

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



Vás pozývajú na 132. prednášku v rámci Kuželových seminárov:

dr. Martin Lukačišin

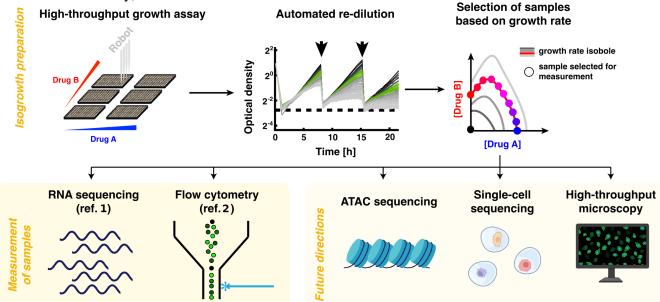
Laboratórium systémovej biológie, Katedra genetiky, Prírodovedecká fakulta, Univerzita Komenského

ISOGROWTH PROFILING FOR PERTURBATION BIOLOGY

ktorá sa uskutoční **29. novembra 2024** (piatok) o **13:30** v miestnosti **CH1-222** Prírodovedeckej fakulty UK

> http://www.naturaoz.org/seminare.html http://www.naturaoz.org/KuzeloveSeminare.html

Martin Lukačišin graduated with honours in Biochemistry from the University of Oxford in 2012. For his master thesis, he studied breast cancer metastasis with Yibin Kang at Princeton University. After a one year stay at the Department of Systems Biology at Harvard Medical School, he enrolled in a PhD at IST Austria, where he worked with Tobias Bollenbach on combinatorial perturbations of yeasts and developed the isogrowth profiling methodology. Martin did his postdoctoral work with Shai Shen-Orr at the Faculty of Medicine at the Technion – Israel Institute of Technology in Haifa, working on computational and systems approaches to human immunity (2019-2024). Since 2024, he has been leading the Systems Biology Laboratory at the Department of Genetics at the Faculty of Natural Sciences, Comenius University, Bratislava.



<u>Synopsis of the lecture</u>: A central goal of systems biology is to predict consequences of specific cellular perturbations. However, cellular perturbations almost always lead to changes in cellular fitness and thus, in growth rate. The growth rate, in turn, is one of the most potent influencers of gene expression, obscuring the transcriptional consequences of the original perturbation. This creates, so to say, a biological version of the Heisenberg uncertainty principle – a stronger perturbation makes the effect more measurable, but also more obscured by the change in growth rate. In my talk, I will present a methodology called isogrowth profiling to decouple growth rate changes from the effects caused by perturbagens – small molecule inhibitors. Using this approach, we were able to identify specific drug effects that enabled us to predict drug interactions, as well as to discover novel effects of well-studied perturbagens on those cellular components that are especially sensitive to changes in growth rate.

Selected publications:

- 1. Lukačišin, M., Bollenbach, T. (2019). Emergent gene expression responses to drug combinations predict higher-order drug interactions. *Cell Systems* 9:423-433. doi:10.1016/j.cels.2019.10.004
- Lukačišin*, M., Espinosa-Cantú*, A., Bollenbach, T. (2022). Intron-mediated induction of phenotypic heterogeneity. *Nature* 605:113–118. doi:10.1038/s41586-022-04633-0; *co-first authors
- 3. Lukačišin, M., Espinosa-Cantú, A., Bollenbach, T., (2022). Single-cell isogrowth profiling: Uniform inhibition uncovers non-uniform drug responses. *Clin. Transl. Med.* 12: e1005. https://doi.org/10.1002/ctm2.1005
- Dubovik*, T., Lukačišin*, M., Starosvetsky, E., LeRoy, B., Normand, R., Admon, Y., Alpert, A., Ofran, Y., G'Sell, M. & Shen-Orr, S.S. (2024). Interactions between immune cell types facilitate the evolution of immune traits. *Nature* 632: 350–356. doi:10.1038/s41586-024-07661-0; *co-first authors