

∞ INFINITY

SCIENTIFIC ASSOCIATION OF MEDICAL LABORATORY SCIENCES

VARASTEGAN INSTITUTE FOR MEDICAL SCIENCES



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The first and only English student magazine for medical laboratory sciences

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Director-in-Charge

Years have passed since the first day the microscope was invented. Many days passed in a row, and slowly centrifuges, cell counters, and auto an-alyzers replaced manual and time-consuming methods and helped us get ac-curate results. We stayed, we fought COVID-19, and we are still strong and stable. We stayed and fixed our eyes on the screens, understood the patient's condition with our hearts, and made decisions with our intellect and knowl-edge. No machine could sacrifice its life to save another human life, and of course we sacrificed many lives. Many white and black days have passed, and now we look to the future with much more hope than before, and we are al-ways trying to help the lives of more of our fellows. In this student magazine, as the first specialized student magazine of medical laboratory sciences in the country, we intend to present the latest news, articles, and information related to our field to serious and interested audiences. Of course, in this way, we welcome your comments and suggestions, and we hope to be able to provide useful and efficient information. We hope that the infinite world of clinical laboratory science will accept this gift from us and lead us to bright horizons of success.

Yours faithfully

Mahoora Rahimi

Editor-in-Chief

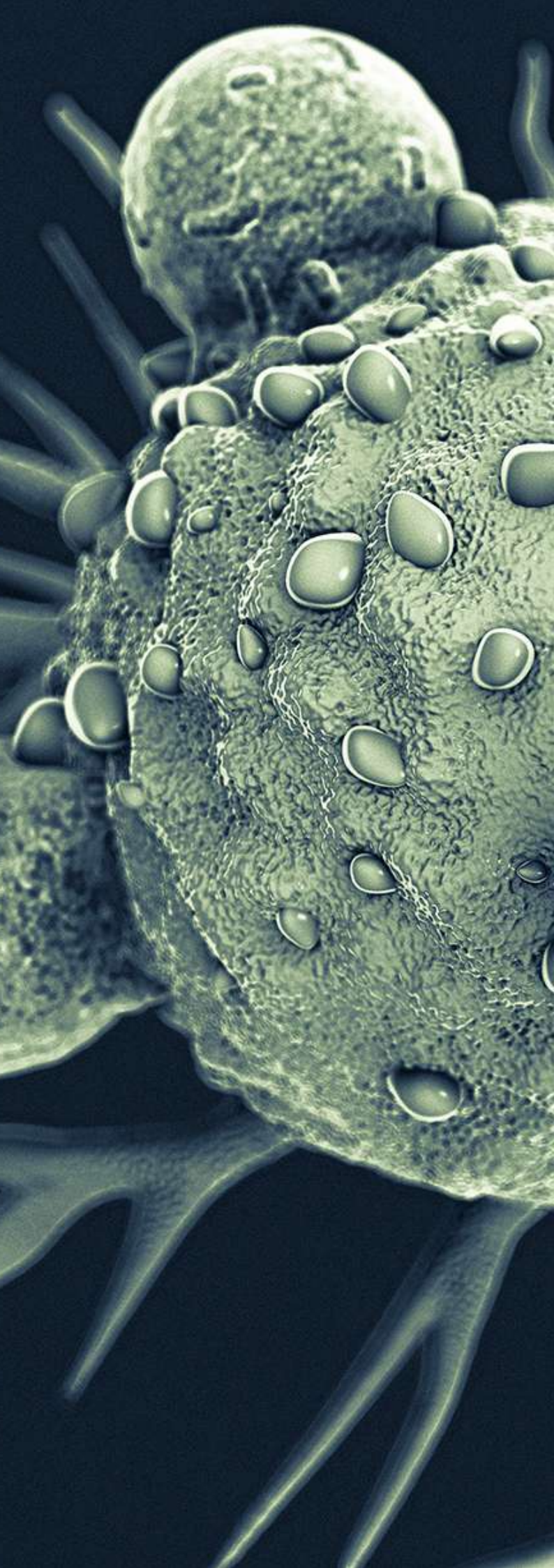
I am writing to express my interest in the publication of the first English student magazine for medical laboratory sciences in the country. The endless world of science requires some pieces of equipment for anyone who wants to enter and continue this journey more easily. Nowadays, learning English has proven to be one of the necessities for all people, regardless of the field in which they are studying or working. No matter what level you are at, the most significant thing is to learn how to begin and continue this way, whether you do it on your own or with an instructor. Our **team** made the decision to start a magazine, which might give motivation to all those who need to begin learning English and to those who like searching and writing academically in this language.

We would eagerly welcome all medical laboratory scientists across the country to join us and take part in any part of this publication they would like.

Kind regards

Arefeh Cheraghchi





Neo antigen Vaccine

IMMUNOTHERAPY

Immunotherapy utilizes methods and principles to target the increased or decreased activity of an organism's immune function and to fortify or weaken the responses of this system to reach the treatment goals. Through immunotherapy, the immune system's capability of recognizing, targeting, and removing tumor cells is reinforced. In comparison to the rest of cancer treatments, immunotherapy is more specific, individualized, and possess fewer side effects. This method is divided into two groups: active immunotherapy, which means using the body's immune system to get rid of cancer cells, and passive immunotherapy, which describes the acquiescence of antibodies, cytokines, or transformed immune cells that can directly target the tumor.

TUMOR VACCINE

Tumor vaccines that recognize the expressed proteins of specific cancer cells, suppress tumor cell growth, forestall cancer recurrence, and remove tumor cells that are left after treatment are one of the most notable active immunotherapy methods. Evoking immune responses against tumor-associated antigens (TAAs) or tumor-specific antigens (TSAs) and promoting the immune system's ability to invade cancer cells are the goals of cancer vaccines. These vaccines comprise nucleic acid, dendritic cell-based, tumor cell, and synthetic long peptide (SLP) vaccines.

NEOANTIGEN

Genetic instability of tumors ends in many gene mutations in both coding and non-coding regions. Neoantigens are non-autologous proteins that are produced by non-synonymous mutations in the genome of the tumor cell. TAAs are proteins that can be found on cancer cells and normal cells at the same time, though their expression on cancer cells is much higher than others. In contrast to TSAs, which are neoantigens emanating from somatic mutations, TAAs, for the reason of being normal host proteins, are subject to both central and peripheral tolerance mechanisms, so targeting them can lead to autoimmune toxicity. On the other hand, TSAs are only expressed on the surface of tumor cells; thus, these tumor antigens can be processed into an ideal, individualized vaccine for precise immunotherapy.

CHALLENGES

The neoantigen vaccine has had many positive re-

sults in clinical trials and has become popular among scientists in the field of immunotherapy. Nonetheless, some inhibitory factors in the production of this treatment exist.

The first obstacle is the low number of antigens. Between the thousands of antigens resulting from mutations in tumor cells, only a few possess the optimal criteria to be used in the development of a cancer vaccine. Insufficient screening methods is another problem that hopefully can be solved by improvements in bioinformatics technology, artificial intelligence, and machine learning. Also, the production of the neoantigen vaccine is long, and patients participating in the trial might not reach the end of treatment due to their short survival period. Also, laboratories feel great pressure as a result of this problem. Preparation and delivery methods, resolving the heterogeneity of the tumor, and the high costs of this process are the other issues that need to be carefully considered.

COMBINATION WITH OTHER THERAPIES

Monotherapy with the neoantigen vaccine has shown inadequate responses; therefore, researchers have experimented the mixture of other therapies with this novel one.

Checkpoint inhibition therapy includes using monoclonal antibodies such as anti-CTLA-4, anti-PD-1, and anti-PD-L1 to block checkpoints and stop the inhibition of T cell function by cancer cells. On one hand, administering the cancer vaccine boosts the number of T cells attacking tumor cells; on the other hand, the

more T cells are present, the more PD-L1 expression on the surface of tumor cells happens. Thus, the combination of immune checkpoint inhibition therapy and the neoantigen vaccine shows promising results.

Applying a cancer vaccine and adaptive T cell therapy have also shown acceptable consequences. CAR-T therapy has limited effects since the tumor's micro-environment blocks CAR-T cells. But scientists did more tests on mice with tumors and found out that the combination of neoantigen and CAR-T therapy could completely get rid of 60% of mouse tumors. This could be a really good treatment in the future.

Studies have shown that both chemotherapy and radiotherapy can raise the number of tumor antigens produced by tumor cells. Additionally, radiotherapy can increase the transportation of T cells into tumor tissue and the strength of specific anti-tumor immune responses. Chemotherapeutic drugs also enhance the anti-tumor activity of adoptive T cells, macrophages, and cancer vaccines. So, using these traditional treatments along with the neoantigen vaccine had positive outcomes.

CONCLUSIONS

Nonsynonymous mutations can result in neoantigen production in tumor cells. In comparison to TAAs, neoantigens are only expressed on the surface of tumor cells. They are not subject to central and peripheral tolerance mechanisms and have more immunogenicity as

well. Researchers are facing many problems in producing these vaccines, and solving those issues is necessary. As monotherapy did not show enough favorable effects, a combination of the neoantigen vaccine with other therapies is needed. More oncologic studies and a better understanding of tumor immunology, immune suppression, and escape mechanisms of tumor tissue can help us develop more efficient drugs.



Arefeh Cheraghchi

GRAVES' DISEASE



An autoimmune disorder termed Graves' disease leads to hyperthyroidism. Your thyroid gland produces an excessive amount of thyroid hormone when you have this disease. One of the most prevalent types of hyperthyroidism is Graves' disease.

Causes

Your immune system wrongly produces thyroid-stimulating immunoglobulins when you have Graves' disease rather than antibodies to specifically target an invader. These antibodies then go for the healthy thyroid cells in your own body. Scientists are aware that the capacity to produce antibodies against one's own healthy cells can be inherited. However, neither the cause nor the prognosis of Graves' disease have been established. Experts believe it's possible that your genes and a virus or other external trigger both play a part in its development.

Symptoms



• **Rapid heart rate (tachycardia)**



• **Sleep problems**



• **Weight loss**



• **Goiter**



• **Hand tremors**



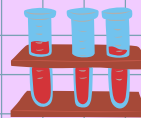
• **Irregular periods**



• **Heat sensitivity**

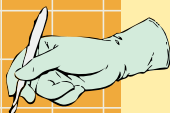
Diagnosis

- **Blood test**
- **Thyroid ultrasound**
- **Radioactive iodine uptake test**
- **Thyroid-stimulating hormone test**
- **Thyroid-stimulating immunoglobulin test**



Treatment

- **Antithyroid drugs**
- **Thyroid surgery**
- **Radioactive iodine therapy**



Zahra Akbarzadeh



Different Control of Energy Homeostasis between Men and Women



Obesity-related metabolic disorders are much less common in premenopausal women than in men.

However, in women, it increases dramatically after menopause. Obesity-related health risks depend on the location of adipose tissue. Adipose tissue distributed in the abdominal viscera is at a much higher risk of metabolic disorders than that distributed subcutaneously. There are clear gender differences in regional fat distribution, with women having more subcutaneous fat and men having more visceral fat. Men and women regulate energy homeostasis differently. Peripheral obesity and hormones such as leptin and insulin directly affect energy balance.

Sex Differences in Body Fat Distribution

As mentioned earlier, women, on average, have more fat under their skin. Men carry more fat into their internal organs. Gonadal steroids have been proposed as regulators of fat distribution. Men have less estrogen and, on average, less total fat, distributed in the center or abdomen. On the other hand, premenopausal women have more total fat and more subcutaneous fat distribution in the buttocks and thighs. Intra-abdominal fat differs inversely with estrogen levels. After menopause and estrogen decline, women develop increased intra-abdominal obesity. But this is not true about women on estrogen replacement therapy, suggesting a specific role for estrogen in limiting intra-abdominal fat mass. Androgens promote the accumulation of abdominal fat. Most women with polycystic ovary syndrome (PCOS), a hyperandrogenic condition, have increased

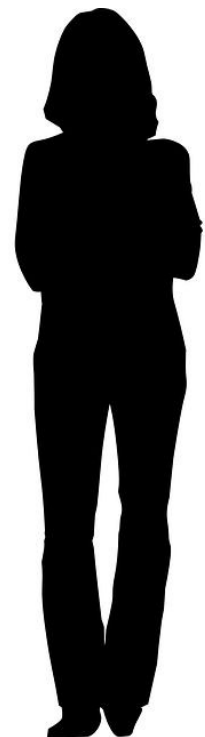
abdominal fat.

Abdominal adipose tissue

Intraperitoneal adipose tissue is metabolically and functionally distinct from subcutaneous adipose tissue. Intraperitoneal adipose tissue has adipogenic, metabolic, proatherogenic, and prothrombotic properties. Intraperitoneal fat has a relatively higher number of capillaries and efferent sympathetic axons per unit volume than subcutaneous fat. Weight loss is characterized by an initial loss of intra-abdominal but not subcutaneous adipose tissue. This is because intraperitoneal adipocytes are more metabolically active. Equal amounts of visceral and subcutaneous fat reduction do not have the same net effect on glucose homeostasis. Surgical removal of intra-abdominal adipose tissue lowers insulin and glucose levels in humans and prevents the age-related development of insulin resistance and diabetes. For example, visceral adipose tissue in men is more active than in women, contributing to gender disparities in obesity-related metabolic and cardiovascular disease.

Subcutaneous fat

Subcutaneous fat, which is widely distributed under the skin, is relatively poorly innervated and vascularized and has a larger average cell diameter than intraperito-



neal adipocytes. Lipid deposition is a favorable process that allows efficient storage of maximal calories per unit volume of tissue. Adipose tissue is designed to absorb fatty acids and store extra calories. The ability to store lipids in subcutaneous reservoirs is key to addressing

subcutaneous adipose tissue are lower in women, but uptake is much higher in premenopausal women than in men. Scientists used fatty acid tracers in food and then biopsied the adipose tissue and found that females had a higher proportion of dietary fat stored in subcutane-

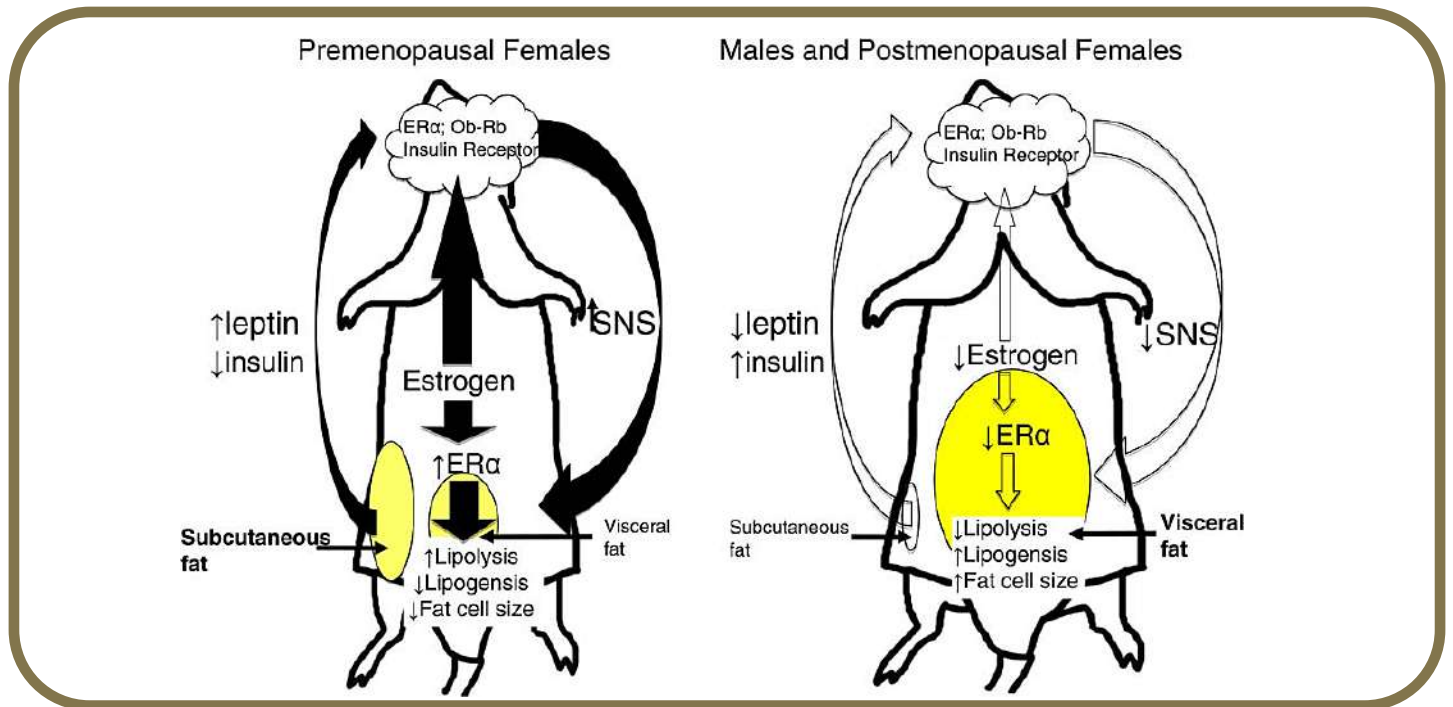


Figure 1. A potential model for how sex hormones and obesity signals interact to regulate body fat distribution. We propose that the female steroid estrogen regulates body fat distribution. Women carry more fat subcutaneously, whereas men with low estrogen levels carry more fat into the internal organs. Estrogen receptors (ER) are expressed in adipose tissue and the hypothalamus.

hunger and calorie restriction, especially in women. Women mobilize the adipose tissue stored in this depot to increase the body's caloric needs during lactation and breastfeeding. Gender differences exist in the release and uptake of fatty acids in subcutaneous adipose tissue. Females have more anti-lipolytic $\alpha 2$ -adrenergic receptors in the subcutaneous region of the buttocks and thighs. In contrast to what was previously reported for intraperitoneal adipose tissue, catecholamine-mediated lipolytic activity and free fatty acid release from

ous and thigh adipose tissue than males. Subcutaneous adipose tissue releases less and absorbs more free fatty acids, resulting in more fat being deposited in the subcutaneous area in women and contributing to regional differences in fat distribution between men and women.

Why do males store visceral fat?

A key question in understanding these important biological differences is the underlying reason why men and women store extra calories in different places. Visceral fat can be mobilized more quickly to meet

short-term, energetic challenges. Therefore, one of the reasons for storing fat in visceral supplies is to make it more available for certain intermittent activities. When men are more responsible for hunting, foraging, or immediate protection, it makes sense to dump the stored calories into more active fats in the shorter timeframes required for these activities.

Why do females store subcutaneous fat?

Given the low rate of lipolysis in subcutaneous adipose tissue, it is much better suited to address chronic metabolic challenges such as those encountered during pregnancy and lactation in women. Female rats gain weight during early pregnancy, and this occurs disproportionately in subcutaneous adipose tissue. Such subcutaneous fat accumulation facilitates a woman's ability to cope with the tremendous chronic metabolic challenges associated with pregnancy and breastfeeding.

Conclusions

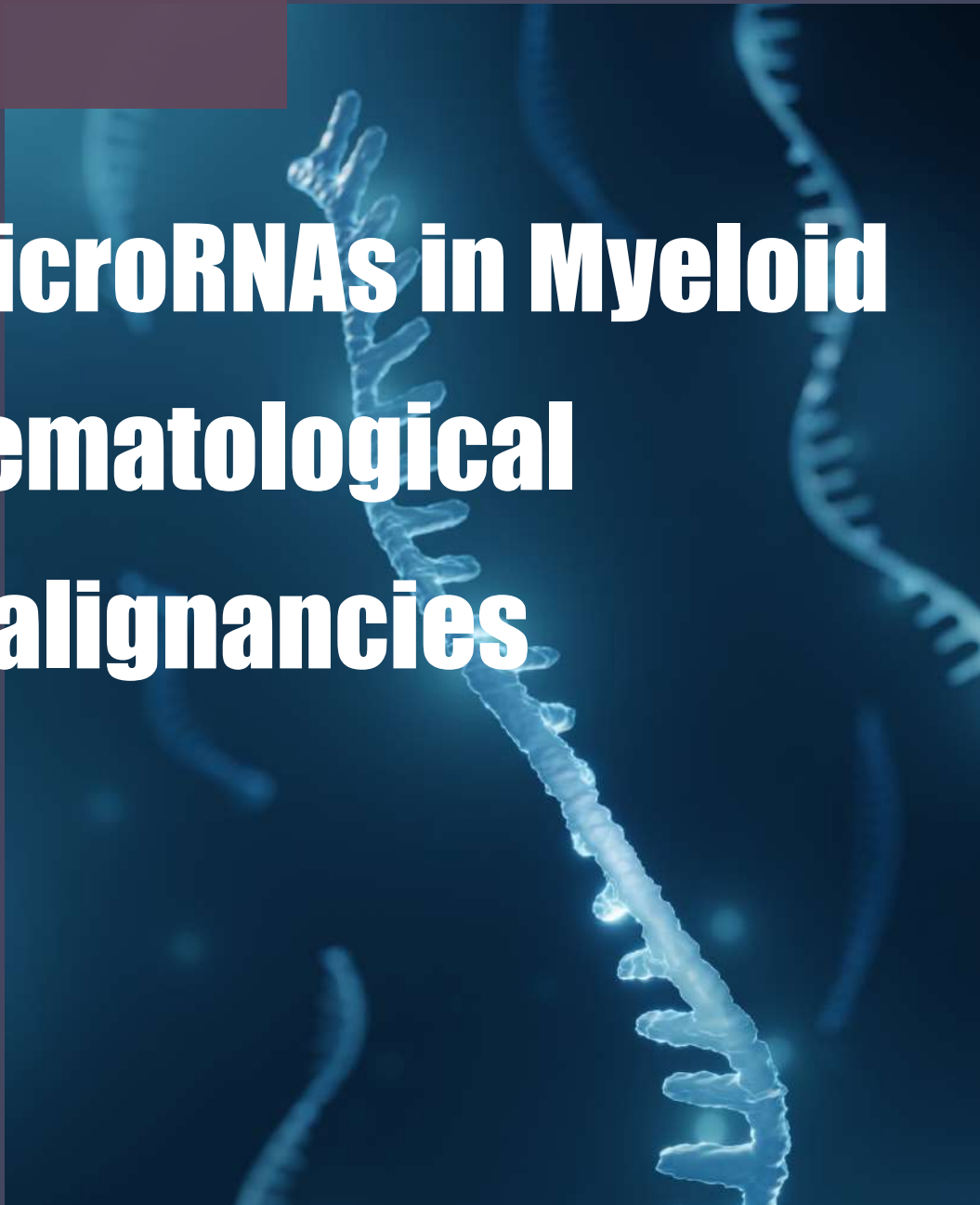
In conclusion, the gender-specific distribution of body fat has important implications for how obesity affects various co-occurring disorders. Widespread evidence links these differences in body fat distribution to gonadal steroids, which also have important effects on regulating energy balance. As a result, there also appear to be important differences in the systems that regulate energy balance and body weight in men and women. Females tend to regulate energy expenditure, while males tend to regulate the energy intake side of the energy balance equation. Men and women respond

differently to obesity signals, with women being more sensitive to leptin and men being more sensitive to insulin. There appear to be similarities in the intracellular signaling pathways activated by leptin, insulin, and estrogen. Leptin and insulin signaling converge on the phosphoinositide-3-kinase (PI3K) pathway, and their actions depend on PI3K activation. Estrogen also activates the PI3K signaling cascade. Further research is needed to better understand the interplay between insulin, leptin, and estrogen signaling at the molecular level.

1. Shi H, Seeley RJ, Clegg DJ. Sexual differences in the control of energy homeostasis. *Frontiers in neuroendocrinology*. 2009 Aug 1;30(3):396-404.
2. Roichman A, Elhanati S, Aon MA, Abramovich I, Di Francesco A, Shahar Y, Avivi MY, Shurgi M, Rubinstein A, Wiesner Y, Shuchami A. Restoration of energy homeostasis by SIRT6 extends healthy lifespan. *Nature communications*. 2021 May 28;12(1):3208.
3. Quirós Cognuck S, Reis WL, Silva M, Debarba LK, Mecawi AS, de Paula FJ, Rodrigues Franci C, Elias LL, Antunes-Rodrigues J. Sex differences in body composition, metabolism-related hormones, and energy homeostasis during aging in Wistar rats. *Physiological Reports*. 2020 Oct;8(20):e14597.



Negin Najmi



MicroRNAs in Myeloid Hematological Malignancies

Tiny RNA molecules that do not undergo protein translation are called ncRNAs. The human genome is made up of around 3 billion base pairs of DNA, of which 5–10% are stably transcribed, although less than 2% of the genome is made up of protein-coding genes. Non-coding RNAs, or ncRNAs, are produced from the remaining 3–8% of the genome. Based on their roles, ncRNAs are split into two groups: housekeeping and regulatory, the latter of which includes miRNAs, circRNAs, and lncRNAs. Regulatory ncRNAs have a significant role in the transcription and translation of genes. They are essential contributors to physiological and pathological processes including angiogenesis, inflammation, and cell differentiation. MicroRNAs (miRNAs) are 19–24 nucleotide non-coding RNAs that are present in all eukaryotes and regulate the expression of a variety of genes involved in hematopoietic stem cell commitment, differentiation, and cancer. A wide range of acute and chronic diseases that result from the clonal transformation of a hematopoietic stem cell are referred to as myeloid malignancies. Myeloid cancers may be distinguished by certain genetic anomalies, such as the translocation t(9;22) that characterizes chronic myeloid leukemia. Recent research has clarified the physiological functions of miRNAs as important hematopoiesis regulators. The finding that key cell machinery may be fine-tuned by miRNAs raised the prospect that mutations in the miRNAs' gene

sequences may lead to the development of cancer. It is interesting to note that miRNA function, as oncogenes or tumor suppressors, depends only on the target genes, although it may also be associated with the particular environment of normal and tumor cells. Recent research supports the idea that the expression of miRNAs may be used to predict therapy response or prognosis in individuals with hematological malignancies.

ACUTE MYELOID LEUKEMIA (AML)

The aggressive hematological malignancy known as acute myeloid leukemia (AML) is characterized by aberrant myeloid cell proliferation and differentiation. The majority of patients still relapse and pass away after remission, and the prognosis is still not optimal despite an expanding array of therapeutic choices. To create more efficient monitoring and treatment programs, novel biomarkers for AML diagnosis, prognostication, and therapeutic targets must be investigated. Noncoding RNAs (ncRNAs) have opened up new avenues for the diagnosis, prognosis, and therapy of AML. AML is one of the primary hematological malignancies, and there is growing evidence that miRNAs, circRNAs, and lncRNAs actively contribute to its development. The most popular diagnostic method for AML is the molecular and cytogenetic criteria as they are currently specified by the 2016 WHO. Each AML subtype appears to have a distinctive miRNA profile that sets it apart from others. For instance, Chen et al. found that

MLL-rearranged AML patients had elevated levels of the carcinogenic miRNA miR-9. MiR-9 expression inhibition may drastically lower cell growth and viability and increase apoptosis. Additionally connected to the morphological subtypes of AML is miRNA expression. AML leukemogenesis is facilitated by changes in the expression of downstream genes caused by variations in miRNA levels. As an oncogenic miRNA, miR-155, for instance, may contribute to the pathogenesis of AML by targeting SHIP1 and suppressing the expression of the transcription factor PU.1. NF- κ B, whose activity was in part regulated by the NEDD8-dependent ubiquitin ligases, was in charge of regulating this miRNA. MiRNAs have become important participants in the gene regulation that underlies certain characteristics of AMLs. To fully comprehend the complicated mechanisms of malignant AML transformation, miRNAs and their regulatory signaling pathways must be considered alongside classic protein-coding oncogenes and tumor suppressors. We are conscious of how shallow and constrained our systems biology knowledge of the miRNA regulatory networks is right now. The expression, function, and regulation mechanisms of miRNAs will be further clarified via in-depth research, which will lead to the development of potential therapeutic options for AML.

MYELOYDYSPLASTIC SYNDROMES

Myelodysplastic syndromes (MDS), which can come before overt AML, are frequently thought to be pre-leukemic disorders. With the advent of next-generation

sequencing (NGS), it has recently become possible to demonstrate the molecular heterogeneity of MDS, offering a greater understanding of its pathophysiology and explaining the various clinical outcomes among afflicted individuals. Studies investigating the expression of distinct miRNA signatures in MDS failed, in some cases, to do what has been seen in AML. However, these findings might be connected to studies analyzing the miRNA profiles of MDS patients using tumor cells derived from unpurified stem cells.

CHRONIC MYELOID LEUKEMIA (CML)

A myeloproliferative illness derived from hematopoietic stem cells (HSCs), chronic myeloid leukemia (CML) is characterized by excessive cell proliferation and aberrant differentiation of the myeloid progenitors. The Philadelphia chromosome (Ph), which is created when the long arms of chromosomes 9 and 22 are translocated, is the distinguishing feature of CML. The t(9;22) mutation results in the production of the oncoprotein BCR-ABL1, a constitutively active tyrosine kinase that grants the hematopoietic progenitors growth factor-independent proliferation. MiR-150 and miR-146 were shown to be elevated in pa-

tients with newly diagnosed CML and after two weeks of therapy, but miR-142-3p and miR-199b-5p were found to be lowered at the same time point compared with pre-treatment levels. Furthermore, blasts from patients with overt CB-CML showed downregulation of miR-150.

MYELOPROLIFERATIVE NEOPLASMA (MPD)

Polycythemia vera, essential thrombocythemia, and primary myelofibrosis are examples of myeloproliferative neoplasms (MPD). Primary myelofibrosis and essential thrombocythemia have been linked to thrombopoietin receptor (MPL) mutations, which cause constitutive activation of the Janus kinase 2 (JAK2) pathway. Compared to stable levels in platelets in healthy people, miR-28 is overexpressed in patients with MPN. It has been suggested that MPL and other proteins necessary for megakaryocyte development are the targets of miR-28's activity. Additionally, terminal differentiation was inhibited by the ectopic expression of miR-28 transfected megakaryocytes derived from CD34. The mechanisms by which miRNAs contribute to the development of myeloproliferative neoplasms are clarified by these findings.

CONCLUSIONS

The crucial role that miRNAs play in myeloid malignancies, such as acute myeloid leukemia, myelodysplastic syndrome, and myeloproliferative neoplasms, has been highlighted by several researchers over the past ten years. MiRNAs can interfere with many pathways involved in the cell cycle, tumor development, and apoptosis. They can also operate as tumor suppressors or oncogenes. It is interesting to note that the expression patterns of various miRNAs vary among leukemic subtypes. The discovery that miRNA expression patterns may predict the prognosis of myeloid malignancies or chemosensitivity to certain drugs suggests that miRNAs be included in the prognostication scheme of these wide-ranging illnesses. The safety and effectiveness of compounds that suppress miRNAs have shown encouraging outcomes in pre-clinical models and in vitro research. To validate the prognostic and predictive abilities of miRNAs and to evaluate their inhibitory compounds, more research and clinical trials are required.



Mahoora Rahimi



Bacterial ghosts

Bacterial ghosts (BGs) are produced by controlled expression of cloned gene E, this cloning will cause forming a lysis tunnel structure within the envelope of the living Gram-negative bacteria. We can describe BGs as bacterial shells with pores. BGs have been used as vaccine delivery systems or as its adjuvants worldwide. They have an inherent immunogenicity, because of the condition of bacterial cell membranes, which enables targeted drug delivery and controlled release. The development of different types of BGs has been facilitated by advances in genetic engineering and chemical biotechnology, which will be important in immobilized enzyme technology, agriculture, and medicine. Using genetic engineering for preparing these novel delivery systems, can help to retain all the structural antigens expressed by pathogenic bacteria, which causes humoral and cellular immune responses strongly and effectively. The structure of BGs contains pathogen-associated molecular patterns (PAMPs), such as lipopolysaccharide (LPS), lipoprotein (LPP), peptidoglycan (PGN), and fimbriae, among others, which are highly conserved structures on the outer cell bacterial wall. Generally, pathogenic serotypes of Bacterial ghosts are well preserved, and high immunogenicity can be provided by high concentrations of BGs. Bacterial ghosts, as a natural bioactive delivery system, can be applied in different ways, including mucosal administration (nasal cavity, gastrointestinal tract, and ocular administration) and intravenous injection. However, clinical applications of BGs are associated with many challenges. Also, investigations should be held to find a way to seal leaking pores, and the stability, as well as mechanisms of the combination of various drugs or antigens with BGs, should also be investigated.

Zahra Mohammadi





Childhood Traumas effects on Genome function in Adulthood (An Epigenetic Matter)

It has long been known that childhood trauma can have a lasting impact on an individual's mental and physical health. Recently, researchers have shown that these traumas can also have a significant effect on genes function in adulthood. Childhood traumas such as sexual abuse, physical or mental maltreatment, lack of adequate maternal care, emotional abuse, war or natural disaster, financial difficulties or poverty, etc.

can affect gene expression but do not change the genome sequences. Traumas impact via transcriptional, post-transcriptional, translational, and post-translational mechanisms such as DNA methylation, DNA hydroxymethylation, non-coding RNA expression, and histone modifications. The most commonly studied epigenetic mark is DNA methylation (DNAm), which refers to the addition of a methyl group (-CH₃) onto a cytosine base followed by a guanine base (i.e., CpG site). It prevents gene transcription in two ways: methylated CpG sites impede the binding of transcriptional activators and promote the binding of transcriptional repressors. DNA methylation causes various impacts, such as:

Acceleration of epigenetic age (which is the natural decline in tissue and cellular integrity, shifts in cellular activity, cellular senescence, and changes in normal physiological function over the lifespan and is associated with frailty, cancer, diabetes, cardiovascular diseases, dementia, and mortality risk).

- Overweight (increased waist circumference)
- Asthma

Metabolic syndrome (which is characterized by at least three of five related cardiometabolic traits: hypertension, insulin resistance or hyperglycemia, raised triglycerides, low high-density lipoprotein, and central obesity)

- Substance use
- Mental disorders (depression, anxiety, PTSD, BPD, bipolar, and schizophrenia)

Learning and memory

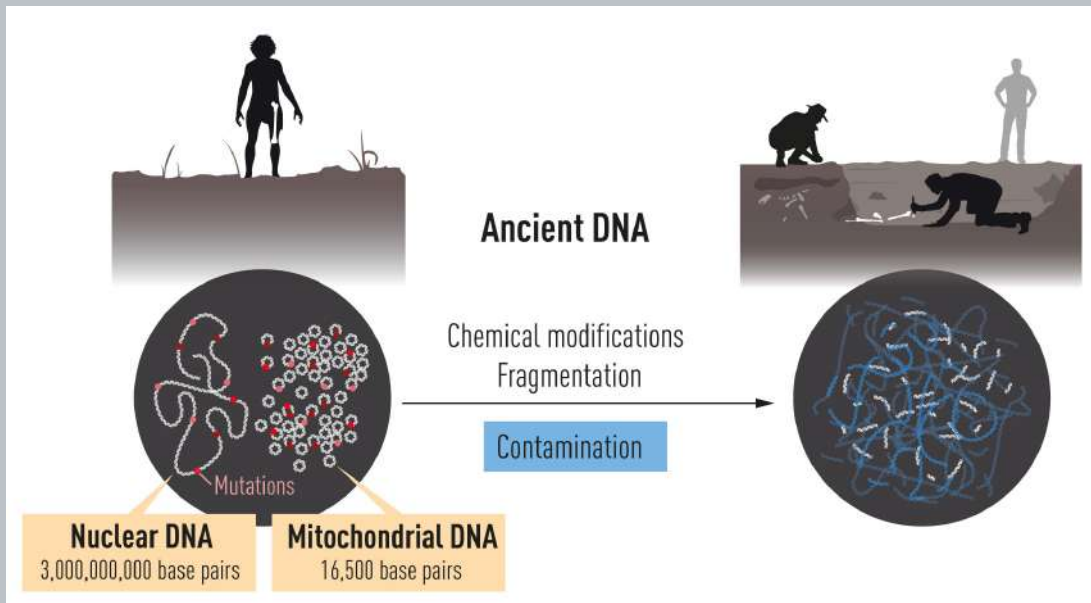
Despite the fact that the change is altering cellular phenotypes by gene expression but not the genome itself, some studies showed that the changes are able to be transferred through cell division, cause a persistent change in gene activity, and make stable alterations in biological processes. Numerous studies also mention that it is intergenerationally biologically embedded, and because it only occurs in male offspring, it is claimed that it's a sex-linked factor. In conclusion, it is important to recognize that these changes can be prevented by early interventions for kids. And we can also use this knowledge to help those who have already experienced childhood adversity by developing treatments targeting the underlying gene activity changes mentioned. But we should not forget that there is a long way ahead and that more research is needed on this subject.





**“The 2022 Nobel Prize in Physiology or Medicine to Svante Pääbo for:
Evolution of the Human Species and Discoveries about
the Extinct Hominin Genome**

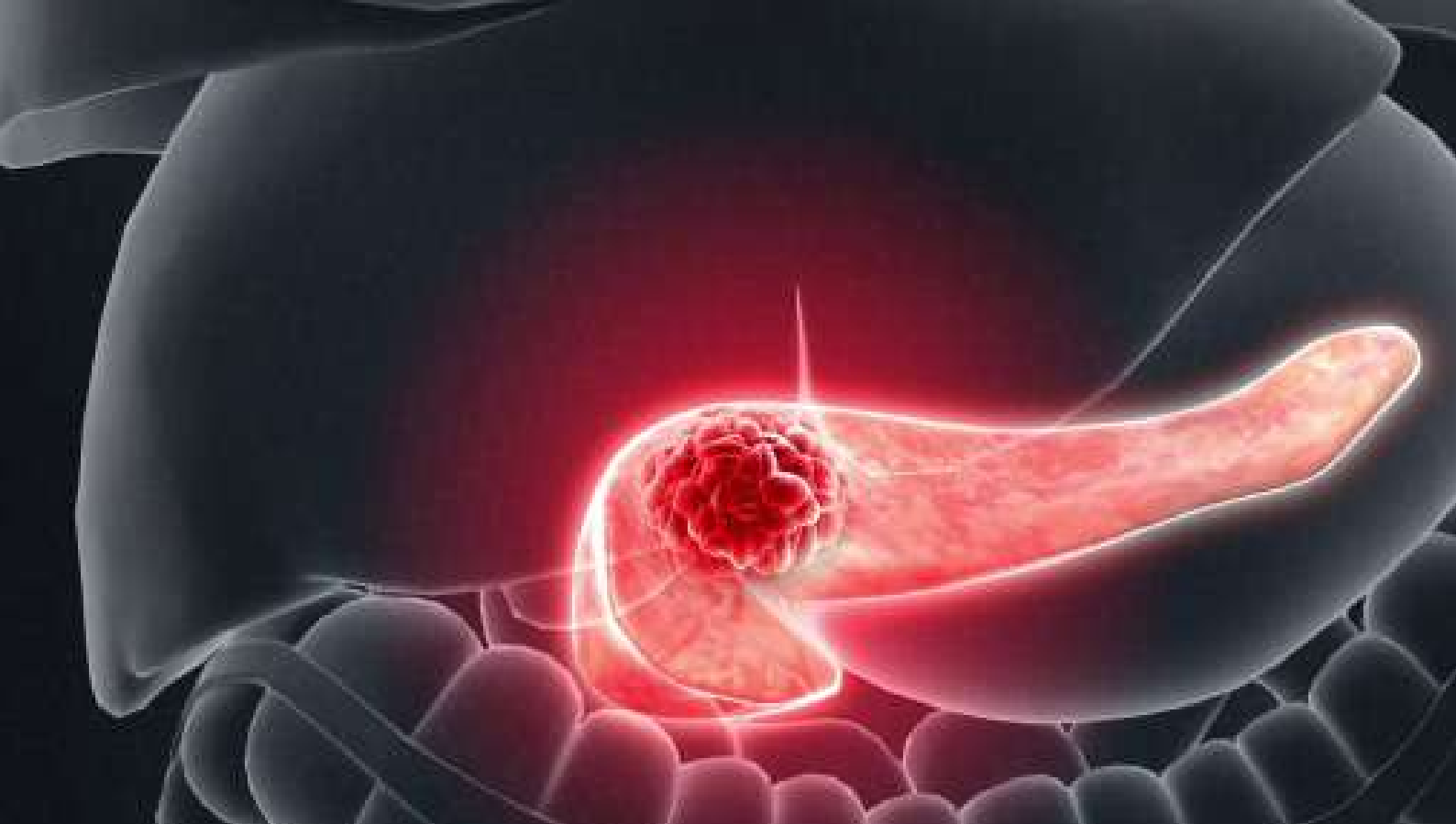
The 2022 Nobel Prize in Physiology or Medicine goes to Svante Pääbo for his work on the genomes of extinct hominins and the development of mankind. The history of humanity has always piqued interest. What is our history, and what connections do we have to those who came before us? What distinguishes *Homo sapiens* from other hominins? By doing ground-breaking research, Svante Pääbo was able to sequence the DNA of the extinct Neanderthal, a cousin of modern humans. The relationship between *Homo sapiens* and extinct hominins has long been a topic of intense study. Paleontology and archeology are extremely useful in studies of human evolution. Our ancient history can be more precisely investigated thanks to modern DNA technologies.



However, it was long debated whether it would be viable to analyze archaic DNA from extinct hominin species due to the significant technical difficulties caused by DNA deterioration over tens of thousands of years as well as pollution by current humans and bacteria. Svante Pääbo obtained the genomic sequence of the Neanderthal, the closest extinct cousin of ours, thanks to considerable technological advancements that set new, strict standards in this difficult field. His astounding discovery of the Denisova, another extinct human, which was made exclusively from genomic information acquired from a little finger bone fragment, came next. According to Svante Pääbo's research, *Homo sapiens* interbred with Neanderthals and Denisovans throughout times of coexistence, resulting in the introduction of ancient DNA into modern people. In a study area that is now quite dynamic, striking examples of ancient gene variations that affect the physiology of modern people have already been documented. Humans today still benefit physiologically from this ancient gene flow because it influences, for example, how our immune systems respond to illnesses. Pääbo's ground-breaking discovery provided a fresh window into our evolutionary history, showing unanticipated complexity in the development and hybridization of prehistoric hominins and establishing the foundation for a greater comprehension of the genetic characteristics that set humans apart from other species.



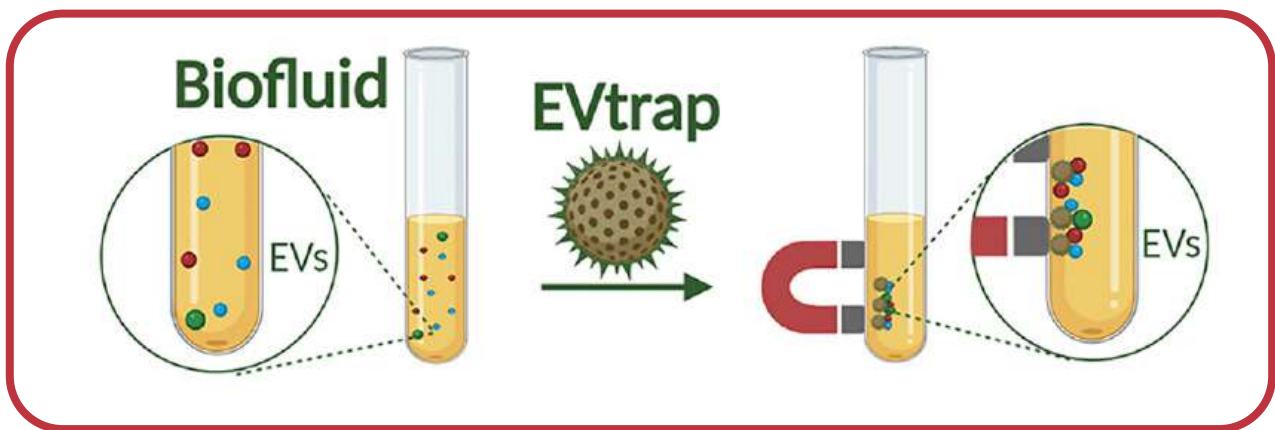
Mahoora Rahimi



Early Pancreatic Cancer Detection in High-Risk Patients Made Possible by AI-Powered Blood Test

Oftentimes, pancreatic cancer, one of the deadliest cancers, is discovered too late for effective therapy. Type 2 diabetes patients have an eight-fold increased risk of pancreatic cancer compared to the general population. Early identification and diagnosis can greatly increase the odds of a successful course of treatment and long-term survival because pancreatic cancer is anticipated to overtake lung cancer by 2030 as the second-biggest cause of cancer deaths. A quick DNA-based blood test can now detect pancreatic cancer in its earliest stages in those who are at high risk for the disease, such as those who have just been diagnosed with type 2 diabetes and are 50 years of age or older.

The Avantect Pancreatic Cancer Test from ClearNote Health (San Diego, CA, USA) measures the biomarker 5-hydroxymethylcytosine (5hmC) with a simple blood draw to identify early-stage pancreatic cancer. The test makes use of ClearNote's epigenomic platform, which keeps track of ongoing biological processes in tumors at the start of cancer development. The exclusive, automated, 5 hmC-based epigenomic approach targets a subset of dynamically demethylated bases to enrich DNA fragments using 5 hmC labeling. This approach makes it possible to quickly and precisely assess biological processes related to gene expression and regulation, which are essential for the growth of cancer. According to recent research, the Avantect test is very effective in identifying pancreatic cancer in high-risk patients, such as those who have just been given a type 2 diabetes diagnosis. Based on 2,150 patient samples, the case-control validation research demonstrated high specificity (96.9%) and early-stage (Stage I/II) sensitivity (68.3%). These results support the use of ClearNote's epigenomic platform for accurately detecting cancer presence in those who are more likely to develop pancreatic cancer, thereby enabling early disease identification and management. In addition to powerful machine learning algorithms, a novel early detection method incorporates fragmentomics, genetic changes, and epigenomics. The ability to identify pancreatic tumors at early, curable stages when longer-term patient survival is still achievable allows us to provide doctors with an early detection test that can be used to guide patient care recommendations.



Mahoora Rahimi

References

Neoantigen Vaccine

1. Zhang Z, Lu M, Qin Y, Gao W, Tao L, Su W, Zhong J. Neoantigen: A new breakthrough in tumor immunotherapy. *Frontiers in Immunology*. 2021 Apr 16;12:672356.
2. Peng M, Mo Y, Wang Y, Wu P, Zhang Y, Xiong F, Guo C, Wu X, Li Y, Li X, Li G. Neoantigen vaccine: an emerging tumor immunotherapy. *Molecular cancer*. 2019 Dec;18(1):1-4.

Different Control of Energy Homeostasis between Men and Women

1. Shi H, Seeley RJ, Clegg DJ. Sexual differences in the control of energy homeostasis. *Frontiers in neuroendocrinology*. 2009 Aug 1;30(3):396-404.
2. Roichman A, Elhanati S, Aon MA, Abramovich I, Di Francesco A, Shahar Y, Avivi MY, Shurgi M, Rubinstein A, Wisner Y, Shuchami A. Restoration of energy homeostasis by SIRT6 extends healthy lifespan. *Nature communications*. 2021 May 28;12(1):3208.
3. Quirós Cognuck S, Reis WL, Silva M, Debarba LK, Mecawi AS, de Paula FJ, Rodrigues Franci C, Elias LL, Antunes-Rodrigues J. Sex differences in body composition, metabolism-related hormones, and energy homeostasis during aging in Wistar rats. *Physiological Reports*. 2020 Oct;8(20):e14597.

MicroRNAs in Myeloid Hematological Malignancies

1. Neaga A, Bagacean C, Tempescul A, Jimbu L, Mesaros O, Blag C, Tomuleasa C, Bocsan C, Gaman M, Zdrenghia M. MicroRNAs Associated With a Good Prognosis of Acute Myeloid Leukemia and Their Effect on Macrophage Polarization. *Front Immunol*. 2021 Jan 15;11:582915. doi: 10.3389/fimmu.2020.582915. PMID: 33519805; PMCID: PMC7845488.

2. Liu, Y., Cheng, Z., Pang, Y. et al. Role of microRNAs, circRNAs and long noncoding RNAs in acute myeloid leukemia. *J Hematol Oncol* 12, 51 (2019). <https://doi.org/10.1186/s13045-019-0734-5>
3. Ciccone M, Calin GA. MicroRNAs in Myeloid Hematological Malignancies. *Curr Genomics*. 2015 Oct;16(5):336-48. doi: 10.2174/138920291605150710122815. PMID: 27047254; PMCID: PMC4763972.
4. Liao, Qiong, Bingping Wang, Xia Li, and Guosheng Jiang. "miRNAs in acute myeloid leukemia". *Oncotarget [Online]* 8, no. 2 (2017).
5. Zuo Z., Maiti S., Hu S., Loghavi S., Calin G.A., Garcia-Manero G., Kantarjian H.M., Medeiros L.J., Cooper L.J., Bueso-Ramos C.E. Plasma circulating-microRNA profiles are useful for assessing prognosis in patients with cytogenetically normal myelodysplastic syndromes. *Mod. Pathol*. 2015;28(3):373-382. doi: 10.1038/modpathol.2014.108.
6. Pardanani A.D., Levine R.L., Lasho T., Pikman Y., Mesa R.A., Wadleigh M., Steensma D.P., Elliott M.A., Wolanskyj A.P., Hogan W.J., McClure R.F., Litzow M.R., Gilliland D.G., Tefferi A. MPL515 mutations in myeloproliferative and other myeloid disorders: a study of 1182 patients. *Blood*. 2006;108(10):3472-3476. doi: 10.1182/blood-2006-04-018879.

Bacterial Ghosts

1. Peng, R., et al., Macrophage-based therapies for atherosclerosis management. *Journal of Immunology Research*, 2020. 2020.
2. Sun, D., et al., Advances in refunctionalization of erythrocyte-based nanomedicine for enhancing cancer-targeted drug delivery. *Theranostics*, 2019. 9(23): p. 6885.

3. Moghimipour, E., et al., Bacteria and Archaea: A new era of cancer therapy. *Journal of Controlled Release*, 2021. 338: p. 1-7.
4. Ding, C., et al., Targeting IL-6 in the treatment of inflammatory and autoimmune diseases. *Expert opinion on investigational drugs*, 2009. 18(10): p. 1457-1466.
5. Holay, M., et al., Bacteria-inspired nanomedicine. *ACS Applied Bio Materials*, 2020. 4(5): p. 3830-3848.
6. Chen, Haojie, Hao Ji, Xiangjun Kong, Pengyu Lei, Qinsi Yang, Wei Wu, Libo Jin, and Da Sun. «Bacterial Ghosts-Based Vaccine and Drug Delivery Systems.» *Pharmaceutics* 13, no. 11 (2021): 1892.

Childhood Traumas Effects on Genome Function in Adulthood

1. Carvalho, C.M., et al., Hyperarousal Symptom Severity in Women with Posttraumatic Stress Disorder Might Be Associated with LINE-1 Hypomethylation in Childhood Sexual Abuse Victims. *Complex Psychiatry*, 2023. 9(1-4): p. 44-56.
2. Čater, M. and G. Majdič, How early maternal deprivation changes the brain and behavior? *Eur J Neurosci*, 2022. 55(9-10): p. 2058-2075.
3. Chubar, V., et al., Mild daily stress, in interaction with NR3C1 DNA methylation levels, is linked to alterations in the HPA axis and ANS response to acute stress in early adolescents. *Psychoneuroendocrinology*, 2023. 150: p. 106045.
4. Comtois-Cabana, M., et al., Association between child maltreatment and depressive symptoms in emerging adulthood: The mediating and moderating roles of DNA methylation. *PLoS One*, 2023. 18(1): p. e0280203.
5. Cuevas, A.G., F.D. Mann, and R.F. Krueger, The weight of childhood adversity: evidence that childhood adversity moderates the impact of genetic risk on waist circumference in adulthood. *Int J Obes (Lond)*, 2022. 46(10): p. 1875-1882.
6. Dye, C.K., et al., Mother's childhood adversity is associated with accelerated epigenetic

aging in pregnancy and in male newborns. *bioRxiv*, 2023.

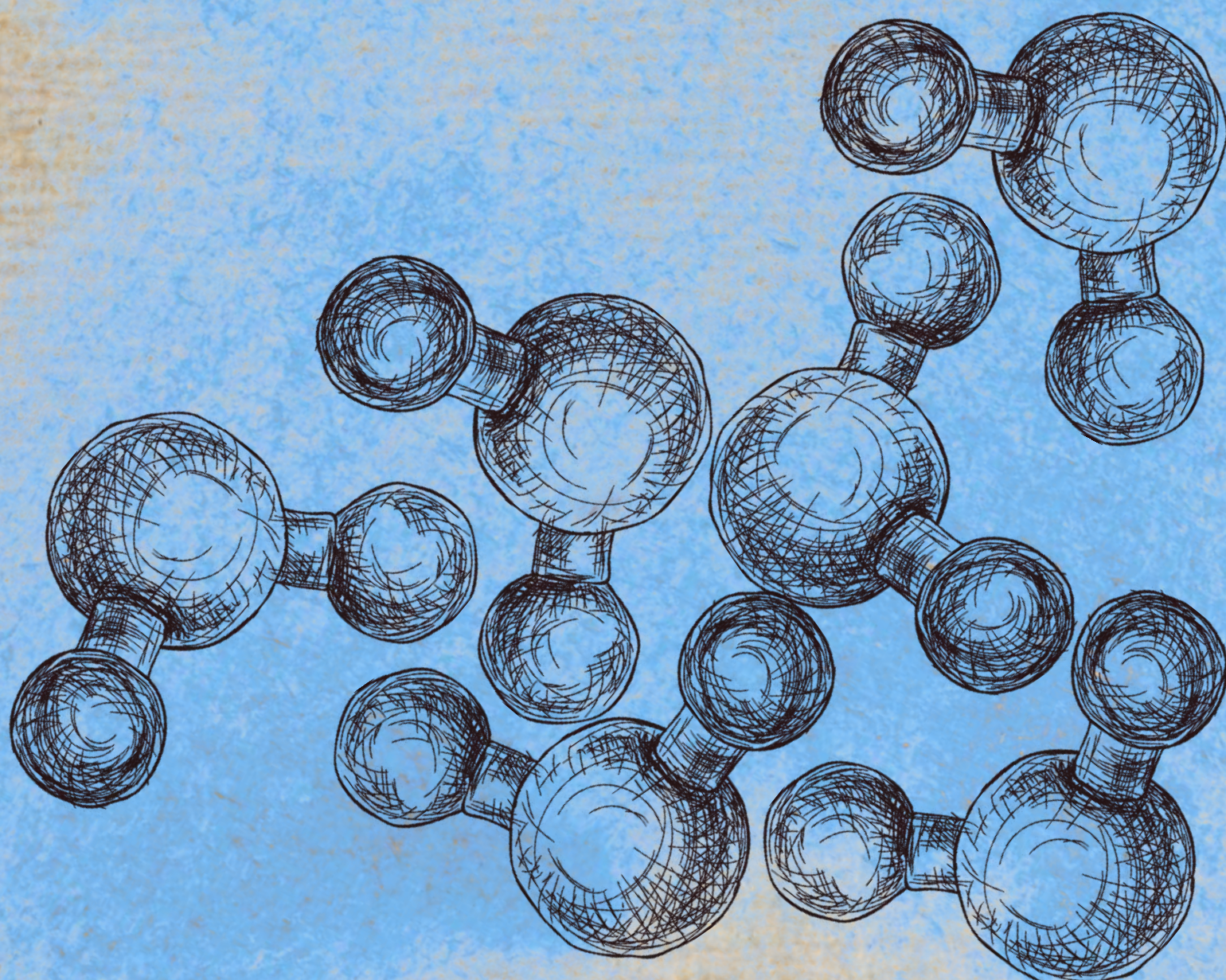
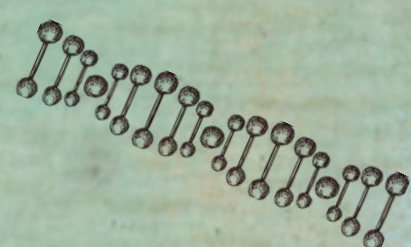
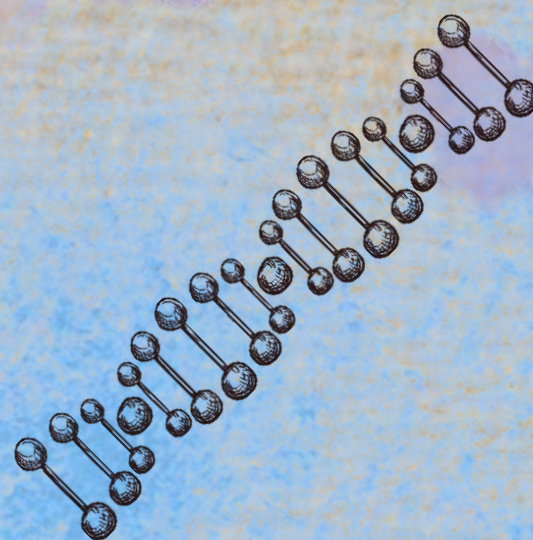
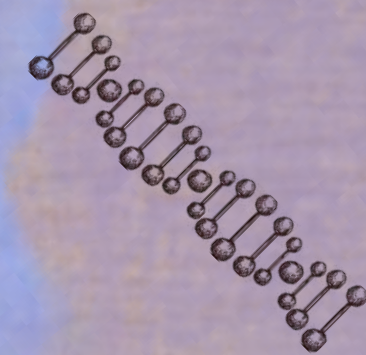
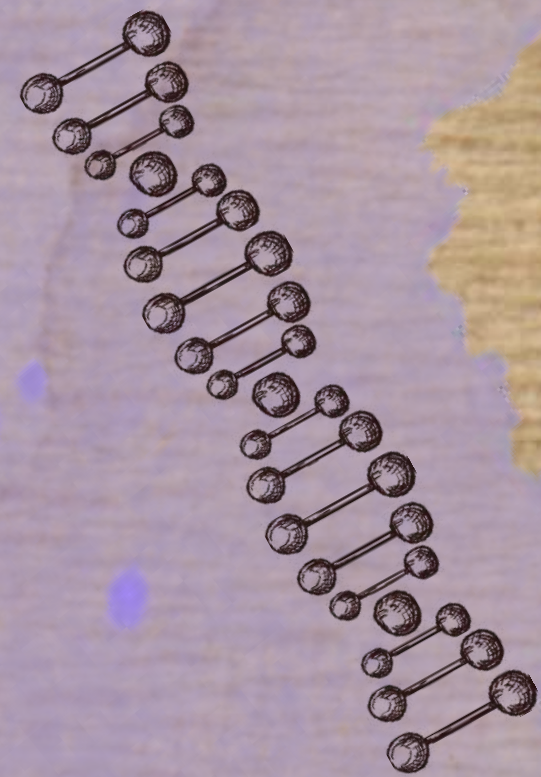
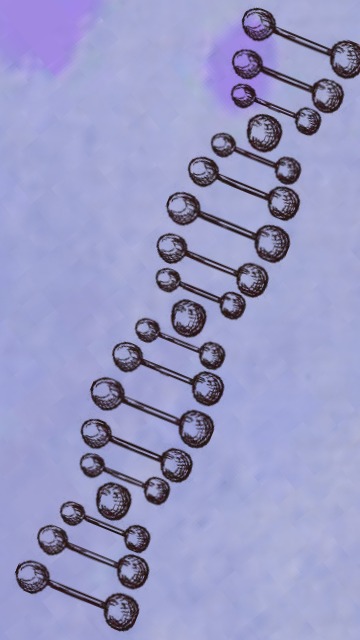
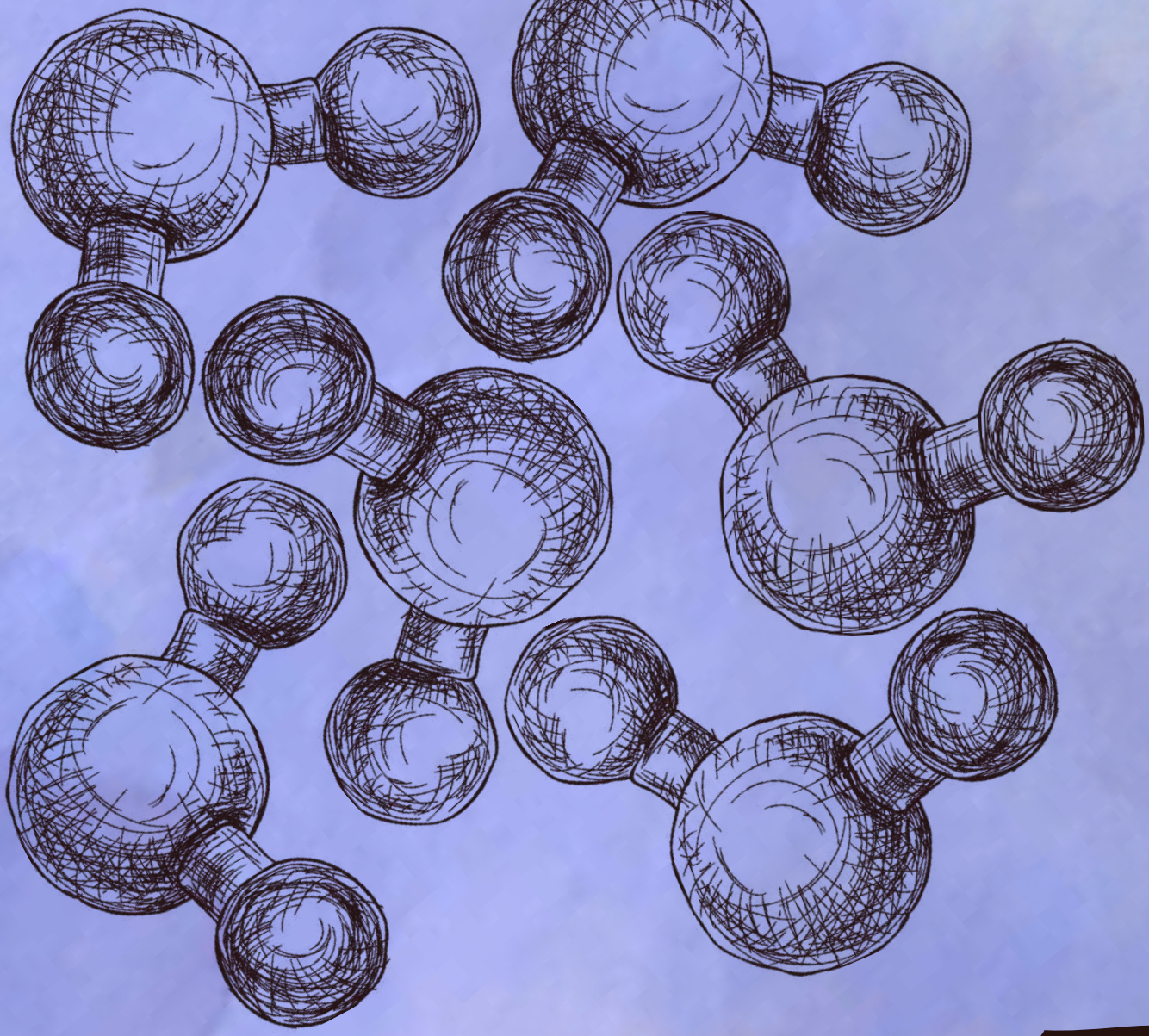
7. Klopach, E.T., et al., Accelerated epigenetic aging mediates link between adverse childhood experiences and depressive symptoms in older adults: Results from the Health and Retirement Study. *SSM Popul Health*, 2022. 17: p. 101071.
8. Lawn, R.B., et al., Psychosocial adversity and socioeconomic position during childhood and epigenetic age: analysis of two prospective cohort studies. *Hum Mol Genet*, 2018. 27(7): p. 1301-1308.
9. McCrory, C., et al., GrimAge Outperforms Other Epigenetic Clocks in the Prediction of Age-Related Clinical Phenotypes and All-Cause Mortality. *J Gerontol A Biol Sci Med Sci*, 2021. 76(5): p. 741-749.
10. Ochi, S. and Y. Dwivedi, Dissecting early life stress-induced adolescent depression through epigenomic approach. *Mol Psychiatry*, 2023. 28(1): p. 141-153.
11. Womersley, J.S., et al., Childhood trauma, the stress response and metabolic syndrome: A focus on DNA methylation. *Eur J Neurosci*, 2022. 55(9-10): p. 2253-2296.
12. Zhou, A., et al., Childhood adverse events and BDNF promoter methylation in later-life. *Front Psychiatry*, 2023. 14: p. 1108485.

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2. Press release. NobelPrize.org. Nobel Prize Outreach AB 2023. Fri. 19 May 2023. <<https://www.nobelprize.org/prizes/medicine/2022>>

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