameters and introduced them as hub genes most of which are miRNAs. The hsa-miR-26b-5p, hsa-miR-124-3p, hsa-miR-93-5p, hsa-miR-16-5p, and hsa-miR-106b-5p are the overlapped miRNAs. Pathway enrichment analysis of miRNAs revealed that they are especially related to proteoglycans in cancer, pathways in cancer, MAPK signaling pathway, focal adhesion, and signaling pathways regulating pluripotency of stem cells. The OIP5-AS1, the lncRNA that was found as a key node, is associated with hepatoblastoma and glial tumors. At the mRNA level, the top genes are especially enriched with pathways related to several types of cancers, adherence junction, VEGF, and chemokine signaling pathways. The CDC42, EGFR, and RAC1 genes are the overlapped nodes with the highest centrality that are considered the key nodes. The mutation analysis of these genes shows 22621 mutations, 14 high-impact mutations, and 0.4% somatic mutation frequency for CDC42 in COSMIC, ICGC, and cbioportal databases, respectively. The 3797 mutations, 152 high-impact mutations, and 3.7% somatic mutation frequency have been reported for EGFR which has 30 target compounds. Also, 672 mutations, 16 high-impact mutations, and 0.7% somatic mutation frequency have been reported for RAC1, respectively. The Kaplan-Meier curve demonstrates the cumulative survival probabilities and a steeper slope indicates a worse prognosis. The CDC42 (P value: 0.0295) and EGFR (P value: 0.0172) results are significant and EGFR correlated with the worse survival prognosis. The low expression and high expression of these genes are associated with 21 and 19.09 months, 18.27 and 14.19 months' median survival, respectively. Also, the expression levels of the genes in several types of cancer were verified by TNMplot and HPA databases.
Conclusion: A holistic assay of HGSOC was performed with the immune characteristics, gene regulatory network, signaling pathways, mutation, and survival analysis. These data revealed several potential genes, miRNAs, lncRNAs, and pathways that may be involved in the progression of HGSOC.
Keywords: High Grade Serous Ovarian Cancer, Immune Infiltration, Bioinformatics

Poster presentation: **Akram Sarmadi**

Whole exome sequencing identifies novel compound heterozygous pathogenic variants in the MYO15A gene leading to autosomal recessive non-syndromic hearing loss

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Objectives: Autosomal recessive non-syndromic hearing loss (ARNSHL) is a highly heterogeneous disease and more than 70 genes have been identified to cause it. MYO15A mutations have been reported to cause congenital severe-to-profound HL. In this study, we applied the whole exome sequencing (WES) to find the cause of HL in an Iranian family.

Methods: A proband from an Iranian non-consanguineous family with hearing impaired parents, was examined via WES after excluding GJB2 mutations as the most common ARNSHL gene via Sanger sequencing. Co-segregation analysis of the candidate variant was done using Sanger sequencing of the family members. Interpretation of variants was according to the American College of Medical Genetics and Genomics (ACMG) guidelines.

Results: WES results showed novel compound heterozygous variants (p.Arg1507Ter and p.Val2815Valfs*10) in the MYO15A gene. These two variants, residing in highly conserved regions, were found to be co-segregating in the family and fulfill the criteria of being categorized as pathogenic, according to the ACMG guidelines.

Conclusion: Our results showed that WES is very promising to diagnosis of the etiology of highly heterogeneous diseases such as HL. Here, we report successful application of WES to identify the molecular pathogenesis of ARNSHL in a patient with ARNSHL. In agreement with previous studies, MYO15A is regarded to be important in causing HL in Iran.

Keywords: Compound heterozygous; Hearing loss; whole exome sequencing; Iran; MYO15A; Pathogenic variant

Poster presentation: **Zahra Vaez**

Fetal Stem Cells in Women's Tissues: A Comprehensive Study on Their Benefits and Risks

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Abstract: In recent studies, fetal stem cells have been detected in various tissues of women who have had successful or even unsuccessful pregnancy experiences. These cells have been reported to have many interesting benefits in the prevention and cure of cancer. However, cases of autoimmune diseases in mothers due to these cells have also been observed. This review paper aims to analyze the benefits and risks of the presence of fetal stem cells in women's tissues from various aspects, including their potential role in cancer prevention and cure, as well as their possible association with autoimmune diseases.

Background and Objectives: This review paper aims to examine the effects of fetal microchimerism on maternal health and its potential role in evolution.

The objective of this review paper is to provide a detailed analysis of the benefits and risks of fetal microchimerism in women's tissues from various aspects, including their potential role in cancer prevention and cure, as well as their possible association with autoimmune diseases. The review aims to analyze the effects of fetal microchimerism on maternal health and its potential role in evolution.

Material and methods: The mixed-methods research of this paper is a systematic and scientific approach to discovering new knowledge, validating existing knowledge, and solving problems. It involves identifying a research question, gathering relevant data from various sources such as scholarly articles, books, and other credible sources, analyzing the data, and drawing conclusions based on the analysis.

Results: Fetal microchimerism is a widespread phenomenon among mammals, and scientists have proposed many theories for how it affects the mother, from better wound healing to a higher risk of cancer. The presence of fetal cells in the mother's body could even regulate how soon she can get pregnant again. The passage further suggests that evolution has always chosen the best fit for the current conditions and natural selection has so far worked to help species survive. Therefore, if some degree of fetal microchimerism has a beneficial effect on the survival of the mother and offspring, it will probably be selected as an adaptive strategy for our species. However, more research is needed to understand the effects of fetal microchimerism on maternal health and its potential role in evolution.

Discussion & Conclusion: It is interesting to note that the phenomenon of fetal microchimerism is widespread among mammals, and scientists have proposed several theories for how it affects the mother, from better wound healing to a higher risk of cancer. The presence of fetal cells in the mother's body could even regulate how soon she can get pregnant again. The passage suggests that evolution has always chosen the best fit for the current conditions and natural selection has so far worked to help species survive. Therefore, if some degree of fetal microchimerism has a beneficial effect on the survival of the mother and offspring, it will probably be selected as an adaptive strategy for our species. However, more research is needed to understand the effects of fetal microchimerism on maternal health and its potential role in evolution. In conclusion, natural selection has so far worked to help species survive by choosing the best fit for the current conditions. Therefore, if some degree of fetal microchimerism has a beneficial effect on the survival of the mother and offspring, it will probably be selected as an adaptive strategy for our species. However, more research is needed to understand the effects of

fetal microchimerism on maternal health and its potential role in evolution. It is important to continue studying this poorly understood phenomenon to gain insights into its effects on maternal health and its potential role in evolution.

Keywords: Fetal microchimerism, Pregnancy, Natural selection, Adaptive strategy, maternal health

Poster presentation: **Sareh Bakhshandeh Bavarsad**

Study Immunodeficiency, Common Variable, 1 in a Family with novel ICOS gene mutation: a case report

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Abstract:

A clinically and genetically heterogeneous collection of diseases known as common variable immunodeficiency (CVID) with autosomal recessive inheritance is defined by a deficiency of antibodies, hypogammaglobulinemia, recurrent bacterial infections, and the failure to mount an antibody response to an antigen. The deficiency is caused by reduced immunoglobulin secretion and impaired B-cell development; whereas circulating B cell counts are often within the normal range, they can occasionally be low. A common variable immunodeficiency with a homozygous mutation at position 2q33 in the Inducible T Cell Costimulator (ICOS) gene as the cause of the disease. Diarrhea is one of the symptoms of immunodeficiency, common variable, 1, also known as antibody deficiency owing to ICOS defect. ICOS gene has several connected pathways and superpathways, including the Innate Immune System and Immune response NFAT. Approximately 10 to 20% of patients with a diagnosis of CVID have a family history of the disorder. In our study, a denovo variant in the ICOS gene has been reported using the next generation sequencing (NGS) technique.

Keywords: NGS| immunodeficiency| common variable| 1| ICOS gene

Poster presentation: **Setareh Arjmanddoost**

Predicting the interaction of miR-122-5p and EZH2 in liver cancer through bioinformatics analysis

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Background: Primary liver cancer is the second leading cause of cancer-related death worldwide and therefore a major public health challenge. Primary liver cancer comprises hepatocellular carcinoma (HCC), intrahepatic cholangiocarcinoma (iCCA), and other rare tumors, notably fibrolamellar carcinoma and hepatoblastoma (1). Liver is the major metabolic center for both carbohydrate and lipid, thereby maintaining glucose homeostasis (2). With the advances in high-throughput profiling techniques and the availability of public data sets such as The Cancer Genome Atlas Program (TCGA), a broad range of coding transcripts have been profiled and their underlying modes of action have been mapped (3). mir122-5p has unique potential as a prognostic biomarker in liver cancer. Mir 122-5p has significantly increased expression in Liver cancer tumor tissue (4). The regulation of many pathways in cell biology is regulated by miRNAs. Obtaining miRNA target genes is effective for negative regulation of this pathways and can also help to understand the regulatory mechanism and gene therapy of cancer. The EZH2 gene, which is expressed in various solid tumors, including liver cancer, can regulate gene transcription and promote the generation and progression of tumors. Our aim was to investigate the relationship between EZH2 and multidrug-resistance of human hepatic cancer cells using RNA interference (5).

Material and methods: In this project, after miRNA target gene prediction by mirwalk database, we analyzed TCGA RNA-seq data and predicted gene expression patterns. (6)

Results: The results showed that EZH2 with a high score in the CDS is targeted by miR-122-5p. Also, the results of TCGA data analysis showed that the expression level of this gene in Liver cancer tumor tissue was significantly Increase.

Conclusion: Predictions showed that increasing the expression of miR-122-5p causes a decrease in EZH2 expression in liver cancer. It is also predicted that the increase in the expression of EZH2, in addition to the role of a biomarker in the diagnosis of liver cancer, can be a factor in the development of liver cancer and the activation of the pathway.

Key word: liver, cancer, has-miR-122-5p

Poster presentation: **Sana Khodadad**

Y chromosome loss in bladder cancer drives growth by evasion of adaptive immunity

Sana Khodadad

Shahrekord University of Medical Sciences

Abstract:

In mammals, the Y chromosome (chrY) determines the male sex and maintains secondary sex characteristics including spermatogenesis. In ageing men, loss of Y chromosome (LOY) has been associated with many adverse health consequences. For example, LOY in haematopoietic cells is associated with an increased risk of several diseases, including cardiac fibrosis9 and multiple cancer types.

It has showed that cancer cells with LOY have a more aggressive growth phenotype and that low LOY gene signature scores are associated with a poor clinical prognosis for patients with cancer. Many studies have shown that losing the Y chromosome puts men at higher risk of getting cancer and of dying from cancer. In bladder cancer, LOY has been found in 10–40% of tumours. This is unsurprising, since bladder cancer is commonly caused by environmental exposures to tobacco and industrial chemicals, which are known to result in DNA damage and LOY

It was showed that the aggressive behaviour of LOY bladder cancer is a consequence of T cell dysfunction. It was reported increased tumour-associated macrophages, high levels of immune checkpoint molecules and CD8+ T cell exhaustion in Ylow tumours. On the upside, loss of the Y chromosome also appeared to make bladder cancer more susceptible to immunotherapy drugs called immune checkpoint inhibitors.

Of note, compared with Y+ tumours, Y− tumours exhibited an increased response to anti-PD-1 immune checkpoint blockade therapy in both mice and patients with cancer.

The chrY is largely heterochromatic and extremely gene-poor. It has determinded that two genes on the Y chromosome whose absence seemed to be responsible for faster growth of Y-negative tumors. The genes, called ubiquitously transcribed tetratricopeptide repeat containing, Y-linked(UTY) and lysine demethylase 5D (KDM5D) that loss of expression these were associated with an unfavourable prognosis in human bladder cancer.

Loss of UTY, the male counterpart of The lysine-specific demethylase6A/UTX (gene name KDM6A) has been reported to promote bladder cancer development.

KDM6A is located on the X chromosome, but both alleles are transcribed in females. As UTY is located on the Y-chromosome, males express one copy each of KDM6A and UTY, and thus possess overall lower total H3K27me2/3 demethylase activity. Recently, KDM6A loss of function mutations have been demonstrated to create a more permissive environment for FGFR3 activating mutations to drive bladder tumorigenesis.

Unlike UTX, UTY possesses very low demethylase activity for H3K2739, suggesting that UTY suppresses bladder cancer development in a demethylase-independent manner.

By contrast, KDM5D negatively regulates the expression of genes involved in tumour cell invasion, such as matrix metalloproteinase family genes, by demethylation of their H3K4me3 marks. Downregulation of KDM5D expression increases H3K4me3 levels at target gene promoter regions, leading to a more aggressive phenotype and the development of metastasis.

It remains to be determined if combinatorial loss of KDM6A and UTY is a requirement for initiation of bladder carcinogenesis in males. Further, identification of KDM5D or UTY loss in human tumours has the potential to be a useful prognostic factor in determining the clinical aggressiveness of bladder cancer.

Key word: Y chromosome ،bladder cancer ،immunotherapy

Poster presentation: **Sina Fekri**

Gastric cancer

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Introduction: Gastric cancer is one of the most common malignancies worldwide and it is the fourth leading cause of cancer-related death. GC is a multifactorial disease, where both environmental and genetic factors can have an impact on its occurrence and development. Early-onset gastric cancer is a good model to study genetic alterations related to the carcinogenesis process, as young patients are less exposed to environmental carcinogens. In this article, with different analyzes, the aim is to find biomarkers for this cancer.
Methods; Microarray analysis was performed on GSE158662 in the field of gastric cancer from the GEO database. GIF gene was selected as a gene with significant expression reduction after checking with ENCORI and GEPIA2 databases. The signaling pathways in which the GIF gene was active were checked by KEGG and Reactome databases. After analyzing the SNPs related to the said gene through the SIFT, miRNASNP and dbSNP databases, after analyzing SNPs related to the mentioned gene through SIFT, miRNASNP and dbSNP databases, A SNP in 3'UTR named rs541677351 was selected and a SNP in coding sequence were selected and their effects on the target gene were analyzed with the Hope database. The protein - protein interaction of the gene was analyzed by STRING database. The interaction between the desired gene and its related miRNAs was checked by miRWalk database.
Results: The deleterious SNP obtained from the SIFT database named rs150884181 after checking by the Hope database showed that it had a change in the 97th amino acid position and this change was from methionine to threonine. post-mutation state of this amino acid is smaller than the normal state and also the normal state is more hydrophobic than the mutated state. The mutation creates an empty space in the core of the protein. The mutation causes the loss of hydrophobic interactions in the protein core. After analyzing the desired gene with its related miRNAs, hsa-mir-6751-3p was selected as the miRNA affecting the 3UTR region. AIRN lncRNA was selected in the lncRResearch database as the lncRNA associated with GIF gene. Finally, the interaction between the selected lncRNA and its related miRNAs was studied.
Conclusions: After microarray analysis on GIF gene, the result of this study was that the said gene has a significant decrease in expression on gastric cancer and can be a biomarker in this cancer. The studies conducted on the protein-protein interaction of this gene showed that the target gene interacts with a significant number of other genes, and there is a possibility that these genes also affect the studied cancer.

Poster presentation: **Shantia Yazdani**

Colon cancer

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Introduction: Colon cancer is the third most common cancer globally. The risk of developing colon cancer is influenced by a number of factors that include age and diet, but is primarily a genetic disease, resulting from oncogene over-expression and tumour suppressor gene inactivation. Colon cancer needs better screening and treatment options. Its incidence in the young population is rising. In this article, with different analyzes, the aim is to find biomarkers for this cancer.

Methods: Microarray analysis was performed on GSE87873 in the field of colon cancer from the GEO database. PTGDR gene was selected as a gene with significant expression reduction after checking with ENCORI and GEPIA2 databases. The signaling pathways in which the PTGDR gene was active were checked by KEGG and Reactome databases. After analyzing the SNPs related to the said gene through the SIFT, miRNASNP and dbSNP databases, after analyzing SNPs related to the mentioned gene through SIFT, miRNASNP and dbSNP databases, A SNP in 3'UTR named rs1248870416 was selected and a SNP in coding sequence were selected and their effects on the target gene were analyzed with the Hope database. The protein - protein interaction of the gene was analyzed by STRING database. The interaction between the desired gene and its related miRNAs was checked by miRWalk database.

Results: The deleterious SNP obtained from the SIFT database named rs41311442 after checking by the Hope database showed that it had a change in the 7th amino acid position and this change was from arginine to cysteine. The post-mutation state of this amino acid is smaller than the normal state, and the mutated state is also more hydrophobic than the normal state. The charge of the normal state was positive; the charge of the mutant state is neutral. After analyzing the desired gene with its related miRNAs, hsa-miR-578 was selected as the miRNA affecting the 3UTR region. TSIX lncRNA was selected in the lncRResearch database as the lncRNA associated with PTGDR gene. Finally, the interaction between the selected lncRNA and its related miRNAs was studied.

Conclusions: After microarray analysis on PTGDR gene, the result of this study was that the said gene has a significant decrease in expression on colon cancer and can be a biomarker in this cancer.

The studies conducted on the protein-protein interaction of this gene showed that the target gene interacts with a significant number of other genes, and there is a possibility that these genes also affect the studied cancer.

Poster presentation: **Tahereh Honarmand**

FBN1 regulates cell proliferation through positive co-expression with MFAP2 in bladder urothelial carcinoma patients

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Objective: Urothelial carcinoma of the bladder is a common malignancy that causes approximately 150,000 deaths per year worldwide. So far, no molecularly targeted agents have been approved for the treatment of the disease. The genetic signature of high-risk bladder cancer has been a focus of investigation and has led to the discovery of potential molecular targets for disease identification, risk stratification, and therapy. In this study, we performed an integrated bioinformatics and systems biology investigation to evaluate a novel regulatory network in urothelial carcinoma of bladder cancer.

Methods: Microarray analysis was performed on the GSE186691 dataset using GEO2R, ENCORI, KEGG, Reactome, and Enrichr performed pathway enrichment and gene ontology analyses. STRING performed Protein- Protein correlation analysis.

Results: Microarray analysis revealed that MFAP2 and MMP11 have significant up-regulation; SGCD has significant down-regulation in bladder urothelial carcinoma patients. Survival analysis based on GEPIA2 and ENCORI revealed that increased expression of MFAP2 and MMP11, and decreased expression of SGCD has significant effects on the survival rate of bladder urothelial carcinoma patients. Furthermore, Pathway enrichment analysis based on the Reactome database showed that MFAP2 regulates cell proliferation in BLCA patients. So, MFAP2 and MMP11 have a significant effect on the Extracellular Matrix Organization R-HSA-1474244 pathway. Elastic fibre formation involves the deposition of tropoelastin onto a template of fibrillin-rich microfibrils. Protein- Protein correlation analysis based on the STRING online website illustrated that MFAP2 has a significant correlation with FBN1 (r: 0.412, p-value < 2.75e-18).

Conclusion: Protein MFAP2 regulates cell proliferation in urothelial carcinoma of bladder patients. MFAP2, as a potential oncogene, has a significant up-regulation in BLCA cancer samples. The high amount of MFAP2 has a significant effect on the survival rate of in urothelial carcinoma of bladder patients and FBN1 interaction.

Keywords: Systems Biology, Microarray analysis, Pathway enrichment, MFAP

Poster presentation: **Atefeh Hersij**

Expression Analysis of Treg-related lncRNAs in Neuromyelitis Optica Spectrum Disorder

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Abstract

Neuromyelitis Optica Spectrum Disorder (NMOSD) is an autoimmune disease affecting the central nervous system (CNS), in which various types of immune cells, including T and B cells, and numerous cytokines and chemokines are implicated. Long non-coding RNAs (lncRNAs) modulating the function or differentiation of regulatory T cells (Tregs) may be involved in the pathogenesis of NMO. To assess the involvement of these lncRNAs in this disease, we studied the expression levels of TH2-LCR, MAFTRR, NEST, RMRP, and FLICR in peripheral blood samples of NMO patients and healthy subjects. All of the lncRNAs listed were found to be up-regulated in NMO patients compared with healthy controls. Although the interaction of group and gender factors significantly affected the expression of NEST, RMRP, and TH2-LCR genes, it is detected no effect of gender factors on the expression of the examined genes. The highest expression correlation was found between RMRP and TH2-LCR among cases with correlation coefficients 0.73. Roc curve analysis indicated that TH2-LCR, MAFTRR, RMRP, and FLICR had significant prospective diagnostic power (AUC ± SD = 0.99 ± 0.002, 0.97 ± 0.01, 0.91 ± 0.01 and 0.84 ± 0.04, respectively). The best of these genes is TH2-LCR with AUC ± SD = 0.99 ± 0.002, sensitivity= 0.97, specificity= 1, P-value= <0.0001. RMRP and TH2-LCR had a positive correlation with age and age at onset and a negative correlation with EDSS start. Cumulatively, TH2-LCR, MAFTRR, RMRP, and FLICR lncRNAs, particularly TH2-LCR, could be considered potential markers for NMO disease.

Keywords: Neuromyelitis Optica Spectrum Disorder, T cells, lncRNAs, Expression

Poster presentation: **Abbas Seyedzadeh**

Bioinformatics study of MMP13 gene in Lung cancer

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Abstract

Cancer is a disease in which cells in the body grow out of control. When cancer starts in the lungs, it is called *lung cancer.* Lung cancer begins in the lungs and may spread to lymph nodes or other organs in the body, such as the brain. Cancer from other organs also may spread to the lungs. When cancer cells spread from one organ to another, they are called *metastases.* Lung cancer is one of the most common types of cancer worldwide. Lung adenocarcinoma (LUAD) is the most frequent histological subtype, taking up 40–50% of lung cancer cases. Smoking tobacco (including cigarettes, cigars, and pipes) is the primary risk factor for lung cancer but it can also affect non-smokers. Other risk factors include exposure to secondhand smoke, occupational hazards (such as asbestos, radon and certain chemicals), air pollution, hereditary cancer syndromes, and previous chronic lung diseases. Lung cancer is a significant public health concern, causing a considerable number of deaths globally. GLOBOCAN 2020 estimates of cancer incidence and mortality produced by the International Agency for Research on Cancer (IARC) show as lung cancer remains the leading cause of cancer death, with an estimated 1.8 million deaths (18%) in 2020. Understanding the molecular mechanisms underlying the development and progression of lung cancer may improve early diagnosis, treatment and prognosis. Bioinformatics also helps in identifying common biomarkers and differentially expressed genes in different cancer types which further improves the process of cancer diagnosis.

Background and Objectives: Lung cancer represents a significant global health issue and is among the central causes of mortality and morbidity around the world. Unfortunately, the majority of lung cancer patients acquire drug resistant to chemotherapy either intrinsically or acquired after Cisplatin treatment. It is indicated that increasing or decreasing the expression of particular genes can affect chemotherapeutic sensitivity or resistance. As a result, gaining a deeper knowledge of the changed expression of genes implicated in lung cancer drug resistance, as well as developing novel therapeutic techniques, are critical targets for continued advancement in lung cancer treatment.

Material and methods: We obtained data from the GEO chip dataset GSE۲۲۹۳۰۱. from the NCBI Gene Expression Omnibus (GEO) and analyzed by GEO2R to show the gene expression profile and determine the gene with features a significant up and down expression regulation. Then, by the analyzed data, suitable gene (Adj.P.Val < 0.05) and modules (Categorized genes) pathways are found and determined by ENCORI [3], gene product protein by UNIPROT, microarray by MIRWALK, SNP by MIRNASNP, lncRNA by LNCRRISEARCH and LNCBASE v3.

Poster presentation: **Ali Asghari Ghomi**

Predicting the negative regulation of ITM2C by miR-218 in prostate cancer progression and metastasis by TCGA data analysis

Ali Asghari Ghomi

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Background: MicroRNAs (miRNAs) are small noncoding regulatory RNAs (19–25 nucleotides) that play a major role in regulation of gene expression. They are responsible for the control of fundamental cellular processes that has been reported to be involved in human tumorigenesis. The characterization of miRNA profiles in human tumors is crucial for the understanding of carcinogenesis processes, finding of new tumor markers, and discovering of specific targets for the development of innovative therapies(1). The aim of this study is to find miRNAs involved in prostate cancer progression comparing the profile of miRNA expressed by localized high grade carcinoma and bone metastasis. miR-218 were significantly overexpressed by all localized high GS, pT3 PC in comparison with metastatic carcinoma(1, 2).

Material and methods: In this project, after miRNA target gene prediction by mirwalk database, we analyzed TCGA RNA-seq data and predicted gene expression patterns(3).

Result: The results of Mirwalk analysis show the strong interaction of miR-218 with ITM2C, and the results of prostate cancer genomics data analysis show a significant decrease in the expression of ITM2C in the tumor sample compared to the normal sample. The decrease in ITM2C expression in metastatic samples is also higher than in non-metastatic samples.

Conclusion: According to the location of miR-218 binding to ITM2C and this negative relationship between increased miR-218 expression in tumor samples and decreased ITM2C expression in tumor samples, as well as decreased ITM2C expression in metastatic samples and increased miR-218 expression in metastatic samples, regulation of ITM2C expression by miR-218 can be predicted.

Keyword: miR-218, ITM2C, prostate

Poster presentation: **Farzaneh Iravani**

RNA seq technology and new insights to clinical cancers Heterogeneity

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Abstract:

High throughput sequencing technology has undergone remarkable advancements in recent decades and now RNA sequencing extensively identified as a powerful tool for profiling the transcriptome. Its significance in the context of single-cell (scRNA-seq) is having a vital role. scRNA-seq not only suggests biological insights into the genetic characteristics of individual tumor cells but also facilitates the examination of factors that contribute to the heterogeneity of gene expression and the identification of its molecular mechanisms. In this study, we explain the important role of RNA-Seq on discovery new insights into clinical cancer heterogeneity.

Cancers belong to an impressive, malignant and lethal diseases, continues to present a very large challenge in the field of medical research and clinical treatment. The application of RNA sequencing involving the identification of tumor biomarkers, characterization of different heterogenic cancerous cells and evolution, examination of drug resistance, evaluation of the oncogenic immune microenvironment and immunotherapy, exploration of cancer neoantigens and etc. Recent studies have displayed that this technology could facilitates the detection of new and targetable oncogenic pathways. For example, single-cell sequencing has improved our comprehension of epigenetic mechanisms which manage tumor heterogeneity by disclosing the distinct epigenetic layers of individual tumor cells like chromatin accessibility, DNA/RNA methylation, histone modifications and nucleosome localization.

In summary, RNA seq technology can revolutionize the management of various diseases especially cancers, leading to improved patient outcomes and it has opened up new avenues for cancer research and therapy.

Key words: RNA Sequencing, transcriptome, Neoplasms

Poster presentation: **Kiana Mohammadi**

Downregulation of occludin expression in patients with melanoma

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Background and Purpose: Malignant melanoma is the most lethal cutaneous neoplasm that is curable with diagnosis. During epithelial-to-mesenchymal transition, the expression of occludin, an integralmembrane protein, is altered. The prognostic significance of occludin expression levels in melanomaremains unclear, although recent studies provide sufficient evidence for the functional importance of occludin in cancer. This study was designed to determine occludin expression and correlate it with clinicopathologic features in melanoma patients.

Methods: Occludin mRNA levels were compared between paraffin-embedded tissues from 40 melanoma patients and 10 normal skin subjects using qRT-PCR.

Results: The occludin mRNA level was decreased fivefold in the melanoma patients compared to the control group. There was no significant difference between male and female cases. Between occluding mRNA level, mitotic count, Clark level, and Breslow level no significant correlation was observed. No significant associations were found between gene expression and clinicopathologic characteristics such age and sex.

Conclusion: In conclusion, downregulation of occludin expression in melanoma patients is a characteristic feature of cancer progression and could be used as a prognostic factor.

Poster presentation: **Matin Kayyal**

Identification of JAK2 mutations bi-clonal pattern in Polycythemia Vera patient

Matin Kayyal, Mohammad Saberi Anvar, Reza Sadria, Maryam Shahrabi Farahani, Behzad Poopak

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Patients with Polycythemia Vera (PV) who do not have JAK2-V617F mutations have exon 12 mutations of JAK2. Rarely, myeloproliferative neoplasms (MPNs) have been shown to harbor dual JAK2 mutations in exons 12 and 14. Our investigation indicated that the 58-year-old PV patient, who exhibited trombocytemia evidence, had two distinct mutations in his peripheral blood, including a positive mutation for JAK2-V617F (exon 14) and exon 12 (deletion mutation). Our findings suggests that IFN therapy can lead to clinical, hematological, histological, and sporadically molecular remission in people with MPNs, as the patient in question is the first occurrence of a bi-clonal pattern in the Iranian community.

Keywords: Polycythemia Vera, dual Mutations, Myeloproliferative Neoplasms, JAK2

Poster presentation: **Dr Mojtaba Baktashian**

Downregulation of AnnexinA5 gene expression in coronary in-stent restenosis – A pilot study

Dr Mojtaba Baktashian[1], Dr Mohammad Hashemi[2], Dr Sara Saffari[3], Dr Mansoor Salehi[4], Dr Omid Iravani[5], Dr Mahsa Rastegar Moghadam[6], Dr Alireza Pasdar[7], Dr Majid Ghayour mobarhan[8]

Background and aims: In- stent restenosis (ISR) is the Achilles heel of angioplasty. AnnexinA5
as an anticoagulant has been shown have anti-inflammatory and anti-atherosclerotic effects. Here
we aim to investigating the mRNA expression of AnnexinA5 in peripheral white blood cell of patients with in-stent restenosis.

Methods: Patients with the history of coronary stent implantation who candidate for re-angiography were entered the study and allocated into two groups according the results of re-angiography; in-stent restenosis (stenosis≥50% in stent) and non-in-stent restenosis (stenosis <50% in stent). Total RNA of WBC was extracted and cDNA was synthesized using commercial
kits. AnnexinA5 expression was assessed with real time PCR and TaqMan probe and reported in relation with GAPDH as a housekeeping gene.

Result: AnnexinA5 expression was investigated in total 50 participants including 25 ISR and 25
non-ISR. Baseline characteristics including age, sex, smoking habits, hypertension, diabetes mellitus, dyslipidemia and stent in LAD were statistically the same in cases and controls. AnnexinA5 expression in ISR patients was 50% lower than controls.

Conclusion: AnnexinA5 is down-regulated in ISR and could be considered as a biomarker for predicting ISR and furthermore it could be used as prevention for ISR occurrence.

Keyword: in-stent restenosis, AnnexinA5, angioplasty, expression

Poster presentation: **Mousareza Shiri**

Nucleic acid drug-based therapies: Progress, challenges and perspectives

Mousareza Shiri [1, *], Hassan Dianat-Moghadam [1,2], Mohammadreza Sharifi [1,2]

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Abstract

Since the identification of gene mutations as the underlying factor of genetic disorders, the site-specific targeting of these defects to correct altered genes or create site-specific changes as well as altering gene expression has been the goal of medicine to treat related diseases. In addition to advances in genetic science and engineering, delivery of the therapeutic construct requires efficient delivery systems, which include viral and non-viral vectors. The advantage of viral vectors is that they transfer DNA into cells with high efficiency and have intrinsic tropism for specific cell types. However, viral vectors induce unwanted immune responses and can also integrate into the genome, especially in germ line cells, which has limited their use in the clinic. To address these challenges, nucleic acid drugs (NADs) are being developed that can have prolonged and even curative effects by targeting the gene product in the cytoplasm. Here, we first review the potential of NADs to treat genetic disorders, then review viral and non-viral vectors for NAD delivery, and finally discuss the challenges and prospects involved.

Key words: Gene therapy; gene delivery; nucleic acid drug; vectors; targeted therapy; clinical application; antisense oligonucleotide; siRNA; miRNA

Poster presentation: **Mohammad Saberi Anvar**

Detection of hemoglobin Hamedan in an Iranian family

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Abstract

The most prevalent monogenic autosomal recessive disease in the world is beta-thalassemia. Consequently, identifying carriers and carrying out prenatal testing can stop the birth of a child with an abnormality. Our study aimed to identify any variant of hemoglobinopathy in an Iranian family's peripheral blood. Father and younger sister's blood was drawn from the family. The hemoglobin Hamedan was discovered in a 4-year-old girl, also this variant was observed in her sister with same clinical status. The proband showed a slight decrease of MCV and normal range MCH levels, Furthermore, in this person, variant common variant HbS with increasing range (44.3%) were seen in Beta globin. The abnormal hemoglobin was 46% of the total hemoglobin as estimated by elution of hemoglobin bands from cellulose acetate after electrophoresis. The proportion of hemoglobin A 2 was 2%. There are few reports of this variant, which makes it difficult to assess the pathogen's clinical status. However, its identification can be useful to assess the prenatal screening program's effectiveness based on the emergence of new thalassemia cases.

Keywords: Beta-Thalassemia, Hemoglobinopathy, Proband, hemoglobin Hamedan

Poster presentation: **Maryam Jalali**

Detection of hemoglobin Hamedan in an Iranian family

MARYAM jalali[1], Mohammad Rezaei[2], Mansoureh Azadeh[3]

Introduction: Lung malignancies are aggressive and lethal tumors that are one of the most important causes of cancer-related mortality worldwide. According to histological classification, lung squamous cell carcinoma (LUSC) and adenocarcinoma (LUAD) account for the majority of cases. Lung cancer may be a profoundly heterogenous illness with wide-range of clinicopathological. Inside the classifications of lung cancer, non-small-cell lung cancer (NSCLC) accounts for around 85% of all cases. NSCLC can advance subdivide into two most common subtypes, lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC), speaking to 50–60% and 20–30% of add up to NSCLC cases, separately Lung carcinomas stay one of the foremost forceful malignancies characterized by the most noteworthy mortality rate among men and ladies around the world. With respect to histological classification lung squamous cell carcinoma (LUSC) and adenocarcinoma (LUAD) account for the lion's share of lung tumors in non-small cell carcinomas (NSCLCs). In any case, later considers have proposed that LUAD and LUSC ought to be classified and treated as distinctive cancers lung adenocarcinoma (LUAD) and lung squamous cell carcinoma (LUSC), have definitely diverse natural marks, however they are frequently treated essentially and classified together as non-small cell lung cancer (NSCLC). LUAD and LUSC biomarkers are rare, and their particular natural mechanisms have however to be explained the improvement of early symptomatic biomarkers and prognostic biomarkers is basic for the precise expectation of clinical results and early discovery of lung adenocarcinoma.

Methods: Initially, the NCBI Gene Expression Omnibus (GEO) was selected to obtain the desired GSE (GSE151102), and thus the gene expression profile was analyzed by R Studio to search for differentially expressed genes in LUAD tissue compared to the control group. Therefore, BMPER were selected for further studies. Pathways related to BMPER genes were selected from the GEPIA2 and ENCORI database. Then, the free online prediction software miRWalk 3.0 was used to select different target miRNAs, and dbSNP and HOPEdatabase snp experimental and predictive modules were used to identify the list of snp.

Results: According to GEO analysis of GSE151102 were indicated 65599up and down regulated genes. Among all these genesBMPER was considered as a Upregulated gene that related to LUAD and also Regulation Of Pathway-Restricted SMAD Protein Phosphorylation (revealed by Enrichr). And miRNAs related to BMPER were determined by using the Free Online prediction software miRWalk 3.0 Including hsa-miR-548o-3p, hsa-miR-301a-5p.

Conclusions: As a result of this study, concluded that hsa-miR-548o-3p, hsa-miR-301a-5p. miRNAs act as a tumor suppressor in LUAD by inhibiting the function of, and eventually represses the *ACTN2* gene which is an important gene for metabolism and biosynthesis. Therefore, this result may be considered as a potential therapeutic purpose for LUAD patients.

Poster presentation: **Maryam Norouz-zadeh**

The SRY translocation on X chromosome, a non-obstructive azoospermia case with normal male phenotypic feature

Maryam Norouz-zadeh[1], Sheyda Shokouh[1], Azadeh Yaghmouri[1], Asra Keykhavani[1], Akram Abdi[1], Maryam Rostami[1], Zahra Sadat Hoseini[1], Shamimeh Mosanan-farsi[1], Elaheh Jahanmehr[1], Shermineh Heydari[2], Hamid Reza Moazeni[2], Ahmad Reza Salehi Chaleshtori[1, †]

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Introduction: The 46,XX testicular disorder of sexual development is a rare condition described in 1964 for the first time and coined as the Chapelle Syndrome. This disorder accounts for approximately 2% of male infertility cases and it is stemming from cross over between X and Y chromosomes. Sixty to ninety percent of 46,XX males are fully virilized and have normal genitalia except small testicles. The clinical presentation of such cases is variable ranging from ambiguous genitalia at birth, failed puberty, up to normal male phenotype with infertility and hypogonadism. While the exact molecular bases are still unclear, 80–90% of all cases are SRY positive. A 33 years old phenotypic male was referred to us with azoospermia and infertility. After genetic counselling and for the first tier of genetic investigation, conventional cytogenetic was conducted. Consequently, we evaluated the patient through molecular analysis of AZF on Y chromosome. The first set of our analyzes showed normal 46,XX female karyotype for this patient. The results of the AZF molecular analysis, showed presence of SRY gene and deletion of other targeted genes on Y chromosome. This inconsistency might be due to a cross over between X and Y chromosomes and translocation of SRY gene to the new location on X chromosome. The investigation of this non-obstructive azoospermia case of infertility has shown that SRY translocation can cause a normal phenotypic male with 46,XX female karyotype. A multidisciplinary approach, including psychological support and genetic counseling, is ideal for the management of these patients.

Keywords: SRY, Chapelle Syndrome, non-obstructive, azoospermia, genetic counseling

Poster presentation: **Mojdeh Mansouri**

Title: Identification of a deletion in the DMD gene in an Iranian child with Duchenne Muscular Dystrophy

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Background and Objectives: Duchenne muscular dystrophy (DMD) is one of the most severe form of neuromuscular dystrophy in early childhood. It is a vital X-linked neuromuscular illness affected by mutations in dystrophin gene. Dystrophin is a protein in the cytoskeleton that promotes firmness, stability, and efficacy of myofibers. The typical clinical manifestations include retrogression of motor development in the majority of children. The initial diagnosis of DMD is based on clinical manifestations, muscular biopsy and electromyography. Molecular diagnosis on Dystrophin gene can confirm DMD. In order to cover the limitations in screening the mutations by conventional methods, new molecular genetics approaches using next generation sequencing (NGS) can be more helpful in finding the causative genes for genetic diseases.

Material and methods: Whole exome sequencing carried out along with a complete physical examination of the family. In silico methods were applied to find the alteration in the protein structure.

Results: The homozygous variant in DMD gene (NM-004006.2) was defined as c.2732-2733delTT (p.Phe911CysfsX8) in exon 21. In addition, phylogenetic conservation study of the human dystrophin protein sequence revealed that phenylalanine 911 is one of the evolutionarily conserved amino acids.

Discussion & Conclusion: Our study indicated a new deletion in the DMD gene in the affected family. This deletion with an X-linked inheritance pattern is new in Iran. These findings could facilitate genetic counseling for this family and other patients in the future.

Keywords: Duchenne Muscular Dystrophy, whole exome sequencing, deletion

Poster presentation: **Mahtab Sadat Tabaeian**

Title: Childhood-Onset Choreo-Dystonia Due to a Recurrent Novel Homozygous Nonsense HPCA Variant

Mahtab Sadat Tabaeian, Nayareh Nouri, Narges Nouri, Seyed Amir Bahraini
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Abstract:

Biallelic variants in HPCA were linked to isolated dystonia (formerly DYT2) in 2015. Since then, the clinical spectrum of HPCA-related disorder has expanded up to including a complex syndrome encompassing neurodevelopmental delay, generalized dystonia with bulbar involvement, and infantile seizures. We report four individuals with a new phenotype of childhood-onset choreo-dystonia belonging to two unrelated Iranian pedigrees and harboring a novel homozygous nonsense pathogenic variant in HPCA. Our case was a 35-year-old right-handed male was born full term to a consanguineous couple. Pre- and perinatal history were uneventful. He had delayed motor milestones. At the age of 18 months, he started experiencing involuntary jerky head movements. Over few years, he developed dysarthria and generalized dystonia affecting his limbs and trunk. He had one younger brother in good health and one younger sister with a milder phenotype of choreo-dystonia.

Our case report expands the pheno-genotypic spectrum of HPCA-related disorder by describing childhood-onset choreo-dystonia as a new phenotype, reporting on a recurrent novel pathogenic nonsense variant in HPCA, and suggesting that exon 2 of HPCA might be a mutational hotspot.

Key words: chorea| dystonia| genetics| hippocalcin| HPCA

Poster presentation: **Mobina Tohidian**

Title: microRNAs as promising biomarkers for diagnosing autism spectrum disorders; a bioinformatic approach

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Background and Objectives: Autism Spectrum Disorder (ASD) is a neurological and developmental condition that profoundly impacts how individuals interact with others, establish connections, learn, and behave (1). Although autism can be identified at any age, it is often characterized as a "developmental disorder" because its signs usually become apparent within the first two years of life. Moreover, recent epidemiological data has shown an increase in the prevalence of this condition, now affecting as many as 1 in 10 individuals (2). Furthermore, numerous studies suggest that microRNAs (miRs/miRNAs) play a crucial role in the development of the disorder, influencing the expression of genes associated with various neural pathways related to ASD (3). The objective of the current study is to introduce a genetic pathway and miRNA to gain a better understanding of the disease's underlying pathology. Additionally, we aim to present an early diagnostic biomarker for this condition by applying bioinformatics methods.

Material and methods: In the current research, we utilized the DisGeNET database (https://www.disgenet.org/) to extract genes associated with the disease (4). Additionally, we employed the STRING website (https://string-db.org/) to identify the network related to the genes we extracted (5). We also used the Gephi software for network analysis, and in this phase, we assessed the top 4 records with the highest betweenness and centrality as our target genes (6). To extract miRNAs, we turned to the mirWalk database (http://mirwalk.umm.uni-heidelberg.de/interactions/) (7). Finally, to identify common miRNAs shared among the genes, we employed an online Venn diagram tool (8) and selected miRNAs common to at least three genes.

Results: Genes related to ASD were successfully extracted (Supplementary Table 1). Additionally, a gene network analysis was conducted among the obtained genes, identifying four essential genes: ACTB, AKT1, CTNNB1, and EGFR (Figures 1 and 2). Subsequently, miRNAs associated with these four genes were identified and upon analysis, six miRNAs were found to be shared among them: hsa-miR-149-3p, hsa-miR-3173-5p, hsa-miR-6775-3p, has-miR-1275, hsa-miR-6794-3p, and hsa-miR-6749-3p (Figure 3).

Discussion & Conclusion: Based on the data obtained in this study, seven miRNAs have been identified, which could serve as potential targets in the development of ASD and even become noteworthy biomarkers. In this context, Zhao et al. demonstrated that hsa-miR-1275 could be a biomarker for synaptic brain disorders such as epilepsy (9). Dwivedi et al. also found that hsa-miR-6775-3p might be a biomarker for improving cognitive disorders like bipolar disorder (10). However, according to the authors' best knowledge, many miRNAs related to the course of autism have not been thoroughly explored. Therefore, these miRNAs could serve as valuable targets for future research and diagnostic applications. In summary, based on the data obtained, hsa-miR-149-3p, hsa-miR-3173-5p, hsa-miR-6775-3p, hsa-miR-1275, hsa-miR-6794-3p, and hsa-miR-6749-3p can be considered as promising research and diagnostic targets in Autism Spectrum Disorder (ASD). However, further research is needed to understand the current issue better.

Keywords: Autism Spectrum Disorder (ASD), microRNAs, biomarker

Poster presentation: **Maryam Sajjadi**

Biallelic loss of LDB3 leads to a lethal pediatric dilated cardiomyopathy

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Abstract:

Autosomal dominant variants in LDB3 (also known as ZASP), encoding the PDZ-LIM domain-binding factor, have been linked to a late onset phenotype of cardiomyopathy and myofibrillar myopathy in humans. However, despite knockout mice displaying a much more severe phenotype with premature death, bi-allelic variants in LDB3 have not yet been reported. Here we identify biallelic loss-of-function variants in five unrelated cardiomyopathy families by next-generation sequencing. In one of the families, we identified a novel homozygous frameshift variant in LDB3 residing within an 8Mb ROH in an 8-year-old girl diagnosed with cardiomegaly and severely reduced left ventricular ejection fraction. Our findings demonstrate that recessive LDB3 variants can lead to an early-onset severe human phenotype of cardiomyopathy and myopathy, reminiscent of the knockout mouse phenotype, and supporting a loss of function mechanism.

Key words: LDB3| ZASP| cardiomyopathy|myopathy

Poster presentation**: Sara Ahmadi Teshnizi**

The role of NDRG1 in breast cancer

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SBMU- Genetics group

Abstract:

NDRG1 could be a part of the α/β hydrolase superfamily that resides within the cytoplasm and takes part in the stress reactions, hormone response, cell development, and differentiation. A few studies have pointed to the significance of NDRG1 in the carcinogenesis. This gene has been found to be up-regulated in a cluster of cancer types such as lung and liver cancers, but being down-regulated in other types of cancers such as colorectal, gastric and ovarian cancers. However, its role in the breast cancer has been mentioned relatively less. The current study summarizes the prove on the part of NDRG1 in the carcinogenic processes of breast cancer.

Keywords: NDRG1| Breast cancer| Carcinogenesis| Biomarker

Poster presentation: **Reihane Khorasanina**

Expression analysis of chorionic somatomammotropin genes (CSH1, CSH2 and CSHL1) in breast cancer tumor

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Background: Increasing growth and changing the expression of genes is one of the characteristics of cancer cells, which is very effective in promoting cancer. Somatomammotropin genes are a pair of genes that are expressed exclusively in the placenta and belong to the growth hormone family. **Objective:** In this study, we investigated the expression of GH1, GH2, CSH1, CSH2, and CSHL1 genes in people with breast cancer, so that they may be used in understanding the expression network of cancer and in the field of its treatment or diagnosis. **Method**: At first, based on evidence and clinical records, 40 tumor samples were prepared along with adjacent tissue and healthy tissue as well as placenta tissue. Then, RNA was extracted from the samples and in the next step, the RNAs were converted into c-DNA. In the next step, specific primers for each gene were designed and ordered, and the expression level of the target genes was checked by Real time PCR method and the results obtained by the method Statistics were analyzed and interpreted. **Results**: *CSH1*, *CSH2*, *CSHL1* genes had increased expression in tumor samples compared to healthy breast tissues.Both CSH1 and CSH2 showed significant elevated expression in Breast cancer tissue comparison with normal breast tissue (P=0.01,P=0.002)Furthermore these two genes showed significant elevated expression in comparision with their Adjacent tissue (P=0.015,P=0.042),in associasion with clinicopathological features of breast cancer tissues specifically the CSH2 gene showed elevated expression in Luminal A subtypes. **Conclusion:** Conclusion: CSH1, CSH2, CSHL1 genes had increased expression in tumor samples compared to healthy breast tissues and tumor margins. In addition, CSH1 and CSH2 can be proposed as a new potential therapeutic or diagnostic target in patients with breast cancer or some of its subgroups such as Lumina A or triple negative, and it may also be possible to evaluate the response to treatment or the progress.

Poster presentation: **Sajjad Biglari**

Monogenic etiologies of persistent human papillomavirus infections: a comprehensive systematic review

Sajjad Biglari[1,2,3], Atefeh Sohanforooshan Moghaddam[4], Mohammad Amin Tabatabaiefar[1], Roya Sherkat[5], Leila Youssefian[6], Amir Hossein Saeidian[2,3], Fatemeh Vahidnezhad[7], Lam C. Tsoi[8], Johann E. Gudjonsson[8], Hakon Hakonarson[2,3,9], Jean-Laurent Casanova[10-14], Vivien Béziat[10-12], Emmanuelle Jouanguy[10-12], Hassan Vahidnezhad[*2,3,9]

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Background: Persistent human papillomavirus infection (PHPVI) causes cutaneous, anogenital, and mucosal warts. Cutaneous warts include common warts, Treeman syndrome, and epidermodysplasia verruciformis, among others. Although more reports of monogenic predisposition to PHPVI have been published with the development of genomic technologies, genetic testing is rarely incorporated into clinical assessments. To encourage broader molecular testing, we compiled a list of the various monogenic etiologies of PHPVI.

Methods: We conducted a systematic literature review to determine the genetic, immunological, and clinical characteristics of patients with PHPVI.

Results: The inclusion criteria were met by 261 of 40,687 articles. In 842 patients, 83 PHPVI-associated genes were identified, including 42, 6, and 35 genes with strong, moderate, and weak evidence for causality, respectively. Autosomal recessive (AR) inheritance predominated (69%). PHPVI onset age was 10.8±8.6 years, with an interquartile range of 5–14 years. GATA2, IL2RG, DOCK8, CXCR4, TMC6, TMC8, and CIB1 are the most frequently reported PHPVI-associated genes with strong causality. Most genes (74 out of 83) belong to a catalog of 485 inborn errors of immunity (IEI)-related genes, and 40 genes (54%) are represented in the nonsyndromic and syndromic combined immunodeficiency categories.

Conclusion: PHPVI has at least 83 monogenic etiologies and a genetic diagnosis is essential for effective management.

Keywords: HPV, inborn errors of immunity, recalcitrant wart, persistent human papillomavirus infection, monogenic disorder

Poster presentation: **Melika Ansari Chaharsoughi**

Cancer pain is not incurable

Melika Ansari Chaharsoughi

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Background and Objectives: Cancer, a complex and devastating disease, continues to be a major global health concern. While genetic mutations have long been recognized as key drivers of cancer development, recent research has shed light on the significant role of epigenetics in cancer initiation, progression, and treatment. In this article, we will explore the fascinating field of epigenetics and its implications for understanding and combating cancer.

Understanding Epigenetics: Epigenetics refers to the study of heritable changes in gene expression that do not involve alterations in the DNA sequence itself. These changes can be influenced by various factors, including environmental exposures, lifestyle choices, and aging. Epigenetic modifications, such as DNA methylation, histone modifications, and non-coding RNA molecules, play a crucial role in regulating gene activity and maintaining cellular identity.

Epigenetics and Cancer: Cancer is characterized by uncontrolled cell growth and the ability to invade surrounding tissues. Epigenetic alterations can disrupt the normal regulation of genes involved in cell division, DNA repair, and cell death, leading to the development and progression of cancer. Aberrant DNA methylation patterns, histone modifications, and dysregulated non-coding RNAs have been observed in various types of cancer.

Epigenetic Biomarkers: Epigenetic changes in cancer cells can serve as valuable biomarkers for early detection, prognosis, and treatment response. By analyzing DNA methylation patterns or histone modifications, researchers have identified specific epigenetic signatures associated with different cancer types. These biomarkers hold great promise for improving cancer diagnosis and tailoring personalized treatment strategies.

Epigenetic Therapies: The discovery of epigenetic alterations in cancer has opened up new avenues for therapeutic interventions. Epigenetic drugs, such as DNA methyltransferase inhibitors and histone deacetylase inhibitors, have shown promising results in clinical trials. These drugs work by reversing abnormal epigenetic modifications, reactivating tumor suppressor genes, and restoring normal gene expression patterns. However, challenges remain in optimizing the efficacy and minimizing side effects of these therapies

Poster presentation: **Haniyeh Eskandari**

Crisper cas-9: a revival of adoptive T cell therapy for cancer immunotherapy

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Background: Chimeric antigen receptor T (CAR-T) cell therapy is regarded as a remarkable cancer treatment strategy especially in refractory B-cell malignancies. the optimal potency of CAR T-cell therapy for many other cancers especially solid tumors is not satisfactory. Accurate designing of CAR T-cells with clustered regularly interspaced short palindromic repeats (CRISPR)/CRISPR associated protein 9 (Cas9) system or other novel gene editing tools can improve the proliferation and persistence of CAR T cells in body.

Methods: This narrative review is the result of data collection from Google scholar, Scopus, Pubmed, Embase and web of science databases. 240 articles vwere founded that 25 of them from 2015 to 2023 were chosen to get studied.

Results: Despite hopefulness of CAR T cells in cancer treatment, a number of patients are enable to receive this therapy because of insufficient t cell numbers, fast progression of disease and inability in immunosuppress tumor microenvironment. CRISPER Cas-9 breaks this limitations, directs Cas protein to the specific DNA site under guidance of a single complementary RNA and causes hereditary changes to particular gene of CAR T cell to produce safe, powerful allogeneic CAR T-cells for on-demand cancer immunotherapy.

Conclusion: Application of CRISPER Cas-9 in CAR T cells prolongs their persistence, reverses exhaustion and promotes the anti-tumor function with higher specificity and accuracy with lower cytotoxicity and costs in contrast with other gene editing methods. Although it has already challenges with heterogenicity and constant mutations of cancer cells, method of delivery along with untargeted mutations of CAR T cells. further studies and trials needed to make the path of CRISPER based immunotherapy brighter.

Keywords: Cancer, CRISPER Cas-9, CAR T cell, immunotherapy

Poster presentation: **Shiva Vaheb**

Homozygous variant in the FKBP10 gene underlie Osteogenesis imperfecta

shiva vaheb[1], motaharesaddat hashemi[2], mohammad moosae[3]

Background: Osteogenesis imperfecta, type XI (Bruck syndrome 1) (OMIM-259450), is characterized by congenital contractures with pterygia, onset of fractures in infancy or early childhood, postnatal short stature, severe limb deformity, and progressive scoliosis, caused by mutations in the FKBP10 gene. It's an Autosomal recessive disease.

Osteogenesis Imperfacta (OI) is a heterogeneous group of connective tissue disorders. Classification of OI included types I to XVII. Types VI to XVII which are the rare formsof the disease. The Burk syndrome (BS) is an autosomola recessive form of OI type XI with conjenital joint contractures. Mutation in the FKBP10 gene leads to this disease. Most of these children have normal length at birth but later in life develop significant short stature. The patients have fragile bones, normal sclerae, no dentinogenesis imperfecta, no hearing loss and normal intelligence. Radiographic features include Wormian bones in the skull, generalized osteo-penia, bowing, bending and fractures of the long bones and osteopenia/platyspondyly of the vertebral bodies.

Case report: Here, we describe 8-years-old girl, a child of consanguineous parents. She had normal growth up. She has She has spondylolisthesis in the L5 vertebra of the spine. In infancy, she underwent surgery due to clubfoot.

In Next Generation Sequencing analysis of whole exome, a homozygous NM_021939.4:c.831dupC (p. Gly278fs) mutation in exon 5 of FKBP10 gene was detected. This variant has been reported for pathogenecity.

Conclusion: this disease is very rare so there is little data about genetic causes. In 2018 Fatemeh Maghami and et.al reprted one case who was 8 years old and had two mutations in FKBP10 that's refer to OI disease.

Poster presentation: **Elahe sadat mousavi**

The impact of epigenetics on male infertility

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Background and Objectives: Male infertility is a prevalent and intricate issue with a significant genetic and epigenetic foundation, impacting approximately 1 out of 20 males. Epigenetic alterations encompass DNA methylation, histone modifications, and chromatin remodeling, serving as crucial regulators of various biological processes, including sperm cell production. Hence, epigenetic modifications play a vital role in determining the expression of specific genes and their temporal activation in distinct cellular contexts. The male infertility phenotype is shaped by the interplay between numerous genes, the epigenetic regulation of gene expression, as well as environmental and lifestyle factors that influence genetic and epigenetic variations. In this comprehensive analysis, we present an overview of the influence exerted by epigenetic mechanisms on spermatogenesis and male infertility.

Material and methods: A comprehensive examination was conducted wherein the search terms "epigenetics," "infertility," and "epigenome" were utilized to investigate the available literature in the PubMed, Google Scholar, and Scopus databases. Additionally, an analysis of related articles was undertaken.

Results: Numerous studies have demonstrated the significance of alterations in epigenetic modifications during the initial and final stages of gametogenesis. This suggests that epigenetic modifications, encompassing DNA methylation, modifications to the histone tail, chromatin remodeling, and non-coding RNAs, might be implicated in idiopathic male infertility. Epigenetic mechanisms regulate several genes in the testes, thereby indicating the direct impact of such mechanisms on spermatogenesis. Epimutations, frequently in the form of hypermethylation, have been observed in several genes, including MTHFR, PAX8, NTF3, SFN, HRAS, JHM2DA, IGF2, H19, RASGRF1, GTL2, PLAG1, D1RAS3, MEST, KCNQ1, LIT1, and SNRPN, in association with parameters such as semen quality or male infertility. Environmental toxins and drugs may influence fertility through epigenetic modifications. Unlike genetic aberrations, epigenetic changes may not cause as much harm since they are potentially reversible. Further investigation could lead to the identification of specific drugs capable of reversing epigenetic modifications.

Discussion & Conclusion: Understanding the genetic mechanisms implicated in male infertility pathophysiology, as well as the impact of environmental and lifestyle factors on gene expression, may help clinicians devise personalized treatment strategies. Additional investigations, encompassing genome-wide association studies, epigenomics studies, and experimental studies, are necessary to more accurately ascertain the determinants leading to these outcomes. Given the relative usefulness of epigenetics, there is still much to be learned regarding the processes and mechanisms governing gene expression regulation.

Poster presentation: **Vajiheh Moayedinasab**

The first report of a pathogenic variant in the disease Desbuquois Dysplasia in the population of Iran

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Background and Objectives: Skeletal dysplasia is Desbuquois dysplasia (DBQD) an autosomal recessive inheritance disorder that is characterized by severe short stature, slackness, dislocation of multiple joints and developmental delay. Desbuquois dysplasia is clinically heterogeneous. Three types of this disease are known and classified. Pathogenic variants in the *CANT1* have been reported in all three types of DBQD. Kim type is characterized by elongated phalanges and short metacarpals. While DBQD types I and II differ by the presence or absence of an ossification center at the distal end of the second metacarpal or delta phalanx. Overlay, the Kim type of DBQD is clinically characterized by a milder phenotype, relatively short metacarpals and elongated phalanges.

Material and methods: whole exome sequencing (WES) was used to enrich all exons of protein-coding genes as well as some important other genomic regions. Next-generation sequencing (NGS) was performed to sequence close to 100 million reads on the Illumina sequencer. In general, the test platform examined >95% of the targeted regions with a sensitivity of above 99%. In this test, point mutations and micro-insertion/deletion and duplication (<20bp) can be simultaneously detected.

A 37-year-old man who referred with short stature, short neck, deformity of fingers and knees, and scoliosis. At first, the *FGFR3* gene was examined with method of PCR-Sanger Sequencing in the patient, who had apparent symptoms of achondroplasia, and no mutation was found in this gene. Subsequently, WES was performed for the patient at the request of a genetic counselor.

Results: After analyzing the results of the gene sequence, we identified a homozygous missense variant (c.467C>T) (p. Ser156Phe) that has been previously reported as a pathogenic variant in 3 Indian patients from 2 separate families but this is the first reported case in Iran that has such a mutation. This variant is not present in population databases (ExAC no frequency). Based on the ACMG 2015 guideline the variant can be categorized as likely pathogenic.

Discussion & Conclusion: Considering the similar phenotypic manifestations in the disease *Achondroplasia* and *Desbuquois Dysplasia*, such as obesity, scoliosis, dwarfism, and macrocephaly with frontal bossing, it should be considered that the cases that initially seem to have achondroplasia, instead of Gene check *FGFR3*, NGS should be requested as the first requested test. Further analysis and exploration into the causative mechanism of these missense mutations are imperative to acquire a greater understanding of both the function and metabolism of the *CANT1* protein.

Keywords:Whole Genome Sequencing, Desbuquois Dysplasia, Kim variant, *CANT1*, chondrodysplasia, skeletal Dysplasia, Iran

ارائه پوستر: **ویس هاشمی نیا**

مطالعه همراهی پلی مورفیسم های کاندید GWAS با ابتلا به پره اکلامپسی در بیماران

ویس هاشم نیا

**نویسنده مسئول: گروه بیوتکنولوژی آبزیان، پژوهشکده آرتمیا و آبزی پروری، دانشگاه ارومیه، ارومیه، ایران،*

سابقه و هدف: پره‌اکلامپسی یک اختلال چند ارگانی مختص دوران بارداری می‌باشد که می‌تواند عوارض خطرناکی بر سلامت مادر و جنین داشته باشد. شیوع این بیماری در سرتاسر جهان بین ۲ الی ۸٪ است. مکانیسم بیماری‌زایی پره‌اکلامپسی تاکنون به طور کامل شناخته نشده است اما با توجه به ماهیت چندعاملی‌اش، مطالعه واریانت‌های ژنتیکی می‌تواند در کشف مکانیسم دقیق این بیماری کمک‌کننده باشد. در پژوهش حاضر، همراهی چندشکلی‌های کاندید GWAS، rs4769612 در ژن *FLT1*[1] و rs259983 در ژن *ZNF831*[2]، با استعداد ابتلا به پره‌اکلامپسی در بیماران ایرانی بررسی شد.

روش بررسی : در مجموع ۶۰۰ نمونه در این مطالعه مورد بررسی قرار گرفت. جهت بررسی اثر ژنوتیپ مادری، نمونه‌ی خون محیطی از ۲۰۰ خانم مبتلا به پره‌اکلامپسی و ۲۰۰ خانم سالم باردار گرفته شد. جهت بررسی اثر ژنوتیپ جنینی نیز، نمونه خون بندناف از ۱۰۰ خانم مبتلا به پره‌اکلامپسی و ۱۰۰ خانم سالم باردار گرفته شد. سپس DNA از نمونه‌ها به کمک روش Salting Out استخراج شد و همراهی واریانت‌های rs4769612 و rs259983 با روش Tetra-Arms-PCR مورد بررسی قرار گرفت.

یافته‌ها: نتایج مطالعه حاضر در جمعیت ایرانی نشان داد که ژنوتیپ جنینی rs4769612 با الگوی توارث مغلوب با بیماری پره‌اکلامپسی همراهی داشت ((۰.۷۳-۰.۱۳) ۰.۳۱ :OR (95% CI) ، ۰.۰۰۴۸ :p value) اما این واریانت از طریق ژنوتیپ مادری با بیماری همراهی نشان نداد. این در حالی است که ژنوتیپ مادری واریانت rs259983 با الگوی توارث غالب با پره‌اکلامپسی همراهی داشت ((۰.۴۰-۰.۹۹) ۰.۶۳ :OR (95% CI) ، ۰.۰۴۳ :p value) اما این واریانت از طریق ژنوتیپ جنینی با بیماری پره‌اکلامپسی همراهی نداشت.

بحث و نتیجه‌گیری: مطالعه‌ی حاضر نشان داد که ژنوتیپ جنینی rs4769612 در *FLT1* و ژنوتیپ مادری rs259983 در *ZNF831* با بیماری پره‌اکلامپسی در جمعیت ایرانی همراهی دارد. نتیجه این مطالعه به خوبی اهمیت بررسی همزمان ژنتیک مادر و جنین را در بیماری پره‌اکلامپسی مشخص می‌کند. این نتایج هم‌چنین می‌تواند به شناخت بهتر مکانیسم بیماری کمک نماید.

واژگان کلیدی: پره‌اکلامپسی، GWAS، rs4769612، rs259983

1 Fms related receptor tyrosine kinase 1
2 Zinc finger protein 831

ارائه سخنرانی : **اکرم عبدی**

جابجایی متعادل دوطرفه کروموزمی در یک نوزاد تشخیص داده شده با همبستگی واکترل

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زمینه: همبستگی واکترل بیماری وخیم و نادری است که در آن بیمار دست کم سه نقص از مجموعه علائم در واکترل را دارد. این علائم شامل: نقص در ستون مهره ها، مقعد، قلب، تراکئوازوفاژیال (نای و مری)، کلیه و اندامها(دست و پا(می باشد. تقریبا" ۹۰٪ از موارد همبستگی واکترل بطور تک گیر روی می دهد، در حالی که ۱۰٪ از این بیماران بطور خانوادگی به این وضعیت گرفتار می شوند. شیوع این بیماری ۱ در هر ۱۰۰۰۰ تا یک در هر ۴۰۰۰۰ نوزاد زنده تخمین زده می شود. عواملی مانند ژنتیک و عوامل مربوط به دوران بارداری در مادر در بوجود آمدن همبستگی واکترل نقش دارند. عوامل خطر ژنتیکی شامل جهش های ژنی و یا ناهنجاری کروموزومی می باشند .

هدف: در این مطالعه ما نوزادی هفت ماهه با تشخیص افتراقی همبستگی واکترل را گزارش می کنیم که با جابجایی متعادل تشخیص داده شده است.

مواد و روش ها: روش بندینگ GTG با قدرت تفکیک بالا (HR) و تجزیه و تحلیل سیتوژنتیکی بر روی خون بیمار بعد از جداسازی اجراء خون بدست آمده از بیمار و بدست آوردن سلول های سفید خونی انجام شده است.

نتایج: بعد از آزمایشات دقیق، این بیمار با نقص شدید قلبی، مقعد بسته، شنوایی کم و انگشتان دفرمه در هر دو دست، تشخیص داده شده است. متاسفانه، و در نتیجه شدت نقص قلبی، بیمار تنها چند روز بعد از ارزیابی ما درگذشته است. از طریق تجزیه و تحلیل سیتوژنتیکی ما بیمار را ناقل جابجایی متعادل در بازوی بلند کروموزوم های ۹ و ۱۶ با کاریوتایپ ۴۶ (XX,t(9;16)(q21.12;q21,تشخیص داده ایم.

نتیجه گیری: تجزیه و تحلیل سیتوژنتیکی متداول اولین رویکرد در هنگام مواجهه با ناهنجاری های مادرزادی و خصوصیات سندرومیک است. اما، تنظیم دقیق و نشان دادن محل شکست دقیق بواسطه روش های پیشرفته تر شدیدا" برای بررسی های آینده توصیه شده است.

کلمات کلیدی: همبستگی واکترل، ناهنجاری کروموزومی، نقص قلبی، نقص اندام

ارائه پوستر: **محمد کرد کتولی**

استفاده از microRNA بر روی ژن تنظیم کننده miR-155 در سرطان کولورکتال

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سرطان کولورکتال (CRC) یکی از شایع ترین و خطرناک ترین سرطان ها در جهان است. که سالانه صد ها هزار نفر به این نوع سرطان مبتلا می شوند و در هر سال ده ها هزار نفر جان خود را از دست می دهند .بنابر این هدف این مقاله بررسی بیان سرمی microRNA-155 (miR-155)در بیماران مبتلا به سرطان کولورکتال (crc) بررسی سودمندی بالقوه این مولکول به عنوان بیومارکر برای تشخیص و پیش آگهی در CRCبود.

و روش‌ها در این مقاله، جستجو پایگاه‌های علمی PubMed، Cochrane Library، EMBASE، Web of Science، scopes و Google Scholar برای تجزیه و تحلیل نقش بیومارکر بودن Mir-155 در داده‌های CRC برای جستجوی microRNAهای مختلف در موارد سرطان کولورکتال مورد تجزیه و تحلیل قرار گرفت.

MicroRNA ها (miRNAs) گروهی از RNA های کوچک غیر کدکننده هستند که طول بین ۲۵-۱۹ نوکلئوتید دارند که نقش عمده ای در تنظیم mRNA دارند. اکثر مطالعات بیان miRNA در نمونه‌های بافتی انجام شده است، و برخی مطالعات پتانسیل تشخیصی و پیش‌آگهی را برای miRNAهای در گردش نشان داده‌اند، زیرا miRNAهای مشتق شده از تومور می‌توانند در خون وجود داشته باشند. و به نظر می رسد به طور پایدار از فعالیت ریبونوکلئاز درون زا محافظت می شود. در گردش، که مهم است زیرا افزایش یا حتی کاهش بیان miRNA های در گردش می تواند نشان دهنده miRNA های تولید شده توسط تومور باشد و ویژگی تشخیصی بیومارکر را افزایش دهد. با سرطان، مانند PTEN،TPM1 و PDCD را تعدیل می کند و در تومورهای مختلف انسانی بیش از حد بیان می شود. علاوه بر این، بیان miR-155 در بافت های CRC تنظیم می شود، یا در طول پیشرفت تومور تنظیم می شود. مطالعه اخیر نشان داد که بیان miR-155 پلاسما به طور قابل توجهی در بیماران CRC بر اساس TaqMan افزایش یافته است. miR-155 با پیش آگهی تومور مرتبط است. علاوه بر این، miR-155 اغلب حتی در ضایعات پیش بدخیم مانند آدنوم کولون، که ضایعات هدف برای غربالگری CRC هستند، تنظیم مثبت می شود. در این مطالعه، ما فرض کردیم که miR-155 مورد خوبی برای اکتشاف به عنوان یک نشانگر زیستی است. در واقع، برای تشخیص زودهنگام و پیش آگهی CRC، با فرض اینکه الگوی بیان miR-155 به عنوان یک نشانگر زیستی جدید استفاده می شود.

کلمات کلیدی: بیومارکر ، سرطان کولورکتال ، miR-155 ، microRNAs

ارائه پوستر: **محمد کرد کتولی**

استفاده از siRNA با کمک نانوذرات در تشخیص و درمان سرطان ریه

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مقدمه :سرطان یکی ازعوامل مرگ و میر در جهان است به طوری که در روده دوم مرگ و میر جهان قرار گرفته است. عوامل ژنتیکی ،اپی ژنتیکی و محیطی در ایجاد سرطان نقش بسیار مهمی دارند . سرطان ریه یکی از سرطان های بسیار شایع در جهان به شمار می آیید. به طوری که سالانه صد ها هزار نفر را به کام مرگ می کشاند. برای راه کار های نوین برای تشخیص و درمان سرطان می توانیم از siRNA استفاده کنیم ، که به کاهش بیان ژن کمک میکنند . که میتوانیم از ویژگی های بیولوژیک خاص سرطان ریه را شناسی کنیم که روش نوین به شمار می ایید.

مواد و روش ها : در این مقاله مروری ضمن برسی سرطان ریه از پایگاه علمیscopus,SID,Pubmed و google scholarبه تجزیه و تحلیل استفاده از نانوذرات و انتقال siRNA در تشخیص ودرمان سرطان ریه و چالشهایی آن در جهان پرداخته شد.

بحث و نتیجه گیری: siRNAها که RNA ها غیر کد کننده هستند و به طول حدود ۲۵-۱۹ نوکلئوتید هستند. بدین ترتیب می توانند برای ما بافت های سرطانی را از بافت سالم تشخیص دهیم ، با استفاده از نانوذرات که می توانند siRNA به محل هدف انتقال بدهد بیشتر از نانوذراتی که خاصیت ضد سرطانی دارند مانند طلا ، الماس ، پلاتین و نقره استفاده میشود. ولی یکی از چالش موجود که با ورود نانوذرات به داخل بدن امکان ورود به خون را دارند که در این موقع توسط خون در سرتاسر بدن منتشر میشوند و پس از جذب سلولی در غدد لنفاوی بدن ، مغز ، قلب و... رسوب ایجاد می کنند . در بعضی از واقع گزارش شده است که این نانوذرات می توانند با القا اکسیداتیو به DNA آسیب زده و باعث سرطان شوند. این مقاله به برسی پیشرفت های اخیرو توانایی انجام و موقعیت کنونی و راه کار های پیش رو بشر در تشخیص و درمان سرطان ریه پرداخته شد.

کلمات کلیدی: siRNA ، سرطان ریه ، نانوذرات

ارائه پوستر : **ریحانه روانبخش**

غنی سازی آرتمیا ارومیانا با ترکیب فیتوژنیک ضدسرطان کورکومین به منظور تولید خوراک زنده مقاوم در برابر عفونت و با خاصیت ضدسرطانی

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مقدمه: صنعت آبزی پروری یکی از صنعت هایی است که رشد سریع در تامین نیاز نیاز پروتئین انسان پیدا کرده است. با توجه به این مسئله، افزایش کیفیت گوشت آبزیان که به مصرف انسان خواهد رسید یکی از اهداف اصلی این صنعت می باشد (۱). یکی از روش های افرایش کیفیت آبزیان، افرایش کیفیت خوراک زنده مورد تغذیه این آبزیان می باشد. از پرکاربردترین خوراک زنده مورد استفاده، آرتمیا ارومیانا است که به عنوان حامل، نقش عمده ای در انتقال ترکیبات موثر به بدن آبزیان و از آنجا به انسان دارد (۲). یکی از ترکیبات فیتوژنیک پرکاربرد با خاصیت ضدسرطانی شناخته شده، ترکیب کورکومین است (۳). بنابراین در این مطالعه برآن شدیم تا به غنی سازی آرتمیا ارومیا با ترکیب کورکومین بپردازیم تا در آینده آبزیان با خاصیت ضدسرطانی برای استفاده انسان تولید شود.

روش اجرا: دراین مطالعه ابتدا سیست آرتمیا (تخم آرتمیا) در محیط مناسب) داخل آکواریوم با دمای آب ۲۸ درجه سانتی گراد و نور کافی و شوری (33 ppt تخم گشایی شدند. سپس لارو آرتمیا (ناپلی) ۱۸ ساعت بعد خارج شد. پس از آن دو دوز مختلف کورکومین 0.03 mg/ml) و ۰.۰۵ (mg/ml به منظور غنی سازی استفاده شد. قبل از استفاده کورکومین، آنرا در مقدار مناسب PBSحل می کردیم. برای این منظور از دستگاه هموژنایزر برقی با سرعت بسیار بالا (15000 rpm) استفاده شد. به منظور شناسایی ورود موفق کورکومین (دارای خاصیت فلورسنت) به بدن آرتمیا از میکروسکوپ فلورسانس استفاده شد .

نتایج : ۲۴ساعت پس از تیمار ناپلی با کورکومین، ناپلی ها در الکل ۷۰ درصد تثبیت شد و سپس روی لام قرار داده شد و زیر میکروسکوپ فلورسانس بررسی شدند. نتایج میکروسکوپ فلورسانس نشان از ورود موفقیت آمیز ترکیب فیتوژنیک کورکومین به بدن آرتمیا دارد. با توجه به خاصیت و عملکرد چندگانه کورکومین (ضد سرطان و صد التهاب و تقویت سیستم ایمنی)، انتظار می رود آبزیانی که از این آرتمیای غنی شده با کورکومین تغذیه می شوند همان ویژگی ها را در خود نشان دهند و همچنین همان ویژگی ها را به انسان که از این آبزیان استفاده می کند نیز انتقال دهد .

نتیجه گیری: استفاده از آرتمیای غنی شده با کورکومین به عنان خوراک زنده می توان خواص چندگانه کورکومین را آبزیان تغذیه شده با این خوراک زنده و از آنجا نیز به انسان منتقل کند.

کلمات کلیدی: آرتیما ارومیانا، کورکومین، ضدالتهاب، ضد سرطان، تقویت سیستم ایمنی

ارائه پوستر : **ریحانه روانبخش**

تاثیر Dendrosomal Nano Curcumin بر بیان long non-coding RNA HULC در رده سلولی سرطانی MCF-7

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مقدمه: مطالعات اخیر نشان می دهد که RNA غیرکدکننده طویل نقش عمده ای در آغاز و پیشرفت سرطان دارند (۱). یکی از ترکیبات موثر در درمان سرطان استفاده از ترکیبات فیتوژنیک می باشد که این ترکیبات از گیاهان استخراج می شوند. یکی از پرکاربردترین گیاهی که سالیان طولانی در طب سنتی استفاده می شود زردچوبه است که اثرات درمانی و غذایی بسیار مطلوب دارد (۲). کورکومین یکی از موثرترین ترکیب فیتوژنیک مستخرج از ریشه زردچوبه است (۳). در این مطالعه تاثیر Dendrosomal Nano Curcumin بر بیان یکی از مهمترین RNAهای غیرکدکننده طویل درگیر در سرطان بنام HULC در رده سلولی سرطان پستان پرداخته شده است.

روش اجرا: دراین مطالعه بیان RNA غیرکدکننده طویل HULC در رده سلولی سرطانی پستان MCF-7 تیمار شده با Dendrosomal Nano Curcumin توسط تکنیک Real-time PCR تحقیق شده است. برای این منظور، ابتدا رده سلولی مذکور در محیط کشت RPMI ده درصد سرم جنین گاوی بطور مطلوب کشت داده شد. سپس این سلول ها به مدت ۲۴ و ۴۸ ساعت با دو دوز مختلف Dendrosomal Nano Curcumin تیمار شدند. پس از این مدت RNA کل از سلول های تیمار شده و کنترل (بدون تیمار) توسط کیت استخراج Trizol استخراج شد. در ادامه سنتز cDNA این RNAها انجام گرفت و در نهایت بیان HULC توسط تکنیک Real-time PCR بررسی شد.

نتایج: نتایج مطالعه کیفی و کمی RNA های استخراج شده از سلول ها توسط بارگذاری RNA استخراجی در ژل آگارز ۱ درصد و همچنین توسط دستگاه نانودراپ انجام شد که نتایج نشان دهنده استخراج با کیفیت مطلوب بود. سنتز cDNA نیز توسط PCR ژن کنترل داخلی مورد ارزیابی قرار گرفت که این نتایج نیز نشان دهنده سنتز موفقیت آمیز cDNA ها بود. در ادامه مطالعه، بیان HULC توسط تکنیک Real-time PCR انجام گرفت (شکل۱) که نتایج نشان داد که بیان HULC در سلول های تیمار شده با Dendrosomal Nano Curcumin در مقایسه با گروه کنترل به میزان ۳/۲ برابر کاهش یافته است ($p<0.002$, 95% CI) (شکل۲).

نتیجه گیری: ترکیب فیتوژنیک کورکومین می تواند بیان HULC دررده سلولی سرطانی پستان MCF-7 به طور معنی داری کاهش دهد.

کلمات کلیدی: long non-coding RNA، HULC، کورکومین، سرطان پستان، MCF-7

ارائه پوستر : **ریحانه روانبخش**

همراهی واریانت احتمالا بیماری زای ژن AP1S2 با سندرم Pettigrew در سه خانواده

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چکیده

مقدمه: سندرم Pettigrew(MRXS5) نوعی از ناتوانی ذهنی است که توسط فرید در سال ۱۹۷۲ برای اولین بار توصیف شد. این بیماری به ویژگی‌های ناتوانی ذهنی و ویژگی‌های اضافی بسیار متغیر از جمله کریواتتوز، هیدروسفالوس، بدشکلی های داندی-واکر، صرع، و رسوب آهن یا کلسیم در مغز مشخص می‌شود.
جهش‌های در ژن *AP1S2* می‌توانند منجر به ایجاد سندرم Pettigrew شوند، هرچند با بهترین وآخرین دانش و علم کنونی ما چنین جهش‌هایی نادر هستند.

هدف: در اینجا، ما چهار مرد در سه خانواده ای که ناقل واریانت احتمالا بیماری زای در ژن *AP1S2* را توصیف می‌کنیم ، ژنی که در سندرمPettigrew با توارث وابسته به X جهش یافته و اولین بار توسط فرید گزارش شد. علاوه بر این، ما طیف بالینی این ناتوانی ذهنی وابسته به X ارثی را گسترش می‌دهیم.

روش‌ها: مطالعه حاضر با بررسی دقیق بالینی بیماران، مشاوره ژنتیکی قبل از آزمایش ودنبال کردن بیمار، با استخراج DNA از لوکوسیت‌های خون محیطی آغاز شد. سپس، ما از توالی کل اگزوم کامل (WES) و تأیید Sanger برای شناسایی کاندید(ها)ی قوی شناسایی شده استفاده کردیم.
نتایج: بررسی بالینی ما سندرم Pettigrew را به عنوان یک تشخیص افتراقی برای بیماران نشان داد، در حالی که در دو بیمار ویژگی‌های فنوتیپی شدیدتری مشاهده کردیم. در نهایت، ما یک واریانت احتمالا بیماری زای در ژن *AP1S2* (NM_003916:exon1:c.-20_-1+2del)شناسایی کردیم. این واریانت توسط روش توالی یابی سنگر تأیید شد و همراهی بیماری در تعداد بیشتر خانواده مطالعه و تایید شد که بیماری با ژن کاملا همراهی دارد.

بحث و نتیجه‌گیری: نتایج ما ایده مشارکت جهش‌های ژن *AP1S2* در سندرم Pettigrew را بیشتر تأیید می‌کنند. علاوه بر این، ما طیف بالینی شناسایی شده برای این بیماری را گسترش داده‌ایم و به صورت دقیق و جالب سه خانواده با سندرم Pettigrew و چهار فرد مبتلا را گزارش میدهیم. برای تحقیقات آینده، تست‌های مولکولی پیشرفته‌تر، مطالعات عملکردی، و مطالعات مدل حیوانی توصیه می‌شود.

کلمات کلیدی: *AP1S2*، سندرم Pettigrew ، WES، توالی یابی سنگر

ارائه پوستر : **ریحانه روانبخش**

کاهش بیان آرنای غیر کدکننده طویل LncUSMycN در رده سلولی سرطانی MDA-MB-231 تیمارشده با نانوکورکومین

ریحانه روانبخش*

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مقدمه: سرطان پستان شایع ترین بدخیمی مهاجم در زنان جهان است و پس از سرطان ریه دومین سرطان شایع می باشد. بطور کلی یک سوم از زنان سرطانی به این نوع سرطان مبتلا هستند (۱). مطالعات نشان می دهد که تغییر در بیان RNAهای غیرکدکننده طویل می تواند از عوامل آغاز و پیشرفت سرطان پستان باشد (۲). یکی از RNAهای غیرکدکننده طویل که در بیماران مبتلا به نوروبلاستوما شناسایی شده است، lncUSMycN می باشد (۳). گزارشات متعددی ثابت می کند که برخی ترکیبات موجود در طبیعت خواص ضد سرطانی دارد. یکی از این ترکیبات کورکومین است که بعلت حلالیت پایین در محیط های آبی، به صورت نانوکورکومین در بسیاری از مطالعات به خواص ضدسرطانی آن پرداخته شده است (۴). در این مطالعه برآن شدیم تا تاثیر نانوکورکومین دندروزومی (DNC: Dendrosomal Nano-Curcumin) بر بیان lncUSMycN در رده سلولی سرطان پستان MDA-MB-231 بپردازیم.

روش اجرا: ابتدا رده سلولی پستان MDA-MB-231 از بانک سلولی انستیتوپاستور (تهران-ایران) تهیه شد. سپس در محیط کشت RPMI1640 غنی شده با L-گلوتامین می باشد کشت داده شد. پس از اینکه سلول ها به تراکم ۸۰ درصد در فلاسک کشت رسیدند، به منظور تیمار با نانوکورکومین دندروزومی به ظروف شش خانه انتقال داده شدند. سپس در دو دوز مختلف و به مدت ۲۴ ساعت و ۴۸ ساعت با این ترکیب تیمار شدند. در ادامه و با اتمام زمان تیمار، RNA این سلول ها (سلول های تیمار شده و گروه کنترل که تیماری در آنها صورت نگرفته است) با استفاده از کیت استخراج RNA بنام Trizol، استخراج شد. RNA های استخراجی از نظر کیفی (بارگذاری در ژل آگارز ۱درصد) و کمی (دستگاه نانودراپ) ابتدا بررسی شدند که در شرایط مطلوبی باشند. سپس cDNA سنتز شد و در ادامه بیان RNA غیر کدکننده طویل lncUSMycN توسط تکنیک Real-time PCR بررسی شد.

نتایج: نتایج بررسی کیفی و کمی RNAهای استخراجی نشان دهنده کیفیت بسیار خوب RNAهای استخراجی بود (شکل۱). همنین کیفیت سنتز cDNAتوسط PCR ژن کنترل داخلی بتااکتین انجام گرفت که تمام cDNA های سنتزی کیفیت خوبی داشتند. در نهایت نتایج تاثیر نانوکورکومین دندروزومی بر بیان lncUSMycN در رده سلولی سرطان پستان توسط تکنیک Real-time PCR انجام گرفت (شکل۲) و این نتایج نشان داد که بیان ژن lncUSMycN در نمونه‌های سلولی تیمار شده با DNC به میزان ۲/۷ برابر کمتر از گروه کنترل مربوطه، می‌باشد ($p<0.007$, 95% CI) شکل (۳).

نتیجه گیری: ترکیب نانوکورکومین دندروزومی (DNC) می تواند با کاهش بیان lncUSMycN باعث تقلیل خواص سرطانی رده سلولی سرطانی MDA-MB-231 شود که گام موثری در درمان سرطان محسوب می شود.

کلمات کلیدی: long non-coding RNA، LncUSMycN ، نانوکورکومین، سرطان پستان، MDA-MB-231

ارائه پوستر: **ریحانه روانبخش**

کاهش بیان آرنای غیر کدکننده طویل HULC در دره سلولی سرطانی کبد HepG2 تیمار شده با (DNC) نانوکورکومین دندروزومی

ریحانه روانبخش

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مقدمه: مطالعات گسترده ای از گذشته تا به اکنون در مورد جنبه های مختلف دارویی کورکومین انجام شده است و نقش آن به عنوان یک ترکیب ضد سرطان مشخص شده است. اما به دلیل ماهیت طبیعی آن که محلولیت کمی در آب دارد، جذب سلولی بسیار کمی داشته و به این دلیل هنگام استفاده از آن در تیمار سلول های سرطانی نمی تواند خاصیت ضد سرطانی خود را در سلول سرطانی به طور مطلوب القاء کند (۱). از اینرو، فرم جدید کورکومین که به حاملهای دندروزومی اتصال یافته و Dendrosomal Nano Curcumin یا DNC نام دارد به طور موثری می تواند در محیط های آبی حل شده و در نتیجه به طور موثرتری از سد غشائی سلول ها عبور میکند می تواند خواص خود را در سلول سرطانی القا کند (۲). یکی از نقش های کورکومین در سلول کاهش بیان ژن ها و RNA های سرطان زاست. یکی از این RNAهای غیرکدکننده طویل شناخته شده در پیشرفت سرطان به ویژه در سلول های سرطانی کبد، HULC می باشد (۳) که در این مطالعه به تاثیر DNC بر بیان HULC پرداخته شد.

روش اجرا: در این مطالعه ابتدا سلول های سرطانی کبد HepG2 در محیط RPMI 10% در فلاسک های 5 ml کشت داده شدند. سپس وقتی تراکم سلول ها به میزان مناسب ۷۵ درصد رسید، سلول ها توسط تریپسین از کف فلاسک جدا شدند و به منظور تیمار با دو دوز مختلف کورکومین و در دو زمان ۲٤ و ٤۸ ساعت، داخل ظروف شش خانه سید شدند. پس از تیمار ۲٤ ساعت و ٤۸ ساعت با کورکومین، RNA کل سلول های مذکور توسط کیت ترایزول استخراج شد و سپس توسط کیت سنتز cDNA فرمنتاز، cDNA نمونه ها سنتز شدند. در ادامه توسط تکنیک Real-time PCR بیان HULC در رده سلولی سرطانی HepG2 بررسی شد.

نتایج: نتایج بررسی کیفی (بارگذاری آرناها داخل ژل آگارز ۱٪) و کمی (دستگاه نانودراپ) آرناهای استخراج شده از رده سلولی سرطانی کبدHepG2 نشان دهنده کیفیت بالای آرناهای استخراجی بود. همچنین نتایج سنتز cDNA که توسط PCR ژن کنترل داخلی بتااکتین انجام گرفت، حکایت از سنتز مطلوب و موفقیت آمیز cDNAها را دارد. در ادامه بررسی بیان HULC توسط تکنیک Real-time PCR (شکل۱) نشان داد که کاهش بیان معنی دار ۳/۹ ($p<0.002$, 95% CI) در سلول های سزطانی کبد تیمار شده با DNC در مقایسه با گروه کنترل در هر دو دوز و هر دو زمان، اتفاق افتاد (شکل۲).

نتیجه گیری: نانوکورکومین دندروزومی می تواند به طور معنی داری بیان RNA غیرکدکننده HULC را در رده سلولی سرطانی کبد HepG2 کاهش دهد و از این رو می تواند یک ترکیب درمانی امیدبخش در سرطان کبد در نظر گرفته شود.

کلمات کلیدی: long non-coding RNA، HULC، نانوکورکومین دندروزومی، سرطان کبد، HepG2

ارائه پوستر : **غزاله فرهمند**

گامی بزرگ در تغییر سبک زندگی و پیشگیری از بیماری ها بر پایه رمز گشایی از ژن ها با تست های Gen Codex

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مقدمه: امروزه با گسترش روزافزون تکنولوژی و مطالعات تخصصی مشخص شده است که DNA نه تنها به عنوان رمزکننده و انتقال دهنده اطلاعات لازم برای حیات و تولیدمثل موجودات زنده، بلکه مرجعی برای انجام تست های مربوط به سلامت مورد استفاده قرار می گیرد. مطالعات بسیاری در راستای رمزگشایی از این کدهای اطلاعاتی در موجودات زنده درحال انجام است. خوشبختانه با پیشرفت های روزافزون در زمینه مهندسی ژنتیک و علم بیوانفورماتیک، رمزگشایی طیف عظیمی از ماده وراثتی انسان DNA میسر شده است.

هدف: علم ژنومیک شخصی (علم مطالعه ژن های موجود بر روی کروموزوم های فرد) شاخه ای از علم است که با استفاده از تکنیک های مختلف مهندسی ژنتیک و بیوانفورماتیک، ژن ها را توالی یابی، تجزیه و تحلیل و تفسیر می کند و تعیین ژنوتیپ (توالی های ژنتیکی) را امکان پذیر کرده است. هنگامی که ژنوتایپ فرد مشخص می شود، اطلاعات بسیار زیادی از جمله ویژگی های ظاهری، سلامت فرد، ویژگی های اخلاقی و شخصیتی، احتمال ابتلا به بیماری های مختلف و... در مورد فرد در دسترس قرار می گیرد. نسل جدید دستگاه های توالی یابی ژن با افزایش سرعت و کاهش هزینه استخراج اطلاعات قادرند تست های ژنتیکی متنوعی را به جهت استفاده مصرف کنندگان فراهم آورند. یکی از مهم ترین نقاط قوت تست های Gen Codex در اصلاح سبک زندگی و پیشگیری از بیماری هاست. با بررسی ژنتیک افراد می توان بیماری هایی که استعداد ابتلا به آنها دارند را شناسایی و مسائل لازم جهت پیشگیری را به آنها ارائه داد.

روش ها: Gen Codex با رمزگشایی از اطلاعات نهفته در ژنوم انسان‌ها، گنجینه‌ای ارزشمند را در اختیار هر فرد قرار می‌دهد که از طریق آن می‌توان یک سبک زندگی ایده‌آل، بر اساس محتوای ژنتیکی فرد طراحی و برنامه‌ریزی کرد. تست ژنتیکی Gen Codex با استفاده از ویژگی های ژنتیکی منحصر به فرد و ارائه راهکار متناسب با ژنتیک هر فرد و حذف آزمون و خطا کمک زیادی در پیشگیری از بسیاری بیماری ها دارد. با روش نمونه گیری بزاق و با استفاده از تکنولوژی روز و بر پایه پشتوانه هزاران تحقیق علمی بدست آمده براساس اطلاعات ژنتیکی هر فرد به جای پیشنهادات موقتی و مد روز که پس از مدتی ناکارآمدی خود را نشان می دهند، دفترچه ای کامل شامل توصیه و راهکارهای اختصاصی متناسب با ژنتیک هر فرد ارائه می شود ما با علم ژنتیک قطعات پازل تناسب اندام و سلامتی مراجعین خود را تکمیل میکنیم و همچنین با ارائه خدمات در زمینه های تغذیه و سلامت، ورزش و تناسب اندام، ویژگی های پوستی و کشف ویژگی های شخصیتی گامی بزرگ در تغییر سبک زندگی بر پایه رمز گشایی از ژن ها برداشته ایم .

نتیجه گیری: امروزه پزشکی شخصی یا پزشکی فردمحور (Personalized Medicine) با بهره گیری از علوم مختلف ژنتیک، بیوانفورماتیک و زیست فناوری و غیره پنجره جدیدی در حوزه پزشکی گشوده که بر روی تشخیص و درمان هر انسان به صورت منحصر به فرد تمرکز دارد. تست های ژنتیکی Gen Codex به دنبال ارائه خدمات پزشکی (سلامت، پیشگیری، تشخیص، درمان و مراقبت) متناسب با ژنتیک فرد است که منجر به پیشگیری از بساری بیماری ها و کاهش هزینه‌های درمانی می‌گردد. هرچند پزشکی شخصی به عنوان شاخه در حال گسترش از پزشکی، قدمت چند هزارساله دارد اما در سال‌های اخیر رویکرد فردمحور، به تدریج در همه شاخه‌های پزشکی گسترش یافته است. این شاخه از علم، روز به روز در پزشکی روزمره کاربردهای بیشتری پیدا می‌کند و به نظر می‌رسد یکی از عرصه‌های عمدهٔ پزشکی در آیندهٔ نزدیک باشد. ما مطمئن هستیم که آینده علم پزشکی شخصی محور است.

کلمات کلیدی: پزشکی شخصی، تست Gen Codex، تغییر سبک زندگی، پیشگیری از بیماری

ارائه پوستر : **پردیس ارجمند**

بررسی بیان ژن و پروتئین ZBTB16 در سلول های جنسی تمایزیافته، تمایزنیافته و سلول های فیبروبلاست

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چکیده

سلول‌بنیادی اسپرماتوگونیال نقطه آغاز اسپرماتوژنز در بیضه است. علیرغم اهمیت ویژه سلول‌های‌بنیادی اسپرماتوگونیال برای تولیدمثل مردان، اطلاعات کمی درمورد ویژگی‌های مورفولوژیکی یا بیوشیمیایی آن وجود دارد. این امر تا حدی ناشی از این واقعیت است که سلول‌های بنیادی اسپرماتوگونیال یک دسته سلولی بسیار کم جمعیت در بیضه هستند. هدف از مطالعه حاضر تجزیه و تحلیل مقایسه ای بیان ZBTB16 در سه گروه سلولی اسپرماتوگونی تمایزنیافته، تمایزیافته و فیبروبلاست ها بود. در این مطالعه‌تجربی، ما بیان ZBTB16 را با روش ایمونوسیتوشیمی آنالیز کردیم به طوریکه نتایج حاصله حکایت از بیان بالا در اسپرماتوگونی تمایزنیافته در مقایسه با سلول های جنسی تمایزیافته داشت؛ همینطور بیان منفی ZBTB16 در سلول های فیبروبلاست نشان داده شد. نتایج حاصل از پژوهش حاضر به عنوان پایه‌ای مفید برای سایر مطالعات پیشرفته در حوضه بیولوژی تولیدمثل مورد توجه خواهد بود.

کلمات‌کلیدی :سلول‌های جنسی تمایزیافته، سلول بنیادی اسپرماتوگونی، لوله اسپرم ساز، ZBTB16

ارائه پوستر : **حنانه محمدی نودهی**

شناسایی واریانت تعداد کپی با نرخ مثبت کاذب کاهش یافته از داده اگزوم از طریق بهینه سازی مراحل پیش پردازش و ساخت مجموعه نمونه مرجع

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تغییر در تعداد کپی بخش‌هایی از DNA، یکی از انواع تغییرات ساختاری در ژنوم است که باعث ایجاد تفاوت ژنتیکی و در برخی موارد بروز صفات متفاوت در میان افراد می‌شود. اندازه این تغییرات که منجر به برهم خوردن تعادل در اندازه ژنوم می‌شود، از ۵۰ جفت باز تا چندمگا جفت باز متغیر است. روشهای سنتی متداول عموما حساسیت و رزولوشن بالایی برای یافتن دقیق این وقایع ژنومی ندارند. در حالی‌که استفاده از توالی‌یابی نسل جدید، علاوه بر اینکه یافتن تغییرات کوچک در مقیاس یک نوکلئوتید را ممکن می‌سازد؛ از تکرارپذیری بالاتری برخوردار است. بنابراین برای یافتن CNVهای کوچکتر از ۱۰۰۰ جفت باز، استفاده از داده‌های توالی‌یابی نسل جدید که امروزه با هزینه اندکی بر روی نواحی اگزوم توالی یابی شده و در دسترس هستند، انتخاب مناسبی محسوب می‌شوند. با این حال چالش‌های مختلفی برای یافتن CNV ها از این داده‌ها نیز وجود دارد. یکی از مهمترین این چالش‌ها، تطابق کم میان نتایج بدست آمده از ابزارهای مختلف و همچنین تعداد بالای CNV مثبت کاذب است. این مشکل بعلت تاثیر مستقیم انواع نویز و بایاس روی سیگنال عمق خوانش، به عنوان اصلی‌ترین اطلاعات موجود برای یافتن CNV ها، ایجاد می‌شود. لذا یافتن راه حل‌هایی برای کاهش نرخ مثبت کاذب در شناسایی CNV از داده اگزوم و همچنین دستیابی به نتایج تکرارپذیر در نمونه‌های مختلف، هدف اصلی و ارزشمند پژوهش جاری خواهد بود. با توجه به اینکه در ابزارهای متنوع موجود جهت فراخوانی CNV روش‌های مختلف نرمالسازی داده و نحوه انتخاب مرجع تصمیم اهمیت به سزایی در عملکرد نهایی هر ابزار دارد، همین موضوع در پژوهش حاضر مورد توجه قرار گرفته است.

واژگان کلیدی: واریانت تعداد کپی، توالی‌یابی کل اگزوم، پیش‌پردازش، مجموعه مرجع، رزولوشن بالا