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БІОЛОГІЧНА СЕКЦІЯ

«ВАЖЛИВІСТЬ ІДЕЙ ГЕОРГІЯ ГАМОВА ДЛЯ БІОЛОГІЇ 21-ГО СТОЛІТТЯ» (19 СЕРПНЯ 2025 Р.) В МЕЖАХ XXV ГАМОВСЬКОЇ МІЖНАРОДНОЇ АСТРОНОМІЧНОЇ КОНФЕРЕНЦІЇ «АСТРОНОМІЯ ТА НЕ ТІЛЬКИ: АСТРОФІЗИКА, КОСМОЛОГІЯ ТА ГРАВІТАЦІЯ, АСТРОФІЗИКА ЕЛЕМЕНТАРНИХ ЧАСТИНОК, РАДІОАСТРОНОМІЯ, АСТРОБІОЛОГІЯ ТА ГЕНЕТИКА», ЯКА ПРОВОДИЛАСЬ 18–22 СЕРПНЯ 2025 Р. В ОНУ ІМЕНІ І. І. МЕЧНИКОВА, ОДЕСА, УКРАЇНА

19 серпня 2025 року в межах роботи Гамовської міжнародної астрономічної конференції відбулося засідання традиційної Біологічної секції «Важливість ідей Г. Гамова для біології 21 століття». Цього року Біологічна секція проводиться сьомий раз. У заході взяли участь 46 науковців, серед яких були як досвідчені і відомі вчені, так і молоді дослідники з України, Німеччини, Молдови, Польщі, Болгарії, Чехії, Швейцарії, Фінляндії та США. Тематика доповідей охоплювала актуальні напрями сучасної молекулярної біології та медицини, зокрема дослідження регуляції експресії генів, епігенетичних механізмів і еволюції геномів, а також вивчення процесів стійкості, патогенезу та розробку прикладних молекулярно-генетичних рішень для потреб сільського господарства, охорони здоров'я і збереження біорізноманіття.

Ключові слова: Біологічна секція, Гамовська міжнародна астрономічна конференція, нуклеотидні послідовності, ген, геном.

THE BIOLOGICAL SECTION "THE IMPORTANCE OF G. GAMOW'S IDEAS FOR BIOLOGY OF THE 21ST CENTURY" IN THE FRAMEWORK OF THE XXV GAMOW INTERNATIONAL ASTRONOMICAL CONFERENCE "ASTRONOMY AND BEYOND: ASTROPHYSICS, COSMOLOGY AND GRAVITATION, ASTROPARTICLE PHYSICS, RADIOASTRONOMY, ASTROBIOLOGY AND GENETICS" HELD ON 18–22 AUGUST 2025 AT ODESA I. I. MECHNIKOV UNIVERSITY, ODESA CITY, UKRAINE

On 19 August 2025, within the framework of the Gamow International Astronomical Conference, a meeting of the traditional Biological Section entitled *"The Importance of G. Gamow's Ideas for 21st-Century Biology"* was held. This year marked the seventh edition of the Biological Section. The event brought together 46 researchers,

including both well-established scientists and early-career investigators, from Ukraine, Germany, Moldova, Poland, Bulgaria, the Czech Republic, Switzerland, Finland, and the United States. The presentations covered key areas of contemporary molecular biology and medicine, including studies of gene expression regulation, epigenetic mechanisms, and genome evolution, as well as investigations into resistance processes, pathogenesis, and the development of applied molecular-genetics solutions for agriculture, healthcare, and biodiversity conservation.

Keywords: Biological Section, Gamow International Astronomical Conference, nucleotide sequences, gene, genome.

In August 2025 biological the on-line section *"The Importance of G. Gamow's Ideas for Biology of the 21st Century"* took place successfully within the framework of the XXV Gamow International Astronomical Conference *"Astronomy and beyond: Astrophysics, Cosmology and Gravitation, Astroparticle Physics, Radioastronomy, Astrobiology and Genetics"* on the basis of the department of molecular biology, biochemistry and genetics. Doctor of biology, professor, a senior scientific specialist, a corresponding member of the National Academy of Agrarian Sciences of Ukraine Sabina Chebotar acted as the event moderator. The participants presented 12 reports on the wide range of current trends in molecular genetics: epigenomics and genome regulation in cereal crops, functioning of cis-regulatory elements, molecular mechanisms of stress responses of plants, human genetics, development regulation, as well as biomedical applications. Both fundamental problems of biology and applied aspects, significant for medicine and agrarian science were discussed.

Among the presenters of the section there were famous scientists, experienced scientific specialists, young researchers and postgraduate students from different parts of the world. Fourty six participants, scientists, postgraduate students, and students took an active part in the work of biological section. The conference took place in the worm and productive atmosphere, bringing together scientists from Ukraine, Moldova, Poland, Bolgaria, the Check Republic, Germany, Switszeland, Finland, and the USA. The ideas of Georgii Gamow, who was one of the first to propose to consider genetic sequences as an information code, were reflected in current genetic and bioinformatics approaches. They are the methods that today provide new possibilities for the analysis of complex biological processes and become the basement for biology of the XXI century.

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THE UTILIZATION OF GENOME-WIDE ASSOCIATION STUDIES (GWAS) FOR THE EXPLOITATION OF PLANT GENETIC RESOURCES – EXAMPLES ON WHEAT AND BARLEY

Understanding the genetic complexity of traits is an important objective of small grain temperate cereals yield and adaptation improvements. Bi-parental quantitative trait loci (QTL) linkage mapping is a powerful method to identify genetic regions that co-segregate in the trait of interest within the research population. However, recently, association or linkage disequilibrium (LD) mapping using a genome-wide association study (GWAS) became an approach for unraveling the molecular genetic basis underlying the natural phenotypic variation. Many causative allele(s)/loci have been identified using the power of this approach which had not been detected in QTL mapping populations. In cereals, GWAS has been successfully applied to define the causative allele(s)/loci which can be used in the breeding crop for adaptation and yield improvement. This promising approach represents a tremendous step forward in genetic analysis of genetic resources stored in genebanks world-wide.

With a total inventory of 150,000 accessions from 3,212 plant species and 776 genera, the 'Federal *ex situ* Genebank of Germany' in Gatersleben holds one of the most comprehensive collections worldwide. It comprises wild and primitive forms, landraces as well as old and more recent cultivars of mainly cereals but also other crops. We will give examples on the utilization of genebank collections of wheat and barley for GWAS analysis.

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PROGRESS IN GENOME EDITING OF CROP PLANTS

The establishment of Cas endonucleases as genome editing tools has expanded the possibilities of plant biotechnology in ways previously thought scarcely possible (Koeppel *et al*. 2019). We demonstrated the power of this technology by generating

gene-specific mutants with agriculturally relevant traits in some cereals and other crops. For example, hulled barley was modified to form naked, edible grains through mutagenesis of *NUD1* (Gerasimova *et al*. 2020), and two-rowed barley was converted into the 6-rowed type via knockout of *VRS1* (Thirulogachandar *et al*. 2024). Genome editing also facilitates the advancement of other plant breeding technologies. By targeted knockout of *PLA1*, haploidy-inducing barley lines were developed that, when used as pollinators, lead to the generation of homozygous maternal recombinants. Utilizing such doubled haploid lines has proven to be extremely effective in crop improvement (Kalinowska *et al*. 2019). Further, we used *cas9*- and (wheat-specific) guide RNA-transgenic maize lines to pollinate wheat. Relying on the phenomenon of uniparental genome elimination, this leads to the immediate generation of *cas9* and guide RNA transgene-free wheat lines that carry newly induced target gene edits in the homozygous state (Budhagatapalli *et al*. 2020). A key challenge of further technological advancement is to go beyond targeted mutagenesis by developing precise genome editing methods at an applicable level. For instance, base-editing Cas9 derivatives were used to precisely mimic specific, still functional barley *eIF4E* alleles that confer resistance to bymoviruses. In another example, the heavy metal transporter HMA3, that had been spontaneously disabled in the context of durum wheat domestication, was functionally restored via Cas9-triggered DNA cleavage followed by repair through homology-mediated end joining. The precise deletion of a mutative 17-bp duplication achieved in this approach is expected to result in a significant reduction of the accumulation of cadmium in the wheat grains.

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CIS-REGULATORY ELEMENTS CONTROLLING TRANSCRIPTION IN BARLEY

Regulation of transcription initiation is the ground level of modulating gene expression during plant development. This process relies on the interactions between transcription factors, non-coding RNA and *cis*-regulatory elements (CREs), such as promoters, enhancers and silencers, which become promising targets for crop bioengineering.

In order to annotate CREs in the barley genome and understand mechanisms of distal regulation in this crop, we conducted genome-wide profiling of several epigenetic features – namely, cytosine methylation, open chromatin and three histone modifications – across four barley developmental stages: developing, maturing and germinating embryo and young leaves. Using machine learning, we integrated the data into seven chromatin states, predicting ~77,000 CRE candidates, collectively representing 1.4% of the barley genome. Chromatin Conformation Capture-based technique HiChIP allowed us to identify activating and repressive chromatin interactions across the genome and assigned part of the CRE candidates to their putative target genes. Numerous elements showed a high degree of evolutionary sequence conservation across Triticeae species, suggesting that they may also be functional in related cereal crops. The applicability of our datasets for predicting distal CREs at other developmental stages was verified on the *Vrn3* locus.

Our study concluded with a comprehensive map of key epigenetic features, genomic interactions and predicted CRE candidates, which can be viewed in the context of gene transcription and evolutionary sequence conservation in an interactive genome browser, termed the BarleyEpiBase, at https://olomouc.ueb.cas.cz/en/resources/barleyepibase.

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CELL TYPE-SPECIFIC ATTENUATION OF ETHYLENE SIGNALING IN FUNCTIONAL STUDIES OF PLANT STRESS RESPONSES

Ethylene is a gaseous plant hormone that controls responses to different environmental and developmental cues, primarily by inhibiting vegetative growth through restriction of cell elongation. However, the cell-type specificity of ethylene signals activating various stress-protective mechanisms remains elusive.

In *Arabidopsis*, ethylene is perceived by a family of transmembrane receptors ETHYLENE RESPONSE 1 and 2 (ETR1, ETR2), ETHYLENE RESPONSE SENSOR 1 and 2 (ERS1, ERS2) and ETHYLENE INSENSITIVE 4 (EIN4), residing in the endoplasmic reticulum membrane. Ethylene signaling cascade is suppressed when the hormone is absent via CONSTITUTIVE TRIPLE RESPONSE 1 (CTR1; a Raf kinase) which inhibits the membrane protein EIN2 by direct phosphorylation. Ethylene binding to the receptors inactivates CTR1 releasing the repression of EIN2. The C-end of EIN2 is cleaved off and moves to the nucleus where it activates the master ethylene transcription factors EIN3 and EIN3-LIKE 1 (EIL1). EIN3 is constantly degraded in the absence of ethylene, a process which is under the control of two F-box proteins EIN3 BINDING F-BOX PROTEIN 1 and 2 (EBF1 and EBF2).

Cell type-targeted expression of the F-box protein EBF2 provokes local ethylene insensitivity and provides efficient approach to identify major sites of ethylene action for regulation of stress responses in *Arabidopsis thaliana*.

EBF2-coding sequence has been put under control of various cell type-specific promoters using double recombination cloning system. The obtained transgenic lines exhibit reduced sensitivity to ethylene in particular root cell types: epidermis and Lateral Root Cap *(pA14::EBF2)*, the quiescent center *(pQ6::EBF2)*, endodermis *(pE30::EBF2)*, pericycle *(pS1::EBF2)*, cortex *(pCOR::EBF2)*, and vasculature *(pS2::EBF2).*

The comparative analyses of these transgenic lines with the wild-type plants (Col-0) and the ethylene double mutant *ein3eil1* subjected to drought outlined the root epidermis and pericycle as major ethylene signaling sites involved in adaptive response to prolonged dehydration. This could be useful for future targeted molecular strategies in stress-resilient crops design.

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GENOMIC ORGANIZATION AND EVOLUTIONARY DYNAMICS OF 5S RDNA REPEATS IN DIFFERENT SUBGENERA OF *ACONITUM*

Over the past decade with the availability of the whole-genome sequencing data the study of diversity and organization of repetitive sequences has developed into a distinct field of genomics – repeatomics. Most existing studies focus on a generalized analysis of repetitive elements (REs) in the genome, whereas detailed investigations of individual RE families are far less common. Tandemly arranged 5S ribosomal RNA genes (5S rDNA) represent a RE family present in the genomes of all eukaryotes. Each 5S rDNA repeated unit consists of an evolutionarily conserved coding sequence (CDS) and a hypervariable intergenic spacer (IGS).

In this study, we conducted a comprehensive analysis of 5S rDNA using genome skimming data from 67 samples representing 40 taxa of the genus *Aconitum*. Repeat organization analysis with the TAREAN tool revealed substantial differences in the genomic organization of 5S rDNA both between and within subgenera. The proportion of 5S rDNA in the genome ranged from 0.025% in *A. anthora* L. and *A. degenii* Gáyer to 0.88% in *A. napellus* L., with up to a fourfold difference observed among individuals of the same species.

The total number of individual repeat variants per species ranged from three (*A. degenii* Gáyer, *A. barbatum* Patrin ex Pers.) to 57 (*A. kirinense* Nakai). In most cases, individual variants could be grouped into one to three classes, differing by numerous SNPs within the IGS. Recombinant sequences between classes were also detected. Notably, in some species (*A. coreanum* (H. Lév.) Rapaics, *A. napellus*, and *A. turczaninowii* Vorosch) possessing relatively few highly similar variants, the genomic proportion of 5S rDNA was high (> 0.5%), which may indicate a recent genomic expansion of this repeat variants.

The comparison of 5S rDNA repeat organization among representatives of the three subgenera (*Aconitum*, *Anthora*, and *Lycoctonum*) revealed substantial diversity both among and within subgenera. Similarities in repeat structure, abundance, and number of individual variants and classes were found only between closely related species. Thus, patterns of 5S rDNA evolution can vary considerably within intrageneric groups of plants.

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CHANGE IN TOMATO GENE EXPRESSION UPON PHYTOPLASMA INFECTION

Phytoplasmas are plant pathogenic intracellular bacteria inhabiting phloem tissue and transmitted to plants by insect vectors. They affect a variety of agriculturally important crops, causing substantial economic losses. Interestingly, phytoplasma has the ability to modify gene expression in both its plant host and insect vector. Understanding the specific transcriptional responses of various crop varieties to phytoplasma infection may help reveal the mechanisms behind plant resistance to this pathogen. The goal of this study is depicting the response of two local Moldovan tomato varieties to infection of *Candidatus* Phytoplasma solani, a causative agent of stolbur in tomato, a disease responsible for up to 70–100% of yield loss.

Total RNA from peduncles of healthy and infected tomato plants of two varieties was extracted and subjected to library preparation and sequencing, which resulted in at least 40 million 150 bps long read pairs.

As a result, 143 genes were identified as significantly (q-value ≤ 0.05) differentially expressed in infected samples compared to uninfected plants of both varieties. Among these genes, 81 were upregulated and 62 were downregulated (fold-change ≥ 2) in infected plants compared to healthy controls. Differentially expressed genes include those involved in hormone regulation, flowering control and floral architecture, plant defense, cell wall structure and stomatal regulation, among others. Differential expression of some genes (Apetala2b, Vacuolar Iron Transporter-like protein) was further confirmed by qPCR, and is the subject of further studies.

This analysis provides insights into the mechanisms by which phytoplasmas regulate host gene expression and how tomato plants respond to phytoplasma infection.

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TAKING STOCK OF HOW EFFECTIVE THE OAT RESISTANCE GENES TO POWDERY MILDEW ARE IN POLAND

Oat (*Avena sativa* L.) is a widely cultivated crop valued for its nutritional quality and multifunctional applications. However, its productivity may be increasingly compromised by fungal diseases. Powdery mildew, caused by Blumeria graminis f. sp. avenae, is one of the most common and economically damaging diseases of oat in Poland, leading to reduced photosynthetic efficiency and yield losses. The most sustainable method of managing this disease is through using genetic resistance. It combines effectiveness, economy and environmental friendliness because it eliminates the need for fungicides and reduces production costs. So far, 13 genes conferring resistance to powdery mildew have been identified, mainly designated as Pm genes. However, the long-term effectiveness of these resistance genes is increasingly challenged by the pathogen's ability to evolve and overcome plant defences. Certain genes can initially confer strong resistance, but their effectiveness often declines over time due to the appearance to new pathogen races capable of breaking down resistance. This phenomenon, known as resistance erosion, is particularly evident in regions where a limited number of genes are used widely, allowing the pathogen to adapt. Therefore, regular monitoring of oat resistance gene effectiveness and changes in the pathogen populations is essential to assess which genes remain effective. In Poland, the effectiveness of individual Pm genes varies due to the high genetic variability and rapid evolution of the pathogen population. For this reason, the effectiveness of these genes was monitored using common oat varieties and lines with known 13 resistance genes, analyzing the degree of Blumeria graminis f. sp. avenae infection from different localizations in Poland. Depending on the gene and pathogen pathotype, effectiveness of powdery mildew resistance genes has been demonstrated to be weak, moderate and high. While Pm genes have provided an essential tool for managing powdery mildew in oats, their effectiveness must be continually assessed. Sustainable disease management will depend on integrating resistant varieties with other agronomic practices and diversifying the genetic basis of resistance in breeding programs.

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MANAGING, CURATING AND SHARING PASSPORT, PHENO- AND GENOTYPING PGR DATA TO PROMOTE AGRO-BIODIVERSITY AND ITS UTILISATION

Large datasets generated in international consortium projects involving partners from different institutions across Europe and beyond can become freely accessible to millions of interested users worldwide. Ensuring that data are FAIR and openly accessible requires the development of well-structured experimental designs, comprehensive metadata descriptions, and standardized experiment templates in accordance with current scientific and data management standards.

In this context, managing, curating, and sharing passport, phenotypic, and genotypic data of plant genetic resources (PGR) plays a crucial role. Data collected and integrated from consortium partners should undergo thorough validation and curation to ensure uniformity and compliance with predefined templates. The resulting standardized datasets should be findable and accessible through open repositories or dedicated web portals, thus promoting transparency, interoperability, and reusability of valuable genetic resource information.

How do the obtained data help to promote agrobiodiversity and its utilisation?

Through standardized phenotyping and genotyping experiments high-quality datasets that capture the genetic diversity and trait variation present within these crops are generated. By ensuring that all data are collected and shared according to the FAIR principles via the web portal, researchers, breeders, and policymakers worldwide can access, analyse, and integrate these datasets into their work.

This openness enables: breeding program enhancement – by identifying beneficial alleles and linking them to phenotypic traits under diverse environmental conditions; conservation strategies by documenting and preserving genetic diversity in a transparent and traceable way, Knowledge transfer by allowing institutions across countries to reuse the same standardized data; increased crop resilience through informed selection and targeted breeding for climate adaptation and disease resistance.

Ultimately, the combination of robust experimental design, FAIR-compliant data sharing, and global accessibility strengthens the link between scientific research and practical agricultural outcomes, fostering both the preservation of agrobiodiversity and its active use in sustainable food systems.

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STREPTOMYCES VIRIDOSPORUS ATCC1462 AS A PLATFORM FOR DEVELOPMENT OF ANTIBIOTICS WITH A NOVEL MODE OF ACTION

Streptomyces viridosporus ATCC14672 is known for the production of phosphoglycolipid family antibiotics, the moenomycins. The latter exhibit a unique (and as-yet medically unexploited) mode of action via direct inhibition of peptidoglycan glycosyltransferases (PGTs). Grampositive cocci resistant to other cell wall active drugs show no cross-resistance to moenomycins, making them an ideal candidate to develop a novel class of antibiotics. The major pharmacological hurdles on the way to moenomycin-based drugs are their very low oral bioavailability and long half-life in the bloodstream. Moenomycins are structurally very complicated molecules, and so the only viable route towars their production would be a microbiological (fermentation-based) one. However, available ATCC14672 strains produce minute quantities of this antibiotic. We discovered the genetic control of moenomycin biosynthesis, which gave us new tools to both increase the production level of these fascinating natural products, and also to alter their structure. A major focus of our current research is to understand global mechanisms governing its production, such as the impact of transcription efficiency as well as genomic instability. To this end, we were able to isolate a number of spontaneous rifampicin-resistant ATCC14672 mutants harboring missense mutations within *rpoB* gene for the beta-subunit of RNA polymerase. Some of these mutations, such as H437Y, appeared to have positive effect on total antibiotic activity of the strain. Also, we demonstrate the occurrence (at a frequency of about $10ê^{-4}$) of spontaneous sporulation-deficient variants within the population of wild type strain which retain the ability to produce moenomycins. One such mutant has been genomically characterized and shown to harbor large (approx. 1 Mbp in size) deletion within the right telomere arm of ATCC14672 linear chromosome.

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RESULTS OF MOLECULAR IDENTIFICATION OF SPECIES OF THE ANOPHELES MACULIPENNIS S.L. COMPLEX IN ODESA REGION

Malaria remains a serious public health threat, while global climate change, increasing migration flows, and international transportation create conditions for the re-establishment of local transmission even in countries where the disease has been eliminated. In Ukraine, seven species of malaria mosquitoes are known [4], with members of the *Anopheles maculipennis* sensu lato (s.l.) complex − a group of morphologically similar but genetically distinct species − playing the leading epidemiological role. Due to considerable morphological similarity and the limitations of cytogenetic methods, molecular approaches have increasing importance [1, 3].

The aim of the study was to determine the species composition of the *An. maculipennis* s.l. complex in biotopes of Odesa Region using ITS2 rDNA markers.

In September 2023, 188 larvae of malaria mosquitoes were collected from biotopes in three localities of Odesa District (Yasky, Mayaky, Velykodolynske). Morphologically identified representatives of the *An. maculipennis* s.l. complex (n = 108) were analysed by PCR with species-specific primers targeting the ITS2 region [1–3]. Amplicons were determined by size following electrophoresis in 7% polyacrylamide gel, visualized with silver nitrate.

Five species of the complex were identified: *An. atroparvus* (117 bp), *An. labranchiae* (374 bp), *An. maculipennis* s.s. (410 bp), *An. melanoon* (224 bp), and *An. messeae* (305 bp). *An. beklemishevi* and *An. sacharovi* were not detected. Additionally, *An. hyrcanus* (not belonging to the complex) was morphologically identified. *An. labranchiae* and *An. melanoon* were recorded for the first time in Ukraine.

Dominance structure varied among the localities: *An. hyrcanus* predominated in Yasky (50.7%), *An. messeae* in Mayaky (50.0%), and in Velykodolynske, *An. hyrcanus* (43.6%) co-dominated with *An. maculipennis* s.s. (34.3%).

Thus, six *Anopheles* species were recorded in the studied biotopes, five of which belong to the *An. maculipennis* s.l. complex. The first detection of *An. labranchiae* and *An. melanoon* in Ukraine is of considerable epidemiological importance. The

use of ITS2 markers confirmed their high efficiency for distinguishing cryptic species, which is important for improving the system of entomological surveillance of malaria vectors in Ukraine.

The results provide a basis for further monitoring of malaria vectors and assessing the risk of re-establishment of local transmission.

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NOVEL CANDIDATE GENES FOR OLIGOGENIC 46,XY COMPLETE GONADAL DYSGENESIS

Sexual development in humans depends on the proper determination, differentiation, and functioning of the gonads. Approximately 50% of 46,XY gonadal dysgenesis (GD) cases are attributed to mutations in genes such as *SRY, NR5A1, MAP3K1*, and *DHX37.* Whole-exome sequencing (WES) allowed the identification of several new candidate genes. Increasing evidence suggests that some cases follow an oligogenic inheritance pattern, where multiple genetic variants collectively contribute to the phenotype. This research aimed to identify novel DSD genetic variants through WES and subsequent genotype-phenotype correlation analysis.

The patient, UKR21, presents 46,XY SRY-positive, complete gonadal dysgenesis (CGD), osteoporosis. After WES analysis, no convincing pathogenic variants were identified in known DSD-related genes, so we extended our analysis to other candidate genes.

Two different mutations in a compound heterozygous state were identified in the *STARD9* gene: NM_020759.3 c.5585_5590del (p.Ser1862_Thr1863del) (rs528276071) – an in-frame deletion (MAF = 0.0019); combined with NM_020759.3 c.3514 C>T (p.Arg1172Cys) (rs12594837) – a missense mutation (MAF = 0.00837). Detected mutant variants were inherited from healthy parents – heterozygous carriers and were not previously implicated in the pathogenesis of any disease.

In mice, Stard9 is expressed in a sex-specific manner during gonadal differentiation, with significantly higher expression in Sertoli cells, supporting its potential role in testicular development.

Considering the oligogenic inheritance of the 46,XY CGD in our patient, we explored whether STARD9 protein interactors contained additional variants. We identified a missense variant in the *CDK5RAP2* gene: NM_018249.5:c.2003A>G (p.Tyr668Cys) (rs137966123), which was inherited from the heterozygous mother and has a MAF of 0.0003284.

Molecular simulation revealed that mutations in both genes can affect some regulatory patterns responsible for the PPI interactions. Cdk5rap2 and Stard9 are expressed in a sex-specific manner, with the highest expression in Sertoli cells during gonadal development in the mouse [1]. Cdk5rap2 plays a critical role in gonadal development, as demonstrated in mouse models [2]. Recently, a missense variant in *CDK5RAP2* was associated with non-obstructive azoospermia [3], while STARD9 was shown to be downregulated in sperm cells of patients with asthenozoospermia [4].

Based on the results of this study and prior evidence we propose that these genes should be considered candidate genes for 46,XY CGD, potentially acting in an oligogenic mode of inheritance.

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GENOME DIVERSITY IN UKRAINE: POPULATION AND HEALTH-RELEVANT VARIATION FROM NATION-WIDE GENOME AND WHOLE EXOME SURVEYS

Large parts of the world remain genomic "deserts," where limited sequence data hinder accurate risk prediction and equitable therapeutic discovery. We present a two-pronged strategy to reduce these gaps. Using a continuously updated, open-access platform that compiles whole-genome and whole-exome datasets from more than 40 international projects, we quantify disparities in sequencing density. Regions such as Eastern Europe, Central Asia, and parts of Africa collectively contribute < 5 % of genomes deposited in public archives.

Leveraging the framework of Genome Diversity in Ukraine initiative, we have created the first country-wide Ukrainian exome reference and expanded local capacity in Ukraine to include: (a) a biobank facility for >30K biospecimens; (b) an accredited molecular-genetics laboratory; and (c) a bioinformatics analysis hub. Currently, within the Ukrainian Type 1 Diabetes Exome Project, more than half of the projected 20,000 case-control exomes + have been collected, biobanked, and sequenced. Preliminary genome-wide association scans, anchored by a custom 2 M-SNP scaffold and imputed, confirm classical HLA-DR/DQ signals and reveal coding variants in genes that appear at elevated frequencies relative to gnomAD Europeans. The data provides background for estimates of local ancestry and historical natural selection on the population level.

The Genome Diversity in Ukraine open-access database and the T1D research data transform Ukraine from a genomic desert into a data-rich landscape, improve imputation accuracy for Eastern-European studies, and supply endemic alleles for global polygenic-risk models. The approach – local biobanking, international sequencing partnerships, open data – offers a scalable blueprint for other under-sampled regions, advancing fair representation in precision medicine.

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