Name	DAVID BALCHIN
Position	Group Leader (1st 6)
Year joined *(Crick or founder institute)*	2020

Career History

2010-2014: University of the Witwatersrand, South Africa - PhD in Biochemistry
2014-2019: Max Planck Institute of Biochemistry, Germany - Postdoctoral fellow

Major Awards, Honours and Prizes

2015: EMBO long-term fellowship
2019: Max Planck Institute Junior Scientists' Publication Award

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

Lab Name	***Protein Biogenesis Laboratory***

Research programme and achievements

The objective of the recently-established Protein Biogenesis laboratory is to understand how cellular factors cooperate to support the folding of nascent proteins. In particular, we focus on the ribosome as the hub that coordinates protein synthesis, folding, chaperone recruitment and quality control.

In my previous role I studied the mechanisms of molecular chaperones. My major achievements in this time were:

1. Determining how the eukaryotic chaperonin complex directs actin folding.
2. Determining how the novel chaperone Hgh1 interacts with elongation factor 2.
3. Demonstrating that the Hsp70 chaperone system is a catalyst of protein folding.
4. Demonstrating that the bacterial chaperonin cavity is a privileged environment that enables rapid folding of endogenous substrate proteins.

Overall, this work provided key support for the new idea that cellular chaperones actively and specifically modulate the folding energy landscape of their client proteins.

Future/current work in my laboratory is focused on two main areas.

1. *In vitro* reconstitution and biophysical analysis of the machineries of protein synthesis and folding in bacteria, with the aim of understanding how the process of translation shapes the folding pathway of nascent proteins on the ribosome.
2. Using mass-spectrometry based approaches to map the pathways of protein biogenesis in bacteria and human cells. From this we hope to discover how proteins are routed through the chaperone network, and how different nodes in the network contribute to overall folding efficiency.

Research outputs

Balchin, D., Miliĉiĉ, G., Strauss, M., Hayer-Hartl, M., and Hartl, F.U. (2018) *Pathway of actin folding directed by the eukaryotic chaperonin TRiC*. Cell 174:1507-1521. DOI: 10.1016/j.cell.2018.07.006
The TRiC chaperonin interacts with ~10% of the nascent cytosolic proteome, and is uniquely able to support the folding of certain essential proteins with complex topologies. Using actin as a model substrate, we applied a range of biophysical methods to establish the protein-folding mechanism of TRiC. This work also put forward the new idea that chaperones can specifically manipulate the folding pathway of some substrates to allow access to the native state.

Moenkemeyer, L., Klaips, C.L., Balchin, D., Koerner, R., Hartl, F.U. and Bracher, A. (2019*) Chaperone function of Hgh1 in the biogenesis of eukaryotic elongation factor 2*. Mol Cell 74:88-100. DOI: 10.1016/j.molcel.2019.01.034
eEF2 is an abundant and essential translation factor with complex biogenesis requirements *in vivo*. We identified Hgh1 as a novel chaperone that cooperates with the TRiC chaperonin to fold EF2 in yeast. These findings allowed us to propose a pathway for EF2 maturation that links multiple chaperone systems with nascent protein folding at the ribosome.

Imamoglu, R., Balchin, D.*, Hayer-Hartl, M.* and Hartl, F.U.* (* Co-corresponding authors). (2020) *Bacterial Hsp70 resolves misfolded states and accelerates productive folding of a multi-domain protein*. Nat Commun 11:1-13. DOI: 10.1038/s41467-019-14245-4
Hsp70 chaperones are the central hub of the protein homeostasis network in bacteria and eukaryotic cells. By reconstituting Hsp70-dependent protein folding under single-molecule conditions, we discovered that Hsp70 can dramatically accelerate folding of a multidomain protein. These findings imply that folding acceleration may be a fundamental feature of chaperone function that underlies both *de novo* protein biogenesis and recovery from proteotoxic stress.