



Stephen Kowalczykowski

University of California, Davis
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Dr. Stephen Kowalczykowski majored in chemistry at Rensselaer Polytechnic Institute, and subsequently received his Ph.D. in chemistry and biochemistry with Dr. Jacinto Steinhardt at Georgetown University. His postdoctoral training was with Dr. Peter von Hippel at the University of Oregon. Dr. Kowalczykowski started his independent faculty career in 1981 at Northwestern University Medical School. In 1991, he relocated to the University of California at Davis with the rank of Full Professor. He subsequently served as the Chair of Microbiology and the Director of the Center for Genetics and Development; currently, he is a

Distinguished Professor of Microbiology & Molecular Genetics, and of Molecular & Cell Biology. Dr. Kowalczykowski's honors include election to the National Academy of Sciences (2007), the American Academy of Arts and Sciences (2005), the American Academy of Microbiology (2003), and the American Association for the Advancement of Science (2001). Professor Kowalczykowski's research focuses on exploring the principles that govern DNA recombination, and how that process contributes to genomic integrity; he has published over 200 papers in this area. His research programs focus on the biochemical mechanisms of recombinational DNA repair; the function of homologous recombination in genome maintenance; the functions of DNA helicases, such as BLM and WRN; single-molecule biophysical analysis of protein-nucleic acid interactions; and roles of BRCA1, BRCA2, and RAD51 in the molecular etiology of breast cancer. The single-molecule approaches permit visualization of enzymes functioning in real-time and provide novel insights into protein behaviors.

Abstract: Watching and Understanding DNA Recombination and Replication, One Molecule at a Time

It is now possible to image individual proteins acting on single molecules of DNA. Such imaging affords unprecedented interrogation of protein-nucleic acid interactions that are essential for chromosome maintenance. We have watched proteins functioning in the recombination, replication, repair, and manipulation of DNA.

Visualization is achieved through the application of two complementary procedures. In one, a single DNA molecule is attached to a polystyrene bead which is captured in an optical trap. The DNA is extended either by the force of solution flow in a micro-flowcell, or by capturing the opposite DNA end in a second optical trap. In the second procedure, DNA is attached by one end to a glass surface. The coiled DNA is elongated either by continuous solution flow or by subsequently tethering the opposite end to the surface. Proteins and DNA are visualized via fluorescent reporters. Individual molecules are imaged using either epifluorescence microscopy or total internal reflection fluorescence (TIRF) microscopy. Molecules are introduced and supramolecular complexes are built, one component at a time, using microfluidic flowcells.