

## About the Axelrod Lectures



**D**r. Bernard Axelrod served as Head of the Department of Biochemistry and is currently Professor Emeritus. His efforts were instrumental in founding the biochemistry program at Purdue University. On the occasion of his 70th birthday, colleagues and friends established this lectureship in honor of Dr. Axelrod's many contributions to the field of biochemistry and its community of scientists.

### Previous Speakers in the Bernard Axelrod Lecture Series

2009	Lee Hood	Institute for Systems Biology
2008	Jasper Rine	University of California, Berkeley
2007	Olke Uhlenbeck	Northwestern University
2005	Carol Greider	Johns Hopkins University of Medicine
2003	Stephen Kent	University of Chicago
2001	Winslow Briggs	Carnegie Inst. of Washington at Stanford University
2001	Gregory A. Petsko	Brandeis University
1997	Klaus Hahlbrock	Max Planck Institute, Germany
1997	Aziz Sancar	University of North Carolina
1995	Paul Nurse	Imperial Cancer Research, London
1995	Danny Reinberg	Robert Wood Johnson Medical School

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The Department of Biochemistry

Presents

The Bernard Axelrod Lectures 2010

October 18—October 19



Robert T. Sauer

Department of Biology

Massachusetts Institute of Technology

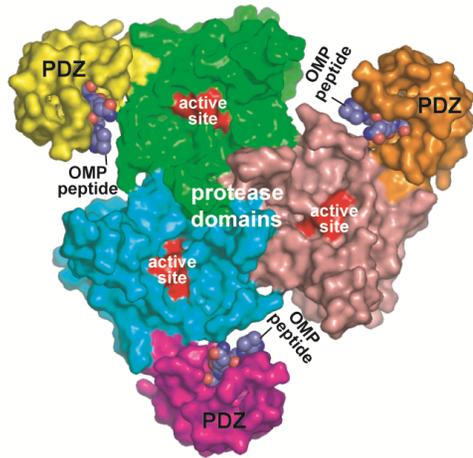
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## Brief Biography

Dr. Sauer is currently the Salvador Luria Professor of Biology at the Massachusetts Institute of Technology, where he has been a faculty member since 1978 and has served as Head of the Department of Biology. After growing up in the Hudson River Valley of New York, he received his undergraduate education at Amherst College (Biophysics) and his Ph.D. training at Harvard University (Biochemistry and Molecular Biology). Using the tools of protein biochemistry, molecular genetics, and structural biology, his lab has studied protein-DNA interactions, protein folding and stability, and most recently, mechanisms of intracellular protein degradation. Bob has coauthored ~300 scientific papers. His honors include the Hans Neurath Award of the Protein Society and election to the National Academy of Sciences and the American Academy of Arts and Sciences.

## “Regulation of the activities of allosteric proteases”

Monday, October 18 at 4:00 PM  
Deans Auditorium, PFEN



Proteases are ubiquitous enzymes that destroy proteins by cleaving their polypeptide chains. In cells, proteases function to maintain protein-quality control and serve as components of regulatory networks. Because proteolysis is irreversible, degradation must be highly specific and carefully regulated. In this talk, I will describe the structure and function of DegS and DegP, which are related periplasmic proteases of *E. coli*. DegS is a sensor protease. Following activation by specific molecular signals that accumulate during envelope stress, it initiates a transmembrane proteolytic

cascade that results in transcription of stress-response genes. DegP is the major sentinel of quality control in the periplasm. In the presence of appropriate unstructured substrates, it assembles into proteolytic cages in which these polypeptides are degraded. Both enzymes contain a trypsin-like protease domain, one or two PDZ domains, and form trimers or higher oligomers. Despite their diverse functions, the mechanisms of allosteric activation of DegS and DegP are highly conserved and require coupling between distinct sequence signals, one which binds to the first PDZ domain and one which binds to the protease domain. In addition, DegS proteolysis is negatively regulated by a second system that responds to defects in LPS biosynthesis and transport to the outer membrane.

## “ATP-fueled proteolytic machines”

Tuesday, October 19 at 4:00 PM  
Deans Auditorium, PFEN

AAA+ family proteolytic machines perform protein-quality control and are used in regulatory circuits in the cytoplasm of bacteria, archaea, and eukaryotes. These machines contain a compartmental protease, with active sites sequestered in an interior chamber, and a hexameric ring built of AAA+ ATPases. Substrate proteins are tethered to the ring, either directly or by adaptor proteins. An unstructured region of the substrate is engaged in the axial pore of the AAA+ ring, and cycles of ATP binding/hydrolysis drive conformational changes that create pulses of pulling that denature the substrate and translocate the unfolded polypeptide through the pore and into the proteolytic chamber for degradation. In this talk, I will discuss our current understanding of the molecular mechanisms that regulate substrate recognition, adaptor function, and ATP-fueled unfolding and translocation for several bacterial AAA+ proteases, including ClpXP and Lon. Efficient proteolysis of many substrates requires coupled recognition of two or more weak degradation signals, often assisted by adaptor proteins. The need to couple the binding energies of inherently weak degrons allows simple sequences to serve as individual degradation signals, allows efficient evolutionary mixing and matching of degrons, and allows proteolysis to be regulated by controlling the way in which these signals are displayed in native proteins or unfolded polypeptides.

