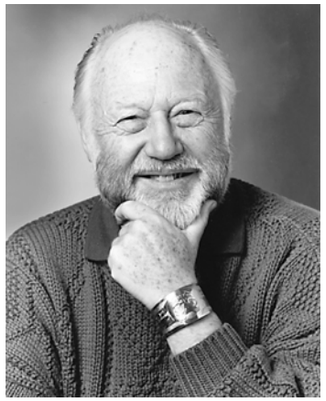

Nobel Prize-winning chemist **Dr. Michael Smith** will be remembered as a great humanitarian who was passionate about research and science. Michael Smith received his PhD in 1956 from the University of Manchester and then undertook his post-doctoral studies with Har Gobind Khorana at the British Columbia Research Council in Vancouver, Canada. In 1966 he was appointed as a Professor of Biochemistry in the UBC Faculty of Medicine. Michael Smith enjoyed a long and productive research career at the University of British Columbia. In addition to being an MRC Career Investigator, he was the founding Director of the Biotechnology Laboratory from 1987 to 1995.

In 1993, Dr. Michael Smith received the Nobel Prize for his development of site-directed mutagenesis, a technique which allows the DNA sequence of any gene to be altered in a designated manner. He donated half of the Nobel Prize money to researchers working on the genetics of schizophrenia, a widespread mental disorder for which research money is scarce. The other half he gave to Science World BC and to the Society for Canadian Women in Science and Technology.

Michael Smith was a distinguished and creative scientist, a humble man known for his humanity. He gave generously to the people of Canada and the world, using his time and energy to reach out to audiences with his message about the importance of science to everyone's life.

10th Annual Michael Smith Distinguished Research Lecture

Presenting

Dr. Robert T. Sauer

Luria Professor of Biology
Massachusetts Institute of Technology

Machines of Protein Destruction

Monday, December 8, 2014 at 4:00pm

Life Sciences Centre
Lecture Theatre #1
2350 Health Sciences Mall

Sponsored by the Michael Smith Laboratories and the Department of Biochemistry and Molecular Biology

UBC

michael smith laboratories

Machines of Protein Destruction

During protein degradation by the ClpXP and ClpAP proteases, hexameric AAA+ unfoldases (ClpX or ClpA) use the energy of ATP binding and hydrolysis to power conformational changes necessary for the mechanical denaturation and translocation of protein substrates into the chamber of ClpP, a self- compartmentalized peptidase. Using a combination of single-molecule studies, solution biochemistry and biophysics, protein engineering and mutagenesis, and X-ray crystallography, we are trying to understand how these fascinating molecular machines work at a detailed molecular level. Our experiments support a power-stroke model of denaturation in which successful enzyme-mediated unfolding of stable domains requires coincidence between mechanical pulling by the enzyme and a transient stochastic reduction in protein stability. We find that ClpA is a more powerful unfoldase than ClpX, apparently because the double-ring ClpA enzyme can grip substrates more tightly than the single-ring ClpX protein. In crystal structures, some ClpX subunits adopt nucleotide-loadable conformations, whereas others adopt unloadable conformations. We find that dynamic interconversion between loadable and unloadable conformations is required to couple ATP hydrolysis by ClpX to mechanical work, possibly as a fail safe to circumvent machine stalling. Interestingly, ATP hydrolysis by different subunits in the ClpX ring does not occur by an ordered or sequential mechanism, but rather by a probabilistic or stochastic mechanism.

Dr. Robert T. Sauer

Luria Professor of Biology

Massachusetts Institute of Technology

I grew up in a working-class town in the Hudson-River valley in New York, interested in science and how “things” work. I attended Amherst College, graduating with a degree in biophysics, and worked as a research technician at Mass General Hospital in Boston, where I first learned and became interested in protein biochemistry. I attended grad school at Harvard University, where I learned molecular biology. I joined the MIT faculty in 1978 and have been there since then. Over the years, my lab has worked on protein-DNA interactions, how proteins fold and unfold, and how ATP-dependent molecular machines destroy proteins and re-sculpt the cellular proteome. My honors include election to the National Academy of Sciences (1996), the Hans Neurath Award (2008), and the Stein and Moore Award (2013).