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Cell Biology

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Born in 1983 in Camrose, Alberta, Canada

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FELLOWSHIP

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### ARBEITSVORHABEN

## Reconstructing the Genome of the Last Eukaryote Common Ancestor

Cellular life can be divided into two forms: simple (prokaryotic) cells lacking internal membranes and devoid of nuclei; and complex (eukaryotic) cells with internal membranous organelles including mitochondria and nuclei. The vast majority of the diversity of complex (eukaryotic) life is unicellular, meaning that only a fraction of eukaryotic diversity is represented by multicellular plants, animals, and fungi. The evolution of the unicellular eukaryotes, therefore, represents THE major evolutionary transition in the history of life. And understanding this transition is perhaps the major goal in evolutionary cell biology. To better understand this transition, a preliminary dataset representing the genomic repertoire of the Last Eukaryote Common Ancestor (LECA) has been reconstructed. These data suggest that LECA contained many genes, making it more complex than many extant lineages.

At the Wissenschaftskolleg, I will use this dataset to establish the theoretical bases and collaborative connections that will form the foundation of my career as an independent investigator. I will analyze the LECA dataset to identify the most promising genes for future study by:

- Phylogenetic screening: to identify unstudied/unrecognized ancient proteins
- Phenotypic screening: to identify phenotype-associated ancient proteins
- Co-gain/Co-loss analysis: to identify putative interacting proteins

It is practically impossible for a single lab to investigate these data effectively; therefore, analyzing the LECA data at the Wissenschaftskolleg, I will have the opportunity to establish collaborative investigations with scientists in Europe and around the world. These interdisciplinary collaborations at the intersection of cell biology and evolution will begin to uncover the molecular details that explain the evolution of complexity and diversity.

### Recommended Reading

O'Malley, M. A., Wideman, J. G., and Ruiz-Trillo, I. (2016). "Losing complexity: the role of simplification in macroevolution." *Trends in Ecology and Evolution* 31, 8: 608-621.

Munoz-Gomez, S., Slamovits, C., Dacks, J. B., Spencer, K. D., Baier, K. A., and Wideman, J. G. (2015). "Ancient homology of the mitochondrial contact site and cristae organizing system points to an endosymbiotic origin of mitochondrial cristae." *Current Biology* 25: 1489-1495.

Wideman, J. G., Gawryluk, R. M. R., Gray, M. W., and Dacks, J. B. (2013). "The ancient and widespread nature of the ER-mitochondria encounter structure." *Molecular Biology and Evolution* 30, 9: 2044-2049.

# A Comparative Anatomy for Cells, an Evolutionary Framework for Cell Biologists

PLEASE BRING YOUR LAPTOPS for a brief (and very simple!) computational lab demo.

The comparative method is essential to the biological sciences. To understand the biology of one organism, we compare it to the biology of another and thereby discover similarities and endeavor to explain differences. In cell biology, the comparative method is implicitly assumed in investigations that use model organisms to illuminate the biology of our own species. However, beyond the use of well-established model organisms, the more proximate biological sciences like biochemistry and cell biology have largely left broad comparison behind. I believe it is much more fruitful to fully embrace the comparative approach and learn from the incredible diversity of life.

Modern cell biologists are pressured to study medically relevant topics and often work directly on human tissue culture (e.g. immortalized cancer cells). Well-established model organisms like the fruit fly (*Drosophila melanogaster*), the nematode worm (*Caenorhabditis elegans*), or a fungus like the brewer's yeast *Saccharomyces cerevisiae*, are still used in cell biological research, but these scientists also feel the pressure to move to more practical systems. Only when investigating photosynthesis do cell biologists regularly turn to the model plant thale cress (*Arabidopsis thaliana*). But these model organisms are all plants, animals, or fungi, and account for only a small fraction of the diversity that encompasses eukaryotes (i.e. complex cells, see Figure), most of which are unicellular. Unfortunately, relatively few scientists study the cell biology of eukaryotes that are not plants, animals, or fungi leading to a misunderstanding of how diversity and the comparative method can inform their science. The near-exclusive focus on multicellular organisms has led to the false notion that evolution proceeds by complexification. This is just not true. Mostly, evolution proceeds by simplification. How can we remedy these misunderstandings?

The first step is to construct a unified conceptual framework for cell biologists. Using computational comparative genomics, we have done this by reconstructing the genome of the Last Eukaryote Common Ancestor (LECA). This provides a single point of comparison for cell biologists and contributes to a better understanding of both the unity and the diversity of life. This not only contributes to understanding the evolution of cell diversity but, ironically, can also be of great benefit to medical and technological advance.

Here at WIKO, I am exploring the theoretical and philosophical implications of reconstructing LECA while completing the project with numerous global collaborators. In my presentation, I will give you insight into this project beginning with an introduction to eukaryote diversity, followed by an interactive computational laboratory demonstration, and finishing with what is yet to come: the plans for an interactive dataset with community engagement and tool development.

Wideman, Jeremy G. (Lawrence, KS,2021)

A functional bacteria-derived restriction modification system in the mitochondrion of a heterotrophic protist

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1763767833>

Wideman, Jeremy G. (London,2019)

Unexpected mitochondrial genome diversity revealed by targeted single-cell genomics of heterotrophic flagellated protists

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1683836944>

Wideman, Jeremy G. (Nature,2019)

Concepts of the last eukaryotic common ancestor

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1665307315>

Wideman, Jeremy G. (Oxford [u.a.],2018)

Cell biology : functional conservation, structural divergence, and surprising convergence in the MICOS complex of trypanosomes

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=104621585X>

Wideman, Jeremy G. (2018)

PDZD8 is not the 'functional ortholog' of Mmm1, it is a paralog : [version 1; referees: 2 approved]

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1029372926>

Wideman, Jeremy G. (2017)

A new mitofusin topology places the redox-regulated C terminus in the mitochondrial intermembrane space

<https://kxp.k10plus.de/DB=9.663/PPNSET?PPN=1041233841>