Katedry genetiky a biochémie PriF UK
a občianske združenie *NATURA*

Vás pozývajú na 138. prednášku v rámci Kuželových seminárov:

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DRIVING FORCES OF CELLULAR PHENOTYPIC FITNESS UNDER STRESS

ktorá sa uskutoční **20. marca 2026** (piatok) o **13:30**
v miestnosti **CH1-222** Prírodovedeckej fakulty UK

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Hostiteľ: dr. Martin Lukačišin

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2022-present	**Tenured group leader** Center for Pathobiochemistry & Genetics Medical University of Vienna, AT
2016-2021	**Junior PI** Center for Stem Cell Biology King´s College London, UK
2010-2015	**Postdoc** Department of Cell Biology Harvard University, USA
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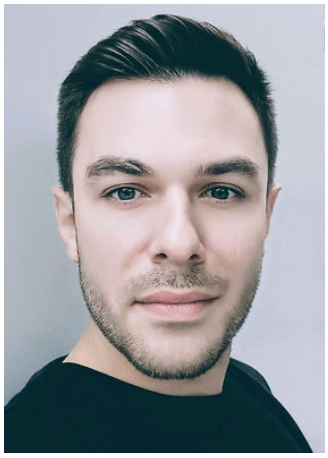

Synopsis of the talk

The classic Luria-Delbrück experiments showed that stress resistance can arise from random genetic mutations. However, cells can also survive stress through reversible, non-genetic phenotypic shifts. Defining the mechanisms that enable phenotypic fitness under stress is an emerging frontier with major biomedical relevance, from cancer therapy to antimicrobial resistance. In my talk, I will present our multiscale approach, combining molecular -omics, quantitative experiments, and modelling, to move from correlative signatures to mechanism and uncover the driving forces behind phenotypic drug tolerance. Guided by the idea that drugs perturb gene and protein networks rather than single targets, we used multi-omics profiling to find that cancer cells tolerating the broad-spectrum chemotherapeutics taxoids enter a dormant-like state by preferentially downregulating evolutionarily ancient translation programs. Functionally, suppressed translation is associated with cytoplasmic accumulation of free amino acids; as potent osmolytes, these are expected to drive water influx and hypo-osmotic–like swelling. Such swelling typically requires adaptive remodeling of the cell surface area-to-volume (SA/V) ratio to avoid lysis, a response also observed in bacteria under translation-targeting drug stress, where SA/V changes can alter drug uptake and intracellular partitioning. I will conclude with preliminary quantitative assays testing this mechanism in mammalian cancer cells and parallel efforts to reconstitute it in designer yeast strains engineered to respond to human taxoids.

Selected publications:

1. Herrera-Fernández V, Hengstschläger M, **Lomakin AJ**. Ameboid cell inchworming: An adaptive phenotype triggered by abiotic-like stress. *Developmental Cell*, 2025.
2. Ju RJ, Falconer AD, Schmidt CJ, Enriquez Martinez MA, Dean KM, Fiolka RP, Sester DP, Nobis M, Timpson P, **Lomakin AJ**, Danuser G, White MD, Haass NK, Oelz DB, Stehbens SJ. Compression-dependent microtubule reinforcement enables cells to navigate confined environments. *Nature Cell Biology*, 2024.
3. Belhadj J, Surina S, Hengstschläger M, **Lomakin AJ**. Form follows function: Nuclear morphology as a quantifiable predictor of cellular senescence. *Aging Cell*, 2023.
4. **Lomakin AJ**, Cattin CJ, Cuvelier D, Alraies Z, Molina M, Nader GPF, Srivastava N, Sáez PJ, Garcia-Arcos JM, Zhitnyak IY, Bhargava A, Driscoll MK, Welf ES, Fiolka R, Petrie RJ, De Silva NS, González-Granado JM, Manel N, Lennon-Duménil AM, Müller DJ, Piel M. The nucleus acts as a ruler tailoring cell responses to spatial constraints. *Science*, 2020.
5. **Lomakin AJ**, Lee KC, Han SJ, Bui DA, Davidson M, Mogilner A, Danuser G. Competition for actin between two distinct F-actin networks defines a bistable switch for cell polarization. *Nature Cell Biology*, 2015.