Organizing living matter: the role of phase transitions in cell biology and disease

Dr. Simon Alberti Technische Universität Dresden Center for Molecular and Cellular Bioengineering (CMCB) Biotechnology Center (BIOTEC) Dresden, Germany

My research group aims to elucidate the molecular principles underlying the spatiotemporal organization of the cytoplasm. We are particularly interested in understanding how the cytoplasm changes upon environmental perturbations and stress. Stressed cells undergo controlled changes on many levels to alter their physiology and metabolism. Many of these changes may directly result from alterations in the organization of the cytoplasm. Indeed, our recent work shows that stressed cells form many membraneless compartments in the cytoplasm via a biochemical process known as phase separation. However, the initially beneficial ability to form compartments becomes detrimental with increasing age, because compartment-forming have a tendency to misfold and aggregate and thus are closely tied to aging and the pathogenesis associated with age-related diseases such as amyotrophic lateral sclerosis. Thus, recent efforts in the lab are focused on understanding the molecular links between subcellular organization, membrane-less compartments and age-related diseases.

Selected publications

Jie Wang, Jeong-Mo Choi, Alex S Holehouse, ..., Rohit V Pappu, Simon Alberti, Anthony Hyman. A Molecular Grammar Governing the Driving Forces for Phase Separation of Prion-like RNA Binding Proteins (2018). *Cell*, 174, doi: 10.1016/j.cell.2018.06.006.

Shovamayee Maharana, Jie Wang, ..., Jared Sterneckert, Pavel Tomancak, Anthony Hyman, Simon Alberti. RNA buffers the phase separation behavior of prion-like RNA binding proteins (2018). *Science*, 360(6391) 918-921.

T. M. Franzmann, M. Jahnel, A. Pozniakovsky, J. Mahamid, A. S. Holehouse, E. Nüske, D. Richter, W. Baumeister, S. W. Grill, R. V. Pappu, A. A. Hyman, S. Alberti (2018). Phase separation of a yeast prion protein promotes cellular fitness. **Science**, 359, eaao5654.

M. C. Munder, D. Midtvedt, T. Franzmann, E. Nüske, O. Otto, M. Herbig, E. Ulbricht, P. Müller, A. Taubenberger, S. Maharana, L. Malinovska, D. Richter, J. Guck, V. Zaburdaev, S. Alberti (2016). A pH-driven transition of the cytoplasm from a fluid- to a solid-like state promotes entry into dormancy. **eLife**, 5:e09347

A. Patel, H. K. Lee, L. Jawerth, S. Maharana, M. Jahnel, M. Y. Hein, S. Stoynov, J. Mahamid, S. Saha, T. Franzmann, A. Pozniakovski, I. Poser, N. Maghelli, L. Royer, M. Weigert, E. W. Myers, S. W. Grill, D. N. Drechsel, A. Hyman, S. Alberti (2015). A Liquid-to-Solid Phase Transition of the ALS Protein FUS Accelerated by Disease Mutation. **Cell**, 162(5), 1066-1077.