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БІОЛОГІЧНА СЕКЦІЯ – "THE IMPORTANCE OF G. GAMOW'S IDEAS FOR BIOLOGY OF THE 21ST CENTURY" XXIII МІЖНАРОДНОЇ ГАМОВСЬКОЇ КОНФЕРЕНЦІЇ, ЩО ВІДБУВАЛАСЯ У СЕРПНІ 2023 р. В ОДЕСЬКОМУ НАЦІОНАЛЬНОМУ УНІВЕРСИТЕТІ ІМЕНІ І.І. МЕЧНИКОВА

Біологічна секція щорічної Гамовської конференції проходила 23 серпня 2023 року в режимі on-line на платформі Zoom. В роботі секції брали участь 44 учасники з України, Німеччини, Великобританії, Швейцарії, Польщі, США, Канади, Аргентини і Казахстану. Робота секції поділялася на модулі – з молекулярної генетики рослин, молекулярної генетики мікроорганізмів – продуцентів антибіотиків, молекулярно-генетичних досліджень людини, що проводяться для вирішення питань генної діагностики і терапії людини. Також на конференції обговорювали окремі питання історії розвитку молекулярних досліджень вірусів.

Серед доповідачів свої дослідження представляли провідні науковці Інституту генетики рослин і досліджень сільськогосподарських рослин імені Лейбніца (IPK) в м. Гатерслебен (Німеччина). Керівник відділу Репродуктивної біології рослин IPK професор Й. Кумлегн виступив з доповіддю – «Cas ендонуклеазна технологія у зернових: від сайт-спрямованого мутагенезу до більш прецизійного редагування геному», в якій продемонстрував такі досягнення відділу, як створення шестирядного ячменю з дворядного, отримання певних сортів голозерного ячменю. Представлені результати вражають не тільки тому, що вони з'явилися майже одразу після оголошення Нобелівської премії у 2020 році за відкриття механізму CRISPR / Cas редагування геномів, але й прецизійною точністю виконаного редагування, коли заміна фактично одного нуклеотиду призвела до появи певних бажаних ознак у рослин.

Про складнощі з визначенням гена короткостебловості пшениці *Rht 8* розповів проф. С. Гріффітс (Центр Джона Іннеса, м. Норвіч, Велика Британія) в доповіді «Гойдалка *Rht 8*».

Цікаві доповіді представили науковці з IPK: професор М. Нагель – «Зміни метаболітів в насінні після 40 років довготривалого зберігання в холоді пшениці та ячменю» і др. М. Ширенбек – «Генетична дисекція стійкості паростків до посухового стресу у панелі сортів озимої пшениці». Родзинкою виконаних др. М. Ширенбеком зі співавторами досліджень, на наш погляд, було те, що поряд з сортами пшениці з низки Європейських країн та країн Південної Америки вивчалися і українські сорти пшениці, деякі з котрих проявили себе як посухостійкі. В доповіді др. Г. Чеботар (IPK) «Як знайти ген-кандидат – GWAS – з особливим наголосом на збереженні життєздатності ячменю», наочно було продемонстровано алгоритм й можливості GWAS для пошуку маркерних послідовностей генів кандидатів, що впливають на життєздатність насіння ячменю при довготривалому зберіганні.

Аспірантка кафедри молекулярної біології, біохімії та генетики ОНУ імені І. І. Мечникова (м. Одеса) Ю. Попович представила результати щодо ефективності застосування самостійно розроблених праймерів для визначення алельного стану багатокопійних генів гліадинів в сортах пшениці, а професор С. Оконь з Природничого університету (м. Люблін, Польща) розповіла про визначення й локалізацію нових генів стійкості до борошнистої роси у вівса – «Ідентифікація та хромосомна локалізація генів стійкості до борошнистої роси *Pm11* та *Pm12* у вівса (*Avena sativa* L.)».

Питання молекулярної організації і еволюції нуклеотидних послідовностей генів 5S РНК у межах триби *Limonieae* (*Plumbaginaceae*) розглянув в доповіді «5S рибосомна ДНК у трибі *Limonieae* (*Plumbaginaceae*): молекулярна організація, поліморфізм та таксономічне застосування» доцент, к.б.н. Ю. О. Тинкевич, який продемонстрував результати досліджень, виконаних в Чернівецькому національному університеті імені Юрія Федьковича на кафедрі молекулярної генетики та біотехнології.

Надзвичайно велику зацікавленість викликала доповідь «Динаміка геному рослин та епігеному в контексті зміни клімату» професора Е. Бучера, керівника групи з дослідження динаміки геному злаків корпорації Agroscope, Швейцарія.

У наступному інформаційному модулі на засіданні секції виступили молоді науковці Львівського національного університету імені Івана Франка – к.б.н. О. Ющук з доповіддю «Гени стійкості до глікопептидних антибіотиків: оновлена точка зору» і аспірантка Г. Качор – «Геномна характеристика штаму актиноміцетів *Mumia* sp. Pv 4–285, виділеного з ризосфери *Phyllostachys viridiglaucescens*». Молоді дослідники продемонстрували традиційно високий рівень молекулярно-біологічних досліджень актиноміцетів, що вивчаються на кафедрі генетики та біотехнології ЛНУ.

Питання з молекулярної генетики людини розглядалися в двох доповідях. У доповіді, представленій Д. Сірохою «Олігогенний вплив мутацій KIAA1210 та CFAP47 на розвиток особливостей DSD у пацієнта з мутацією C.34G>C GATA4» згідно досліджень, виконаних під керівництвом професора Л. Лівшиць, яка очолює лабораторію геноміки людини в Інституті молекулярної біології і генетики НАН України (м. Київ) і в доповіді др. Ю. Мончака – «Молекулярний ДНК-трекінг трансплантації стовбурових клітин пуповини з мультидонорських пулів: коли одного донора замало» стосовно результатів досліджень, що виконані у відділі експериментальної медицини в МакГілл університеті, (м. Монреаль, Канада). Обидві доповіді продемонстрували визначальну важливість дослідження нуклеотидних послідовностей певних молекулярних локусів.

На завершення роботи біологічної секції пролунала доповідь професора Дж. Сегре з Пенсільванського університету, якій вже вдруге бере участь в Гамовській конференції і є автором біографічної книги «Звичайні генії: як два диваки проклали шляхи сучасної науки», присвяченої Георгію Гамову і Максу Дельбрюку. Цього року професор Дж. Сегре в доповіді «Друг Джорджа Гамова Макс Дельбрюк, засновник сучасних досліджень вірусів» приділив визначну увагу другу Георгія Гамова, лауреату Нобелевської премії Максу Дельбрюку.

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Kumlehn J.
Leibniz Institute of Plant Genetics and Crop Plant Research (IPK) Gatersleben, 06466 Seeland, Germany
e-mail: Kumlehn@ipk-gatersleben.de

CAS ENDONUCLEASE TECHNOLOGY IN CEREALS: FROM SITE-DIRECTED MUTAGENESIS TOWARDS MORE PRECISE GENOME EDITING

The establishment of Cas endonucleases as genome editing tools has expanded the possibilities of plant biotechnology in ways previously thought scarcely possible. We demonstrated the power of this technology by generating gene-specific mutants with agriculturally relevant traits. Two-rowed barley was converted into the 6-rowed type via knockout of *Vrs1*, and hulled barley was modified to form naked, edible grains through mutagenesis of *Nud1*[1]. Genome editing also facilitates the advancement of other plant breeding technologies. By 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. Further, we used *cas9*- and (wheat-specific) guide RNA-transgenic maize lines to pollinate wheat. Relying on uniparental genome elimination, this leads to the immediate generation of *cas9* and guide RNA transgene-free wheat lines that carry newly induced genome edits in the homozygous state [2]. A key challenge of further technological advancement is to develop 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 approach, a heavy metal transporter that had experienced a spontaneous knockout in the context of wheat domestication was functionally restored by employing microhomology-mediated DNA repair. The precise deletion of a mutative 17-bp duplication performed for this purpose is expected to result in a significant reduction of the accumulation of cadmium in the wheat grains.

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Griffiths S.[1], Lister C.[1], Slafer G.[2], Kondić-Špika A.[3]
[1] John Innes Centre, Norwich, United Kingdom
[2] University of Llieda, Llieda, Spain
[3] Institute of Field and Vegetable Crops, Novi Sad, Serbia
e-mail: simon.griffiths@jic.ac.uk

THE *RHT8* SEESAW

Rht8 is a semi dwarfing gene that provides an alternative to the gibberellic acid insensitive *Rht1* alleles of the Green Revolution. *Rht8* was introduced into Italian wheat in the early twentieth century. We present evidence that *Rht8* confers a specific yield benefit under Mediterranean conditions in stark contrast to a negative effect in the UK. Fine mapping of *Rht8* carried by the variety Mara has allowed us to reduce the genetic interval to two genes within an 8kb interval. The two genes occur together in the *Triticeae* and are very tightly co-regulated. When the expression of one increases the other goes down, like a seesaw! We speculate that the *Rht8* height reduction effects results from the disturbance of this coregulation. Gene editing has now been used to delete each gene and we await functional validation of the effect on height.

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Nagel M.
Leibniz Institute of Plant Genetics and Crop Plant Research (IPK), 06466 Seeland, Germany
e-mail: nagel@ipk-gatersleben.de

CHANGES OF SEED METABOLITE AFTER 40 YEARS OF LONG TERM COLD STORAGE IN WHEAT AND BARLEY

Seed deterioration is of great importance for agriculture, food security and the conservation of plant genetic resources. Here we study spring barley (*Hordeum vulgare* L.), the fourth most important cereal. Its high seed quality is crucial for the brewing industry and genebanks, where more than 460 thousand accessions are stored. For the analysis of seed deterioration, 184 unique, long-term cold-stored accessions were selected according to a broad distribution of germinations in the Gatersleben genebank and genotyped. Seeds from the so-called EcoSeed panel were analysed for seed viability traits, nitric oxide content and metabolites. Overall, barley seeds of 184 genotypes germinated in a range between 0 and 99% total germination percentage

after 40 years of cold storage. Thereby, the germination percentage was independent of the nitric oxide concentration, but negatively correlated with the accumulation of 4-amino-butanoic acid, gluconic acid, glycerol, adenine, proline and ribonic acid. Based on 5,844 SNP markers, a genome-wide association mapping analysis revealed 43 marker-trait associations (MTAs) for seed viability traits on six chromosomes, of which 30 MTAs co-localised with proline and 14 MTAs with valine, suggesting a genetic relationship between seed viability traits and metabolites. Overall, the results provide new insights into the mechanisms of seed deterioration after long-term dry and cold storage.

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Schierenbeck M.[1,2,3*], Alqudah A. M.[4], Thabet S. G.[5], Avogadro E. G.[1], Lohwasser U.[1], Simón M. R.[2,3], Börner A.[1]
[1]Leibniz Institute of Plant Genetics & Crop Plant Research (IPK) OT Gatersleben, 06466 Seeland, Germany
[2]Cereals, Faculty of Agricultural Sciences and Forestry, National University of La Plata, La Plata, Argentina
[3]CONICET CCT La Plata, La Plata, Argentina
[4]Department of Biological and Environmental Sciences, Biological Science Program, College of Art and Science, Qatar University, Doha, Qatar,
[5]Department of Botany, Faculty of Science, Fayoum University, Egypt
schierenbeck@ipk-gatersleben.de

GENETIC DISSECTION FOR SEEDLING DROUGHT STRESS TOLERANCE IN A WINTER WHEAT PANEL

Drought is a major constraint in wheat (*Triticum aestivum* L.) production worldwide. The present work aimed to identify quantitative trait nucleotides (QTNs)/ candidate genes influencing drought tolerance-related traits at the seedling stage in 261 accessions of a diverse winter wheat panel (including 11 Ukrainian genotypes). Seeds from three consecutive years were exposed to polyethylene glycol 12% (PEG-6000) and a control treatment (distilled water) and grown in chamber conditions. The Farm-CPU method was used for the association analysis with 17,093 polymorphic SNPs. Data analysis revealed extensive phenotypic variation in all studied traits suggesting the suitability of the used panel for association genetic studies. All variables analyzed were significantly influenced by the years, genotypes and G × Y (environment) interactions ($p<0.001$). PEG treatment reduced shoot length (SL) (–36.3%) and root length (RL) (–11.3%) compared with control treatments, while the coleoptile length (CL) was increased by 11% under drought conditions, suggesting that it might be considered as an indicator of stress-tolerance.

Interestingly, three Ukrainian genotypes (Odesska 267, Podoljanka and Polisska 90) showed tolerance for seedling drought stress. Furthermore, we revealed 70 stable QTN across 17 chromosomes. Eight QTNs related to more than one trait were detected on chromosomes 1B, 2A (2), 2B, 2D, 4B, 7A, and 7B and located nearby or inside candidate genes within the linkage disequilibrium (LD) interval. For instance, the QTN on chromosome 2D is located inside the gene *TraesCS2D02G133900* that controls the variation of CL_S and SL_C. The allelic variation at the candidate genes showed significant influence on the associated traits, demonstrating their role in controlling the natural variation of multi-traits of drought stress tolerance. The gene expression of these candidate genes under different stress conditions validates their biological role in stress tolerance. Our findings offer insight into understanding the genetic factors and diverse mechanisms in response to water shortage conditions that are important for wheat improvement and adaptation at early developmental stages.

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Chebotar G., Börner A., Nagel M.
Leibniz Institute of Plant Genetics and Crop Plant Research, 06466 Seeland, OT Gatersleben, Germany
e-mail: Chebotar@IPK-gatersleben.de

HOW TO FIND CANDIDATE GENE – GWAS – WITH SPECIAL EMPHASIS ON BARLEY LONGEVITY

The identification of candidate genes involved in genetic traits of specific interest is crucial in various fields. Genome wide association study – GWAS – "calculate" associations between each marker and a phenotype of interest in the diverse collection of 100–500 distantly related and heterogeneous individuals. Single seed descendants, should be grown and isolated for several growing seasons, with balanced genetic diversity and allele frequency at ≥ 5%. This material should be genotyped, for example with SNP chip or with the help of other technologies such as genotype by sequencing etc. and phenotyped. In the last decades, modern methods of high-throughput phenotyping developed extremely fast. After genotyping, the population structure should be defined and LD (Linkage disequilibrium) evaluated.

At the next step investigator chooses the software, packages and models for marker trait association (MTA) analysis. For example, genome association and prediction integrated tool (GAPIT) that run in the R software environment is free and available for public (https://zzlab.net/GAPIT/) and include several models. Genetic positions of significant MTAs can be identified using genome browsers developed for the crop of interest, e.g. for barley – Barlex (Colmsee et all., 2015). According to genetic positions candidate genes can be identified at the genome browser integrated in the GrainGenes database – database for *Triticea* and *Avena* (https://wheat.pw.usda.gov/GG3/).

To identify the genetic factors that affect longevity of barley seeds stored under ambient storage conditions at the Federal Ex-situ GeneBank for agricultural and horticultural plants in Gatersleben, Germany. The 'Ecoseed panel' (Nagel et al. (2019)) consisting of 184 spring barley accessions from 23 countries (116 two-rowed, 68 six-rowed) was investigated. It was genotyped by the Illumina HD9K chip and 4.343 markers were mapped on the chromosomes after removal of monomorphic markers and applying minor allele frequency of >10%. Population structure was analyzed with STRUCTURE2.3.4 software (Pritchard et al., 2000) and an average LD decay was ±1 cM. Using GAPIT FarmCPU method (Liu et al., 2016) 85 significant (–log(p)>5) marker trait associations (MTAs) were detected. Genetic positions of significant MTAs identified using genome browser Barlex (Colmsee et all., 2015) and about 70 candidate genes were define based on the GrainGenes database (Monat et al., 2019). Thus, GWAS allow to identify genes whose effect on the trait was not known.

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Popovych Yu. A.[1], Blagodarova O. M.[2], Chebotar S. V.[1,2]
[1] Odesa I. I. Mechnikov National University, Odesa, Ukraine
[2] Plant Breeding and Genetics Institute – National Center of Seed and Cultivar Investigations, Odesa, Ukraine
e-mail: s.v.chebotar@onu.edu.ua

PREFERENCE OF MOLECULAR MARKERS FOR DETECTING ALLELIC VARIANTS OF GLIADINS

The main method of studying allelic variants of gliadins is electrophoresis in acidic PAGE, which actually shows the phenotype determined by the set of genes of the gliadin-encoding locus. This method is difficult to use, because peptides encoded by all gliadin-encoding loci are present on one lane of the gel and may overlap. Therefore, there is a need for molecular markers that would allow the determination of allelic variants of gliadins using PCR. This will help to use gliadins for marker-asissted selection, to identify allelic variants of gliadins even before obtaining grain suitable for electrophoresis of storage proteins. In this regard, the aim of study was to analyze polymorphism of *Gli-1* loci using allele-specific molecular markers and microsatellites and find suitable molecular markers for detecting allelic variants of gliadins by PCR method.

The collection of bread wheat cultivars from different countries, which reflects the maximum diversity of allelic variants of gliadins encoded by the *Gli-B1* locus (provided by Dr. E. Metakovsky) and collection of the modern Ukrainian wheat cultivars and lines from different breeding centers were analyzed using allele-specific primers to loci *Gli-A1, Gli-B1* and *Gli-D1* developed by Zhang et al. (2003) and *Taglgap* microsatellite marker described by Devos et al. (1995).

PCR with allele-specific primers to the *Gli-B1* locus permit to differentiate wheat genotypes with the *Gli-B1.1* or *Gli-B1.2* alleles, but we also revealed polymorphism within *Gli-B1.1* or *Gli-B1.2* alleles caused by a microsatellite within the amplified sequence that have been described Devos et al. (1995). Seven alleles were sequenced, and the presence of microsatellite with a CAA cor-motif which vary in number of repeats was confirmed. By using *Taglgap* microsatellite marker we revealed 12 alleles in the investigated wheat collections. The correspondence between "SNP allele of the *Gli-B1* locus – allele of the *Taglgap* microsatellite – allelic variant of gliadins" have been shown.

PCR analyze of the *Gli-A1* locus with two pairs of allele-specific primers developed by Zhang et al. (2003) permit to revealed *Gli-A1.1* and *Gli-A1.2* alleles which were of the same length. Based on the results obtained for the *Gli-A1* locus, correspondence between the *Gli-A1.1/Gli-A1.2* alleles and allelic variants of gliadins encoded by the *Gli-A1* locus was established. Bioinformatics analysis of the sequences coding

Gamma gliadin-A1 gene help to develop a pair of primers MsA1 to microsatellite in this locus. Eight different alleles that correspond to allelic variants of gliadins encoded by the *Gli-A1* locus were identified by using MsA1-primers.

Correspondence between alleles determined in PCR with allele-specific primers to the *Gli-D1* locus has not been established.

As a conclusion, we recommend to use *Taglgap* primers for detecting allelic variants of gliadins encoded at *Gli-B1* and new developed primers MsA1 for detecting allelic variants of gliadins encoded at *Gli-A1* locus.

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Okoń S., Ociepa T., Nucia A., Kowalczyk K.
Institute of Plant Genetics, Breeding and Biotechnology, University of Life Sciences, Lublin, Poland
e-mail: sylwia.okon@up.lublin.pl

IDENTIFICATION AND CHROMOSOMAL LOCALIZATION OF *PM11* AND *PM12* POWDERY MILDEW RESISTANCE GENES IN OAT (*AVENA SATIVA* L.)

Identification and introduction of effective resistance genes into cultivated crops is a very important element of the integrated plant protection system. Powdery mildew is one of the most dangerous diseases of oat. However, modern oat cultivars are characterised by very low level of resistance against powdery mildew. Also small number of effective genes may lead to the pathogen breaking their resistance. Because of this fact we have made an attempt to identify new and effective sources of resistance against powdery mildew in wild oat species *A. sterilis*. We identify two *A. sterilis* genotypes which were resistant against powdery mildew pathotypes collected in different geographical regions and in different years.

Crosses carried out with these genotypes and a susceptible oat cultivar have shown that resistance segregates according to Mendel's law and is conditioned by single dominant genes. In addition, physiological tests of the host-pathogen type showed that the infection profile of genotypes with new sources of resistance is different than infection profiles of genotypes with described so far powdery mildew resistant genes. Segregating populations of the F_2 generation were genotyped using

the DArTseq method. Analysis of the obtained results allowed to locate new genes on the genetic map of oats. The *Pm11* gene was located on chromosome 13A, and the *Pm12* gene on chromosome 7C.

The conducted research allowed the identification of two new, effective genes of resistance to powdery mildew in oats, which can be successfully used in breeding to increase the resistance of cultivated forms.

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Tynkevich Y. O., Moysiyenko I. I., Panchuk I. I., Volkov R. A.
Department of molecular genetics and biotechnology, Yuriy Fedkovych Chernivtsi National University, Chernivtsi, Ukraine
e-mail: r.volkov@chnu.edu.ua

5S RIBOSOMAL DNA IN THE TRIBE LIMONIEAE (PLUMBAGINACEAE): MOLECULAR ORGANIZATION, POLYMORPHISM AND TAXONOMIC APPLICATION

Tandemly arranged repetitive regions (repeats) encoding 5S ribosomal RNA (5S rDNA) are an essential element within eukaryotic genomes. Typically, the 5S rDNA repeats in a genome exhibit high similarity, owing to the concerted evolution characteristic of this type of repeats. Each repeat of 5S rDNA comprises an evolutionarily conserved coding sequence (CDS) and a variable intergenic spacer (IGS). 5S rDNA is a popular model for studying the molecular evolution of repetitive sequences, and the elevated mutation rate within the IGS makes it a useful tool for phylogenetic analysis among closely related taxa. Still, information on the molecular organization of 5S rDNA is lacking for many groups of angiosperms, including the Plumbaginaceae family. Certain taxa from this family are endemic to southern Ukraine and listed in the Red Book. However, their taxonomic status remains controversial. Resolving this taxonomic uncertainty requires the application of molecular phylogenetic methods. This study focuses on elucidating the molecular organization of 5S rDNA within four genera of the tribe Limonieae, the largest in the family Plumbaginaceae.

The 5S rDNA repeats for Ukrainian representatives of three *Limonium* species and two *Goniolimon* species were amplified by PCR. Subsequently, the PCR products underwent cloning using a plasmid vector and were sequenced by Sanger method. Additionally, *de novo* assembly of 5S rDNA was performed for five *Limonium*

species, two *Armeria* species, and one species each of *Ceratolimon* and *Goniolimon* using Illumina short-read libraries.

The analysis revealed that the CDS of 5S rDNA in *Limonium*, *Armeria*, and *Ceratolimon* genera exhibited single mutations that do not affect the folding the secondary structure of 5S rRNA. In contrast, *Goniolimon* species' genomes not only contain functionally normal 5S rDNA repeats but also numerous pseudogenes. These pseudogenes display non-concerted evolution and harbor multiple mutations in the CDS, disrupting the secondary structure of 5S rRNA. The considerable phylogenetic divergence observed between subgenera *Pteroclados* and *Limonium* within the *Limonium* genus suggests that *Pteroclados* may warrant consideration as a distinct genus. The accelerated molecular evolution of the 5S rDNA IGS region proved to be a valuable tool for reconstructing phylogenetic relationships within the studied genera of the Limonieae tribe and for barcoding Ukrainian endemics of the genus *Limonium*.

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Bucher E.
Agroscope – Federal Department of Economic Affairs, Education and Research (EAER), 1260 Nyon, Switzerland
e-mail: etienne.bucher@agroscope.admin.ch

PLANT GENOME AND EPIGENOME DYNAMICS IN THE CONTEXT OF CLIMATE CHANGE

Climate change represents one of the greatest challenges to agriculture in Europe and worldwide. It is therefore of key importance to better understand how plants respond to climate change related stresses at both the genetic and epigenetic levels. DNA methylation is a key epigenetic mark, regulates important traits in crops. Stresses can lead to DNA methylation changes in strawberry and some of these changes can be transmitted during clonal propagation.

The role of stress-responsive transposable elements (TEs) as important drivers in genome evolution will be disscused. We hypothesized that because numerous TEs respond to stresses, they could be adaptive as they can create novel gene regulatory pathways that respond to these stresses. To address this, we created Arabidopsis lines that carry novel heat-stress responsive TE insertions and investigated how these lines then respond to stress. The many different ways by which novel TE insertions can impact gene expression and stress adaptation will be discussed.

Our research is aimed to investigate possibilities to mobilize TEs in important crops, such as wheat and rice and to test if we can use TEs to adapt them to climate-change related stresses. It proved to be unexpectedly challenging to mobilize TEs in crops and even more challenging to then test these plants in field experiments.

However, we did find that we could mobilize TEs in both rice and wheat thereby obtaining numerous interesting phenotypic changes that are of agricultural importance.

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Yushchuk O.[1,2], **Marinelli F.**[2], **FedorenkoV.**[1]
[1] Department of Genetics and Biotechnology, Ivan Franko National University of Lviv, 79005 Lviv, Ukraine
[2] Department of Biotechnology and Life Sciences, University of Insubria, 21100 Varese, Italy
e-mail: oleksandr.yushchuk.lnu@gmail.com

GLYCOPEPTIDE ANTIBIOTIC RESISTANCE GENES: AN UPDATED POINT OF VIEW

Glycopeptide antibiotics (GPAs) are non-ribosomally synthesized glycosylated natural products from Gram-positive soil-dwelling actinomycetes. GPAs are at the top of the World Health Organization list of antibiotics critically important for human medicine. Natural GPAs such as teicoplanin and vancomycin are effective weapons against multidrug-resistant (MDR) pathogens. All GPAs inhibit the growth of Gram-positive bacteria by binding to the lipid II (a key cell-wall biosynthesis intermediate). Unfortunately, more and more GPA-resistant pathogens emerge, placing this successful class of antibiotics at risk of obsolescence. GPA-resistance is mediated by the so-called *van* genes, which might include combinations of the *vanHAX* operon, *vanY* gene (coding for cell-wall remodeling enzymes), and *vanRS* operon (coding for a two-component regulatory system controlling the expression of other *van* genes). Notably, *van* genes in GPA-producers (which obviously require them for auto-resistance) and pathogens are very similar, implying a common evolutionary source. An alternative hypothesis suggests that GPA-resistance genes might have independently originated in GPA-producers and other soil Gram-positives.

In this study, we aimed to investigate the distribution of *van* genes in phylum *Actinobacteria* and beyond, reconstructing the scenario of their evolution and spread. By analyzing more than 7000 publicly available actinobacterial genomes, we found *van* genes in one-tenth of them. The presence of *van* genes was not limited to the GPA-producers. Our phylogenetic reconstructions for VanY-like proteins, the VanHAX triads, and for VanRS regulatory pairs revealed complex stories of evolutionary independent acquisitions of the corresponding genes. We continued our search, describing *van* genes from other *Eubacteria* and discovered *van* genes in three novel classes – *Anaerolineae*, *Erysipelotrichia*, and *Ktedonobacteria* – as well as in new genera of *Clostridia* and *Bacilli* classes. The majority of these *van* genes were co-localized with genes of mobile genetic elements. Extended phylogenetic reconstruction revealed that all these *van* genes are most likely derived from

Actinobacteria through several horizontal gene transfer events, which we were able to reconstruct.

Taken altogether, our data portrays the phylum *Actinobacteria* as an incredibly vast original source of GPA resistance determinants. Moreover, it was observed that these GPA-resistance genes are actively migrating to other bacterial taxa, which might mediate their transition to pathogens. Interestingly, such variability of *van* genes in *Actinobacteria* is not easily explained by means of self-defence against GPA-producers (which are a very minor fraction of *Actinobacteria*). Hence, we are tempted to speculate that *van* genes might have other physiological roles in *Actinobacteria*; this possibility merits further investigation.

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Kachor A.[1, 2], Samborskyy M.[2], Rebets Y.[2], Gromyko O.[1]
[1] Ivan Franko National University of Lviv, Lviv, Ukraine
[2] Explogen LLC, Lviv, Ukraine
e-mail: smu62@ukr.net

GENOMIC CHARACTERIZATION OF ACTINOMYCETE STRAIN *MUMIA* SP. PV 4–285 ISOLATED FROM *PHYLLOSTACHYS VIRIDIGLAUCESCENS* RHIZOSPHERE

The genus *Mumia*, belonging to the family *Nocardioidaceae*, was established in 2014 and contains three species, *Mumia flava*, *Mumia xiangluensis*, and *Mumia zhuanghuii* [2]. The members of the genus were isolated from different sources, namely, from mangrove soil [1], rhizosphere [3], and the intestinal contents of plateau pika [2]. In the search for producers of new biologically active compounds, rhizosphere soil was collected in 2008 from *Phyllostachys viridiglaucescens* growing in the Nikitsky Botanical Garden (Crimea, Ukraine). From this soil sample, strain Pv 4–285, which is affiliated with the genus *Mumia*, was isolated by direct inoculation on humic vitamin agar.

Sequencing of *Mumia* sp. Pv 4–285 using Illumina and Oxford Nanopore technology resulted in a chromosome of 4,649,352 bp with G+C content of 70.43%. Further analyses indicate that it contains 4,398 protein-coding sequences, 46 tRNA and 9 rRNA genes. RAST server for annotation predicted the highest genes encoding for metabolism (596 genes), followed by energy subsystem (216 genes), protein processing (200 genes), stress response, defense and virulence (112 genes), DNA processing (86 genes), cellular processes (61 genes), membrane transport (40 genes), RNA processing (40 genes), cell envelope (16 genes), regulation and cell signaling (9 genes), and miscellaneous (12 genes). In *Mumia* sp. Pv 4–285 genome were predicted by antiSMASH v. 7.0.0 five biosynthetic gene clusters (BGCs) with low similarity to known clusters: 1 terpene, 1 betalactone, 1 NRPS-independent siderophore, 1 PKS-I BGC, and 1 RiPP-like BGC.

To clarify the taxonomic relationship of *Mumia* sp. Pv 4–285 with *M. flava* DSM 27763, *M. xiangluensis* DSM 101040 and *M. zhuanghuii* DSM 106288 average nucleotide identity (ANI) analysis and *in silico* DNA-DNA hybridization were performed. Strain Pv 4–285 had 77.2, 85.8 and 85.8% ANI values with *M. flava*, *M. xiangluensis* and *M. zhuanghuii* respectively and 20.7, 30.1 and 30.1% DNA-DNA relatedness values with *M. flava*, *M. xiangluensis* and *M. zhuanghuii* respectively.

Based on the results obtained in current study, our isolate *Mumia* sp. Pv 4–285 potentially could be a novel species of this genus. Moreover, further analysis of secondary metabolites will possibly discovery of new bioactive compounds.

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Sirokha D.[1], Kalynovskyi V.[2], Zelinska N.[3]; Gorodna O. [1], Livshits L.[1]
[1] Laboratory of Human Genomics, Institute of Molecular Biology and Genetics, National Academy of Sciences of Ukraine, Kyiv, Ukraine
[2] Taras Shevchenko Kyiv National University, Kyiv, Ukraine
[3] Ukrainian Scientific and Practical Center for Endocrine Surgery, Transplantation of Endocrine Organs and Tissues, Ministry of Health of Ukraine, Kyiv, Ukraine
e-mail: livshits@edu.imbg.org.ua

THE OLIGOGENIC IMPACT OF *KIAA1210* & *CFAP47* MUTATIONS ON THE DEVELOPMENT OF DSD FEATURES IN A PATIENT WITH A C.34G>C *GATA4* MUTATION

Differences in sexual development (DSD) are an important class of rare human diseases involving numerous genes. Nevertheless, about half of 46, XY DSD cases remain genetically unsolved. To investigate disease-causing gene variants combination and genotype-phenotype correlation we analyzed 46, XY DSD patient and family members carriers of c.34G>C (p.Gly12Arg) in *GATA4*, which had not been previously described in DSD patients. Moreover, a *GATA4* mutation c.34G>C was registered in ClinVar in a 46, XY person without DSD features. The aim of our study was to look for potential causative variants previously not implicated in DSD to analyze the oligogenic origin of described DSD phenotype.

Clinical, hormonal, and histological investigations as well as whole exome sequencing for 46, XY DSD patient were performed. 46, XY SRY+ patient had a female phenotype, with both gonads being dysgenetic and hypoplastic. Heterozygous missense mutation c.34G>C (p.Gly12Arg) in *GATA4* gene (MAF = 0.0001752) was not previously identified as DSD-causing.

Moreover, two rare hemizygous mutations: c.8212T>C (p.Ser2738Pro) in *CFAP47* (MAF unknown) and c.1214G>A (p.Arg405His) in *KIAA1210* (MAF=0.008459) located on the X chromosome and involved in spermatogenesis were identified in our patient, but previously not described for DSD patients. Bioinformatic analysis revealed that all these variants are considered pathogenic.

Based on obtained results we hypothesize, that in *GATA4* gene c.34G>C allele together with c.8212T>C in *CFAP47* and c.1214G>A in *KIAA1210* are resulting in oligogenic DSD features exclusively in 46, XY individuals.

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Monczak Y., Peltier L., Laneuville P.
Division of Molecular Genetics McGill University Health Center,
Department of Experimental Medicine of McGill University
McGill University, Canada
e-mail: yury.monczak@mcgill.ca

MOLECULAR DNA TRACKING OF CORD BLOOD STEM CELL TRANSPLANTATION WITH MULTI-DONOR POOLS: WHEN ONE DONOR IS NOT ENOUGH

Human hematopoietic stem cells (HSC) used for therapeutic transplantation can be obtained from several donor sources, including bone marrow aspirates and post-induction peripheral blood. Umbilical cord blood has also proven to be a rich source of HSC, and banking of cord blood specimens for potential autologous transplantation has become a routine alternative. The number of HSC found in cord blood samples varies greatly, and most cord blood specimens collected during childbirth are not conserved or banked, since they have suboptimal numbers of HSC.

Novel alternatives have been tried in research studies that aim to increase the numbers of transplanted HSC from cord bloods. One such method combines a few MHC-compatible cord blood HSC into one graft, but this method is limited by the availability of haplo-identical donors. *Ex-vivo* expansion, or cultivation, of HSC before transplantation aims to increase the number of HSC to an acceptable threshold, but this has not always proven to give acceptable results. Furthermore, these post-collection techniques have the disadvantage of increased costs of transplantation.

In the present pilot study, a small cohort of pooled cord bloods from several donors was combined in a successful series of transplantations. Molecular identity methods (short-tandem repeats (STR), or micro-satellites markers) allowed a careful mechanism of following the engraftment of a HLA-matched donor in a pooled HSC graft.

(This study was part of Dr. Linda Peltier's PhD thesis, co-directed by Dr. Pierre Laneuville and Dr. Yury Monczak at the Department of Experimental Medicine of McGill University).

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Segrè G.
University of Pennsylvania, Philadelphia, USA
e-mail: segre@physics.upenn.edu

GEORGE GAMOW'S FRIEND MAX DELBRUCK – THE FOUNDER OF MODERN VIRUS STUDIES

George Gamow and Max Delbruck were very close friends and fellow physicists in the 1930s. They then decided to start in new fields, Gamow in astrophysics and cosmology, while Max Delbruck began studying, virus replication as a key to biology. Both succeeded and remained pioneers.

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