WYKŁADY PLENARNE
(PLENARY LECTURES)

Jacek Majewski (McGill University, Montreal)
Genetics to Epigenetics and Beyond: A Journey Towards the Nucleome of Pediatric Glioblastoma

Nils Stein (Leibniz Institute of Plant Genetics and Crop Plant Research)
'Personal genomics' in small grain cereals – does it make a difference in breeding?

Barbara Wallner (University of Veterinary Medicine, Vienna)
Let's talk about influential sires: A Y-chromosome perspective on the history of horse breeding

Pedro W Crous (Westerdijk Fungal Biodiversity Institute)
„*The Evolution of Phytopathogenic Fungi*"

Bartosz Piotr Wasąg (Gdański Uniwersytet Medyczny) – 28.06, 9:50, LH-A
Mutational analysis of BRCA1/2 and beyond

Patrick K. H. Lee (City University of Hong Kong)
Accuracy of Using the Skin Microbiome as a Forensic Tool

Maria Jędrzejowska (Warszawski Uniwersytet Medyczny)
Rdzeniowy zanik mięśni - od badań podstawowych do terapii celowanej
(*Spinal muscular atrophy – from basic Research to targeted therapy*)

Boutros Maroun (Medical Affairs, Illumina)
Whole Genome Sequencing to diagnose Rare Genetic Diseases

Agnieszka Ciesielska (10x Genomix)
Single Cell Multiomics Profiling in Contemporary Genetics

Genetics to epigenetics and beyond: a journey towards the nucleome of pediatric glioblastoma

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Keywords: genomics, epigenetics, cancer, glioma

The past decade has been witness to the democratization of high throughput DNA sequencing methodologies and their implementation in mainstream biological research. Exome sequencing provided an early breakthrough, allowing affordable sequencing of most coding DNA and leading to elucidation of the genetic causes of many rare diseases and cancers. As a geneticist involved in many hereditary disease projects, I was exhilarated to be able to use my computational skills to identify dozens of new disease genes. We were gaining unprecedented insights into gene functions and phenotypic manifestations of various mutations. Surprisingly, we found that a large number of disease causing and oncogenic mutations targeted epigenetic modifiers. While genetic material, DNA, is the primary carrier of intergenerational inheritance, epigenetic modifications help maintain transfer of information along cell lineages within an organism. Disturbance of those processes leads to developmental abnormalities and can facilitate oncogenic transformation. One of our landmark discoveries was the identification of driver mutations in histone genes, particularly H3K27M in pediatric gliomas [1]. The primary effect of this mutation is inhibition of PRC2, the complex responsible for depositing H3K27 methylation. However, by disturbing H3K27me, this initial genetic change leads to a subsequent cascade of epigenetic aberrations, which we believe lock the mutant cells in an immature developmental state and allow it to proliferate uncontrollably [2]. In this presentation, I will describe some of our experiences, starting from purely genetic studies, through using epigenomic techniques to understand normal development and cancer, all the way to our most recent results in elucidating three-dimensional chromatin conformation defects in pediatric gliomas.

References

[1] J. Schwartzentruber et al. Driver mutations in histone H3.3 and chromatin remodelling genes in paediatric glioblastoma. *Nature*, 482:226-31, 2012.

[2] A. Harutyunyan. H3K27M induces defective chromatin spread of PRC2-mediated repressive H3K27me2/me3 and is essential for glioma tumorigenesis. *Nature Communications*. 10:1262, 2019.

Let's talk about influential sires: A Y-chromosome perspective on the history of horse breeding

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Keywords: horse, Y chromosome, genealogy, breeding, paternal lineage tracing

The male specific part of the Y-chromosome is inherited without recombination from a father to his sons and hence perfectly mirrors the male demography of a population. Stallion mediated improvement and the establishment of sire lines have an important role in horse breeding.

Genetic sire line tracing was hampered over several decades by the low sequence diversity on the horse MSY, which prevented the discovery of meaningful markers. Over the past years we developed workflows to perform robust Y-chromosomal haplotype analysis in horses based on NGS data. For haplotype inference, we currently screen up to 5.8 Megabases of the MSY for variants in whole genome or target enriched sequencing data [1]. Based on the called variants, we reconstruct haplotypes and create haplotype trees from parsimony informative sites. I will present our current tree in domestic horses which is built from more than 200 sequenced horses and represents modern as well as rural breeds. The horse Y-chromosomal tree depicts two pronounced expansion events, that are both mediated through human intervention after domestication. By linking the Y-chromosomal haplotypes with sire line information documented in their pedigrees, we determined the Y signatures of several influential stallions [1,2]. We can now straightforwardly trace the paternal legacy of those sires by genotyping the respective haplotype determining variant in populations in question. Y haplotype spectra in horse breeds around the globe give an impression how recent stallion mediated refinement breeding (via English Thoroughbreds, Arabian or Iberian Horses) influenced present horse populations.

References

[1] Felkel S et al. The horse Y chromosome as an informative marker for tracing sire lines. *Sci Rep. 2019 Apr 15;9(1):6095.*

[2] Remer V et al. Y-Chromosomal Insights into Breeding History and Sire Line Genealogies of Arabian Horses. *Genes (Basel). 2022 Jan 26;13(2):229.*

The evolution of phytopathogenic fungi

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Keywords: biodiversity, fungal evolution, genome-based prediction, lifestyles

Recent results from large-scale DNA sequencing projects have shown that most biodiversity on earth is actually very small, represented in insects and microbes. The kingdom *Fungi* forms a highly diverse, relatively unexplored lineage of eukaryotes that shares a common ancestor with animals. Both comprise heterotrophic organisms, but *Fungi* form (chitinous) cell walls and are exclusively osmotrophic; that is, nutrient uptake is extracellular. Although nearly 150,000 species of *Fungi* have been described, between 2.2 and 3.8 million are estimated to exist. Many habitats, ecosystems and host plants have, however, never been investigated, and thus their microbial inhabitants remain unexplored, unknown, and underutilised. Over the past 10 years, mycologists have on average described 2000 species per year, meaning that it will take more than 1000 years to simply describe the number of fungal taxa we estimate to occur on earth. Phytopathogenic fungi are important agents of plant disease, resulting in major annual losses to agricultural and forestry industries. The *Dothideomycetes* is the largest and most diverse class of ascomycete fungi, with thousands of phytopathogenic species, comprising an incredible diversity of lifestyles, many of which have evolved multiple times. Studying the evolution in *Dothideomycetes* has significant implications for our fundamental understanding of fungal evolution, and practical implications regarding the effects of climate change on these pathogens in agriculture. The availability of whole-genome data produced a high-confidence overall phylogeny of *Dothideomycetes*, providing a clearer picture of the relationships among the various families, indicating that pathogenicity evolved multiple times within this class. Using machine-learning methods we classified fungi into lifestyle classes with >95 % accuracy and identified a small number of gene families that positively correlated with these distinctions [1]. Ancestral character state analyses support a terrestrial saprobic lifestyle as being ancestral within the class, also at ordinal and family levels, and that several transitions have occurred to evolve lichenised, plant and human parasitic, ectophytic (sooty blotch and flyspeck) and more recently epiphytic (sooty mould) lifestyles.

References

[1] S. Haridas *et al.* 101 *Dothideomycetes* genomes: a test case for predicting lifestyles and emergence of pathogens. *Stud. Mycol.*, 96:141–153, 2020.

Accuracy of Using the Skin Microbiome as a Forensic Tool

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The community of microorganisms or microbiome on our skin is important for modulating skin health. In addition to health, there is also great interest in using the skin microbiomes as fingerprints for forensic purposes to identify individuals and to match individuals to objects they have touched. There have been some successful demonstrations in using skin microbiome to match people to objects and locations, but the application of microbiome matching as a forensic technology still requires further development. Unlike fingerprints, which are generally stable during the lifetime of a person and which can persist on a surface for a long period of time, a person's skin microbiome is less stable and can shift over weeks or months due to factors such as the person's physiology, external environmental conditions, dispersal from external sources, and stochastic assembly processes. In order to better understand utility of the skin microbiome as a forensic tool over different time scales, we have performed a series of study to track the skin and surface microbiomes within households every 12 hours for 10 consecutive days and over four seasons to determine accuracy of the microbiome-based matching of individuals to their households. For the seasonal study, household surface microbiomes could be matched to the correct occupants' skin microbiomes with 67% accuracy in the same season, but the accuracy decreased substantially when skin and surface samples were collected in different seasons. For the short-term 10-day study, a person skin microbiome could be accurately matched to their household surface microbiomes without substantial decay in accuracy. Over the 10-day study period, specific species were found to exhibit a significant variation in abundance between morning and evening. Taken together, in addition to considering the decay or stability of microbiome traces over short and long time scales, diurnal patterns in the human skin microbiome assemblage must also need to be considered in developing skin microbiome as a reliable forensic tool.