

Integrative Biology

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Bacterial genetics and structural biology for decoding the ubiquitin code

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Ubiquitin (Ub)-signals virtually regulate all cellular pathways. However, two major challenges impede our ability to identify and characterize associations within ubiquitylation cascades: Ubiquitylation cascades are multiplex, i.e., few E1s, dozens E2s and hundreds of E3s ubiquitylate thousands of substrates. Moreover, many substrates possess more than one cognate E3-ligase. About a hundred deubiquitylases rapidly and efficiently reverse the ubiquitylation. To circumvent these limitations we took an integrating biology approach including structural based *in silico* search, bacterial genetics, biochemical, biophysicals and X-ray crystallography to establish a productive interdisciplinary research. A novel bacterial genetic selection system for ubiquitylation and its utilization in identifying and characterizing new E3s, Ub-receptors and ubiquitylation substrates will be presented. Using bacterial expression of a functional ubiquitylation apparatus we purified and crystallized and determined the structure of an ubiquitylated-Ub-receptor for the first time. We took a multidisciplinary approach and uncovered a novel UBD within this receptor. A surprising function of the Ub-receptor ubiquitylation will be presented. As the findings derived from the genetic selection system we developed and the crystal structure of ubiquitylated-ubiquitin-receptor are still under review so I will share the full result and discussion at presentation time.

Biography

Gali Prag has earned his PhD from the Hebrew University, Israel. With his supervisor Prof. Oppenheim, he has studied bacterial genetics and obtained two EMBO Fellowships to determine the structures of several chitin-degrading enzymes in complex with their native substrates. He has completed his Postdoctoral studies at the NIH with Professor James Hurley, where he determined the first structures of ubiquitin-receptor complexes with ubiquitin and some of the ESCRT complexes. In 2008, he returned to Israel and established a structural-biology and bacterial genetic laboratory in TAU.

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