Bin Xu

Current Position: Postdoctoral research fellow in Basic Sciences Division at Fred Hutchinson Cancer Research Center in Seattle, Washington

Education: Ph.D. in Biochemistry (2004) from Case Western Reserve University in Cleveland, Ohio (mentor: Professor Michael A. Weiss)

Non-scientific Interests: Travel, sports, nature

I have long been interested in structural mechanisms in biology. However, it was not until I joined the laboratory of Professor Michael Weiss to pursue a Ph.D. (my thesis: "How Insulin Binds to the Insulin Receptor") that I began to understand how fascinating the mechanisms of receptor recognition could be. At the time that I started this work, extensive structural studies of insulin had already been described, both in classical crystallographic literature and more recently by NMR. Together, these had provided significant insights into structure-function relationships, and yet the central mystery of how insulin binds to its receptor was unsolved.

I was fortunate to join the laboratory of Professors Weiss and Panoyatis Katsoyannis (Mt. Sinai School of Medicine, NY) when they initiated an approach based on chemical biology—systematic probing of functional surfaces of insulin by "photo-scanning mutagenesis." This required the construction of an extensive set of synthetic azido-derivatives of the hormone. Over the course of this study, we encountered many exciting moments, generated by novel and intriguing—sometimes even striking—findings. Progress was advanced by development of a rapid and convenient method for mapping photo-products. With this method in hand, we identified an unusual feature of receptor recognition: alternating contacts by the B-chain β-strand of insulin. Such alternation not only revealed that consecutive residues in insulin contact widely separated sequences in the receptor, but also implied that the B-chain β-strand acts as an "arm" to insert between receptor domains. A beautiful coherence emerged from the mutual relationship between these data and the anomalous structural effects of D-amino-acid substitutions at the base on this β-strand, whereby segmental unfolding enhances biological activity, as shown by Dr. Qing-xin Hua and colleagues in the companion paper.

Together, these two papers demonstrate that insulin employs a detachable arm to augment receptor binding and highlight the multiple levels of selection that constrain protein evolution. The utility of photo-scanning in decoding the active conformation of insulin may encourage use of this method in other receptor-ligand systems refractory to conventional structural methods.

I am now a postdoctoral fellow at Fred Hutchinson Cancer Research Center, working on structural biology of innate immune receptors and their viral decoys.

Read Dr. Xu's articles:

Enhancing the Activity of a Protein by Stereospecific Unfolding: *Conformational Life Cycle of Insulin and Its Evolutionary Origins* … http://www.jbc.org/cgi/content/full/284/21/14586

Decoding the Cryptic Active Conformation of a Protein by Synthetic Photoscanning: *Insulin Inserts a Detachable Arm Between Receptor Domains* … http://www.jbc.org/cgi/content/full/284/21/14597