Name	MARKUS RALSER
Position	Group Leader (2nd 6)
Year joined *(Crick or founder institute)*	2013

Career History

2006-2007: Post-doctoral scientist, Max Planck Institute for Molecular Genetics (DE)
2009: Visiting Scientist, Clinical Metabolomics Lab, Dept of Clinical Chemistry, VU University Amsterdam (NL)
2007-2011: Junior Research group leader, Max Planck Institute for Molecular Genetics (DE)
2011– 2018: Group Leader, Wellcome Beit Fellow, Department of Biochemistry, University of Cambridge
2013- 2018: Group Leader, The Francis Crick Institute
2018- present: Einstein foundationProfessor of Biochemistry, Charité Universitätsmedizin Berlin
2019- present: Senior Group leader, The Francis Crick Institute (20% FTE)

Major Awards, Honours and Prizes

2007: The BioMed Central Research Award, Biology
2011: Wellcome Beit Prize (Wellcome Trust)
2014: Südtiroler Wissenschaftspreis (‘South Tyrolean Science Award))
2012- 2015: European Molecular Biology Organisation (EMBO) Young Investigator
2018: The Colworth Medal, The Biochemical Society, UK
2012- 2018: Research Associate, St John’s College, Cambridge, UK
2019: The Starling Medal, The Endocrinological Society, UK

Notable program grants and fellowships
2011- 2016: European Research Council (ERC) starting grant
2011- 2017: Wellcome-Beit fellowship (Wellcome Trust)
2017- 2023: Investigator Award in the Life Sciences (Wellcome Trust)
2020- 2026: National Research Node for for Mass Spectrometry (Co-PI, BMBF)

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

Commissions of trust

2020 Novo Nordisk foundation, Denmark, NNF Data Science Committee, in the panels for emerging, ascending and distinguished awards as well as infrastructure grants
2018 HCRES Scientific Review Board, Institute Jacques Monod, Paris France
2017- 2020 Fundação para a Ciência e a Tecnologia, Portugal, participation in several national grant panels
2016 – 2019 Independent Research Fund, Denmark, member of the national grant panel (Biochemistry and Experimental Biology)

Lab Name	*The Molecular Biology of Metabolism Laboratory*

Research programme and achievements

The Molecular Biology of Metabolism lab is known for fundamental discoveries that have improved our understanding of how cells can coordinate hundreds of biochemical reactions assembled in the metabolic network, and for the development of high-throughput mass spectrometry technologies required to study metabolism.

The major publications from the Ralser lab have linked each yeast gene to its role in Metabolism, and have shown that metabolism is much more flexible and integrated into the physiology of cells than was expected only a few years ago. Moreover, results obtained by the group have provided fundamental insights into how central carbon metabolism could have evolved in early life forms, how reactions can co-occur within a cell despite competing chemistries, and how yeast and cancer cells reconfigure metabolism to be protected against oxidative stress.

Current work concentrates on two major research areas. First, all cells export and import many metabolites. This situation enables individual cells to cooperate and to specialise in metabolism. We have evidence that this specialisation underlies major aspects of a biological property known as phenotypic heterogeneity. We further have evidence that it underlies treatment failures in fungal infection. We are currently developing the methods and concepts to uncover the metabolic contribution of phenotypic heterogeneity.

Second, major progress in the field has been hindered by a lack of high-throughput capacity in the proteome technologies required to quantify the concentration and activity of hundreds of metabolic enzymes in parallel, so that we can understand metabolism in the complexity of the dynamic network it represents. We have joined forces with industry and developed new and faster mass spectrometry technologies. We now apply these not only to study metabolism in yeast and humans, but also to conduct epidemiological investigations to achieve disease prediction.

Research outputs

Messner CB, Demichev V, Wendisch D, Michalick L, White M, Freiwald A, Textoris-Taube K, Vernardis SI, Egger AS, Kreidl M, Ludwig D, Kilian C, Agostini F, Zelezniak A, Thibeault C, Pfeiffer M, Hippenstiel S, Hocke A, von Kalle C, Campbell A, Hayward C, Porteous DJ, Marioni RE, Langenberg C, Lilley KS, Kuebler WM, Mülleder M, Drosten C, Suttorp N, Witzenrath M, Kurth F, Sander LE, Ralser M. (2020) *Ultra-High-Throughput Clinical Proteomics Reveals Classifiers of COVID-19 Infection*. Cell Systems 11(1):11-24.e4. DOI: 10.1016/j.cels.2020.05.012
This paper describes a new platform for clinical proteomics, and applies it to COVID19 patient sera, where we identified 27 biomarkers. These not only reflect key pathological features of severe COVID19, but enabled us to classify patients according to the WHO ordinal scale. I have chosen this paper as it demonstrates the translation capacity of the technologies we have developed.

Demichev V, Messner CB, Vernardis SI, Lilley KS, Ralser M. (2020) *DIA-NN: Neural networks and interference correction enable deep coverage in high-throughput proteomics*. Nature Methods 17, 41-44. DOI: 10.1038/s41592-019-0638-x
We developed a computational strategy that can deconvolute data complex mass spectra in high-throughput proteomics. I have chosen this paper as it demonstrates the power of neural networks in deconvoluting complex biological data.

Olin-Sandoval V, Yu JSL, Miller-Fleming L, Alam MT, Kamrad S, Correia-Melo C, Haas R, Segal J, Peña Navarro DA, Herrera-Dominguez L, Méndez-Lucio O, Vowinckel J, Mülleder M, Ralser M. (2019) *Lysine harvesting is an antioxidant strategy and triggers underground polyamine metabolism*. Nature 572(7768):249-253. DOI: 10.1038/s41586-019-1442-6
We describe a new and powerful metabolic anti-stress mechanism. I have chosen this paper as it demonstrates the importance of metabolism in the cellular network that mediates stress tolerance.

Mülleder M, Calvani E, Alam MT, Wang RK, Eckerstorfer F, Zelezniak A & Ralser M. (2016) *Functional Metabolomics Describes the Yeast Biosynthetic Regulome*. Cell 167(2):553-565.e12. DOI: 10.1016/j.cell.2016.09.007
In this paper we described genome scale metabolomic mapping, associating each non-essential gene to its metabolic function. I have chosen this paper as it shows the power of high-throughput approaches in systematically capturing missing gene function.

Alam MT, Zelezniak A, Mülleder M, Shliaha P, Schwarz R, Capuano F, Vowinckel J, Radmanesfahar E, Krüger A, Calvani E, Michel S, Börno S, Christen S, Patil KR, Timmermann B, Lilley KS, Ralser M. (2016) *The metabolic background is a global player in Saccharomyces gene expression epistasis*. Nature Microbiol 1:15030. DOI: 10.1038/nmicrobiol.2015.30
We showed here that metabolism affects gene expression responses across the genome, and largely in a non-linear manner. I have chosen this paper as it shows that metabolism is intrinsically intertwined in the cellular signalling system.