Name	SNEZHANA OLIFERENKO
Position	Seconded Group Leader (King's)
Year joined *(Crick or founder institute)*	2016

Career History

1996- 2000: PhD student, Institute of Molecular Pathology (IMP), Vienna.
PhD advisor: Lukas A. Huber
2000- 2002: Research Fellow, Institute of Molecular Agrobiology, Singapore
Postdoctoral advisor: Mohan Balasubramanian
2002- 2004: Young Investigator (Career Development Fellow), Temasek Life Sciences Laboratory, Singapore
2005- 2010: Principal Investigator, Temasek Life Sciences Laboratory; Adjunct Assistant Professor, National University of Singapore
2010- 2013: Senior Principal Investigator, Temasek Life Sciences Laboratory; Adjunct Associate Professor, National University of Singapore
2013- 2017: Reader in Cell Biology, Randall Centre for Cell and Molecular Biophysics, King's College London, UK
2016- present: Group Leader, The Francis Crick Institute, London, UK (on secondment)
2017- present: Professor of Evolutionary Cell Biology, Randall Centre for Cell and Molecular Biophysics, King's College London, UK

Major Awards, Honours and Prizes

Membership of external committees, editorial boards, review panels, SABs etc

Community service

Organizing conferences:
ASCB|EMBO Cell Bio 2020, Program Committee member
British Yeast Group meeting 2020 (currently on hold), Program Committee member
Co-organizer of the European Cell Cycle Meeting, Trieste, June 2019

Reviewing papers:
Current Biology, *Nature Cell Biology*, *eLife*, *The Journal of Cell Biology*, *Cell Reports*, *PNAS*, *PLoS Genetics*, *Molecular Biology of the Cell*, *Genetics*, *Yeast, The Journal of Cell Science*

Reviewing grants:
BBSRC, Leverhulme Trust, Wellcome Trust, Swiss National Science Foundation, ANR (France), FRM (France), Singapore Ministry of Education

Research evaluation/advising:
Quinquennial review of the Institute of Biochemistry and Cell Biology, Bordeaux (HCERES, 2021); review of promotion/tenure/habilitation applications in France, Singapore, Japan, US; faculty interview panels at the University of Warwick and King's; thesis committee chair/member at King's, Crick, ETH, University of Lausanne, University of Strasbourg, etc (~10 at steady state).

Lab Name	*Comparative biology of mitotic division laboratory*

Research programme and achievements

We have pioneered the use of the fission yeasts *S. pombe* and *S. japonicus* as a composite system for evolutionary cell biology studies. Their similar genetic makeup and experimental amenability allow comparative and reverse engineering analyses, facilitating discovery of the core cellular components and interactions and illuminating the origins of evolutionary innovation. Our comparative approach has come of age in the last five years. We now appreciate its power not only in elucidating the core principles and evolution of specific cell biological mechanisms but also in illuminating unexpected functional links to the rest of cellular and organismal physiology. Several highlights are outlined below.

We discovered that the divergent strategies of mitotic nuclear envelope remodeling in *S. pombe* and *S. japonicus* are necessitated by the distinct phosphoregulation of the phosphatidic acid phosphatase lipin acting as a rheostat to control phospholipid biosynthesis and hence, nuclear membrane expansion [Current Biology 26: 237 (2016)]. We discovered that cellular membranes in these species are made of structurally distinct phospholipids due to the difference in fatty acid synthase activities, and showed that evolutionary changes in lipid metabolism require extensive adaptation of the membrane-associated proteome [Current Biology 30:367-380 (2020)]. We discovered a conceptually novel function and the mechanism for the ESCRT-III/Vps4 machinery in regulating interactions between the inner nuclear membrane proteins and heterochromatin and explained how it impacts nuclear envelope reformation [Developmental Cell, 53:27-41 (2020)]. In the process of working on these projects, we realized that the striking differences in nuclear envelope management between the two species are just the tip of the iceberg. We found that *S. pombe* has evolved an unusual medial division ring assembly mechanism based on neofunctionalization of a recently duplicated anillin paralog but *S. japonicus* regulates ring formation similarly to metazoans [Current Biology 25: 1187 (2015)]. Following this, we made important contributions to illuminating ring organization and function in *S.japonicus* [eLife 210.7554/eLife.21383 (2016); J Cell Biology 216: 2657 (2017)] and discovered the organismal-level function for cellular geometry scaling in maintaining medial division site positioning [Nature Communications 10: 268 (2019)].

We are now wrapping up several projects, including: (1) elucidating the Aurora kinase-dependent mechanism of NE breakage during mitosis; (2) understanding the regulation of the major activator of Lipin, Spo7-Nem1 phosphatase; (3) investigating the divergence of central carbon metabolism between *S. pombe* and S*. japonicus* (an exciting and completely new project started at the Crick with the help of the Crick-King's PhD fellowship)

We are beginning a major effort to define how lipid metabolic capacity controls membrane organization and cellular physiology, by exploiting the natural divergence in membrane lipid composition between *S. pombe* and *S. japonicus*. This program will be funded by my new Wellcome Trust Investigator Award (awarded in August 2020). Our research will explain how changes in the architecture of glycerophospholipid fatty acyl tails affect membrane properties. It will provide insights into the organization and evolution of genetic networks regulating membrane homeostasis. Finally, it will test if acquisition of new lipid metabolic functionalities engenders diversification of cellular pathways and organismal physiology.

Additionally, we will continue working on elucidating the molecular mechanisms underlying cellular geometry scaling (funded by BBSRC) and probing the functional

interactions between the inner nuclear membrane and chromatin organization, including venturing into mammalian cell biology, in collaboration with Jez Carlton at the Crick.

Research outputs

Pieper, G., Sprenger, S., Teis, D. and S. Oliferenko. (2020) *ESCRT-III/Vps4 controls heterochromatin-nuclear envelope attachments*. Developmental Cell 53:27-41. DOI: 10.1016/j.devcel.2020.01.028
Here we show that the inner nuclear membrane Lem2-Nur1 complex serves a substrate for the nuclear ESCRT-III/Vps4 machinery and explain how the dynamic tethering of chromosomes to this complex during interphase is linked to the establishment of nuclear compartmentalization following mitosis.

Makarova, M, Peter, M., Balogh, G., Glatz, A., MacRae, J., Lopez Mora, N., Booth, P., Makeyev, E., Vigh, L. and S. Oliferenko. (2020) *Delineating the rules for structural adaptation of membrane-associated proteins to evolutionary changes in membrane lipidome*. Current Biology 30:367-380. DOI: 10.1016/j.cub.2019.11.043
This work revealing co-evolution of cellular lipidome and transmembrane proteins may lead to a conceptually new understanding of the relationship between the underlying metabolic makeup and the evolution of cellular properties.

Gu, Y. and S. Oliferenko. (2019) *Cellular geometry scaling ensures robust division site positioning*. Nature Communications 10:268. DOI 10.1038/s41467-018-08218-2
Here we describe our discovery that preservation of specific cellular geometry across a range of cell sizes is essential for correct division site positioning and survival, demonstrating the organismal-level function for scaling.

Makarova, M., Gu, Y., Chen, J-S., Beckley, J., Gould, K. and S. Oliferenko. (2016) *Temporal regulation of Lipin activity diverged to account for differences in mitotic programs*. Current Biology. 26: 237-243. DOI 10.1016/j.cub.2015.11.061
Using *S. pombe* and *S. japonicus* we uncovered a molecular basis for variability in nuclear envelope expansion during mitosis. We showed that cells undergoing closed mitosis expand their nuclear envelope prior to division by entraining inactivation of the phosphatidic acid flux regulator lipin to high CDK activity.

Gu, Y., Yam, C. and S. Oliferenko. (2015) *Rewiring of cellular division site selection in evolution of fission yeasts*. Current Biology. 25:1187-1194. DOI: 10.1016/j.cub.2015.02.056
Here we show that placement of the division apparatus is determined by positioning of the actomyosin-plasma membrane linkers and that both identity of the linker and control of its subcellular targeting are subject to evolutionary plasticity.