University of Birmingham

Dr Damon Huber PhD

Birmingham Fellow

School of Biosciences (/schools/biosciences/index.aspx)

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About

Damon Huber is interested in using a combination of biochemistry and molecular genetics to address complex biological problems in bacteria. The research in his lab is focused on the transport of proteins across the cytoplasmic membrane by the Sec machinery in bacteria, protein folding, and the connection between folding and transport. Damon is a Birmingham Fellow who joined the Institute of Microbiology and Infection in 2013 as a joint appointment between the schools of Biosciences (LES) and Immunity and Infection (MDS).

Qualifications

BSc Microbiology, minors in Chemistry and Music (Iowa State University)
PhD Microbiology and Molecular Genetics (Harvard University)

Biography

Damon attended Iowa State University from 1996 to 2000 where he majored in Microbiology and minored in Chemistry and Music. As a student, he worked in the lab of Greg Phillips, who piqued Damon's interest in bacterial genetics. After graduating with his Bachelor's of Science in 2000, he attended Harvard University where he studied bacterial genetics with Jon Beckwith at Harvard Medical School. During his time in Dr Beckwith's lab, Damon developed a fascination for the connection between protein folding and the transport of proteins across biological membranes, and he was awarded a PhD for his work on these subjects in 2006. He subsequently moved to Bernd Bukau's lab at the University of Heidelberg in Germany, where he was an Alexander von Humboldt Fellow. While in Dr Bukau's group, he discovered a novel pathway for the cotranslational recognition of substrate proteins by the Sec translocation pathway. In 2012, Damon was selected for a Birmingham Fellowship, and he moved into the newly created Institute for Microbiology and Infection at the University of Birmingham in 2013.

Postgraduate supervision

Postgraduate students interested in pursuing a Master's or PhD in Damon's group are encouraged to visit **http://www.findaphd.com/search/ProjectDetails.aspx?PJID=43831&LID=124 (http://www.findaphd.com/search/ProjectDetails.aspx?PJID=43831&LID=124)** or to contact him directly by email at **D.Huber@bham.ac.uk (mailto:D.Huber@bham.ac.uk)** .

Research council studentships are available to UK applicants and are awarded yearly by the School of Biosciences on a competitive basis. EU residents of the UK may also be eligible for these studentships. Other sources of funding, including studentships from the Darwin Trust, may be available for international students.

Research

The main pathway for the transport of proteins across the cytoplasmic membrane in bacteria is the Sec pathway. The research in my lab is currently focused on understanding how the Sec pathway recognizes newly synthesized protein substrates and targets them for transport across the cytoplasmic membrane. Research in my lab combines the relative strengths of biochemistry and bacterial genetics to investigate the mechanistic details of Sec-dependent protein transport in Escherichia coli.

The mechanism of cotranslational targeting by the "posttranslational" branch of the Sec pathway by SecA.

The central component of the Sec pathway is an integral membrane protein complex, SecYEG, which forms a channel in the cytoplasmic membrane through which substrate proteins are transported. There are two main branches of the Sec pathway by which substrate proteins are delivered to SecYEG: the posttranslational branch and the cotranslational branch. The posttranslational branch is responsible for the export of the majority of soluble periplasmic and outer membrane proteins in E. coli. However, until recently very little was known about how substrate proteins were recognized by the posttranslational branch. Export of substrates of the posttranslational branch typically begins either very late in the process of protein synthesis or after synthesis is complete, which has led to the widespread assumption that substrate recognition is independent of protein synthesis. (In contrast, substrates of the cotranslational branch are recognized very early in translation by the SRP, and the ribosome is directly coupled to SecYEG.) However, I recently discovered that a component of the posttranslational Sec machinery, the ATPase SecA, binds to the ribosome and appears to play a role in cotranslationally channeling proteins into the "posttranslational" translocation pathway. My lab is currently investigating the details of the molecular mechanism of substrate recognition by SecA.

The role of targeting in the folding of substrate proteins in the periplasm.

The mechanism of delivery to SecYEG can significantly affect the folding of substrate proteins. For example, several recent studies report that cotranslational export of outer membrane proteins can lead to misfolding and defective assembly into the outer membrane. However, the molecular basis for these differences in folding is still unclear. I am interested in understanding how the mechanism of delivery to SecYEG can affect folding of proteins on the periplasmic side of the cytoplasmic membrane.

Other activities

Member of the American Society for Microbiology, the American Chemical Society (Biological Chemistry Division), and American Association for the Advancement of Science (AAAS)

Publications

Oh E, Becker AH, Sandikci A, **Huber D**, Chaba R, Gloge F, Nichols RJ, Typas A, Gross CA, Kramer G, Weissman JS, Bukau B. (2011) Selective ribosome profiling reveals the cotranslational chaperone action of Trigger Factor in vivo. *Cell*. *147*:1295-308.

Huber D, Rajagopalan N, Preissler S, Rocco MA, Merz F, Kramer G, and Bukau B. (2011) SecA interacts with ribosomes in order to facilitate posttranslational translocation in bacteria. *Mol Cell*. *41*:343-53

Mogk A, **Huber D**, and Bukau B. (2011) Integrating Protein Homeostasis Strategies in Prokaryotes. *Cold Spring Harb Perspect Biol*. 3(4). pii: a004366. doi: 10.1101/cshperspect.a004366

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Huber D and Bukau B. (2008) DegP: A Protein Death Star. *Structure*. *16*:989-90

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Huber D and Beckwith J. (2006) Phage Display extends its reach. *Nat Biotechnol*. *24*:793-4

Huber D, Cha M, Debarbieux L, Planson AG, Cruz N, López G, Tasayco ML, Chaffotte A, and Beckwith J. (2005) A selection for mutants that interfere with folding of *E. coli* thioredoxin-1 *in vivo*. ***Proc Natl Acad Sci USA.*** *102*:18872-7

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Schierle CF, Berkmen M, **Huber DR**, Kumamoto C, Boyd D, Beckwith J. (2003) The DsbA signal sequence directs efficient, co-translational export of passenger proteins to the *E. coli* periplasm via the SRP pathway. *J Bacteriol*. *185*:5706-13

Leeds JA, Boyd D, **Huber DR**, Sonoda GK, Luu HT, Engelman DM, Beckwith J. (2001) Genetic selection for and molecular dynamic modeling of a protein transmembrane domain multimerization motif from a random Escherichia coli genomic library. *J Mol Biol*. *313*:181-95

Phillips GJ, Park SK, and **Huber D**. (2000) High copy number plasmids compatible with commonly used cloning vectors. *Biotechniques*. *28*: 400-402, 404, 406

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