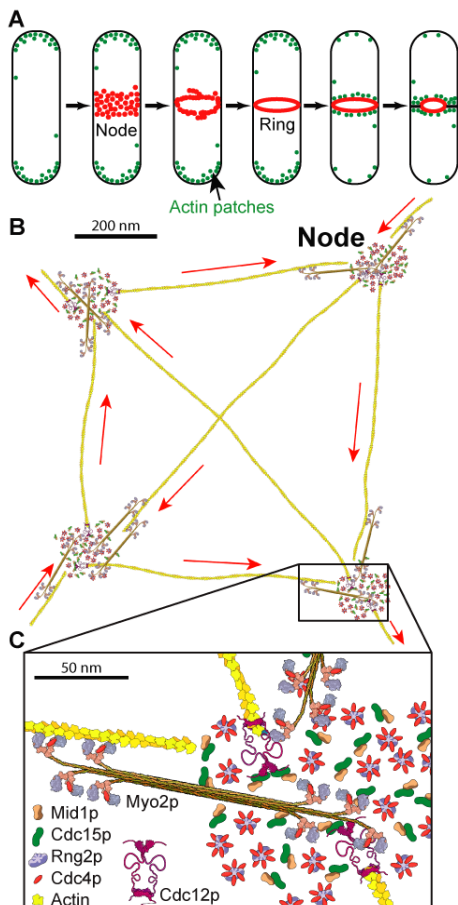


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**The long-term goal of my laboratory is to understand the roles of cytoskeletal and signaling proteins in cellular asymmetry and cell division in normal and cancer cells. In the near term, I am focusing on the molecular mechanisms of cytokinesis in the fission yeast *S. pombe*.** Cytokinesis partitions cellular constituents into two new daughter cells at the end of the cell cycle. When coordinated with the generation of cellular asymmetry, cytokinesis can produce diverse cell types in multicellular organisms. Thus, cytokinesis plays a crucial role in both cell proliferation and cell differentiation.

Contractile rings consisting of actin filaments and myosin-II motor proteins are the common machinery for cytokinesis and other processes including erythrocyte enucleation, morphogenetic epithelial closure, epithelial wound healing, and apoptotic cell extrusion. Furthermore, increasing amounts of evidence suggests that muscles and contractile rings share many common features in composition, assembly, and contraction. It would seem that the ancient cytokinetic contractile ring has been evolutionarily adapted for a variety of cellular functions. Thus, studying contractile-ring assembly, constriction, and function in cytokinesis will also help us to understand these other cellular processes. For example, homologs of several proteins involved in cytokinesis have been implicated in tumors and other human diseases. Thus, studying roles of these proteins in cytokinesis will contribute to the understanding of the pathogenesis and eventual cure of cancer and other human diseases.



The fission yeast *S. pombe* has emerged as an important model system for the analysis of cytokinesis. Not only is it genetically tractable and favorable for microscopic analysis, but it also has highly efficient homologous recombination, a small (13.8 Mb) and fully sequenced eukaryotic genome, and perhaps most importantly, it carries out cytokinesis much like animal cells. The majority of proteins involved in cytokinesis are evolutionarily conserved and thus much of what we learn about these proteins in the fission yeast *S. pombe* is applicable to human cells. Beginning with Paul Nurse's pioneering work on the cell cycle, geneticists have identified >50 evolutionarily conserved genes contributing to cytokinesis in *S. pombe*, but we still do not know how they cooperate during cytokinesis.

My previous research has established the temporal pathway for the assembly and constriction of the contractile ring in fission yeast (Wu et al., *Dev. Cell*, 2003). We measured the global and local concentrations of 28 cytokinetic proteins (Wu et al., *Methods in Cell Biol.*, 2008; Wu and Pollard, *Science*, 2005). We also discovered "nodes" (each containing at least seven proteins) as precursors for the contractile-ring assembly by a lateral contraction mechanism (Wu et al., *J. Cell Biol.*, 2006, Fig. 1). To test my lateral contraction model rigorously, we used high spatio-temporal resolution microscopy and mathematical modeling to study

the assembly of the contractile ring. We found that nodes condense into a contractile ring through a search, capture, pull, and release mechanism (Vavylonis and Wu et al., Science, 2008; Co-first author).

During the next several years, my laboratory will continue to work on the molecular mechanism of cytokinesis in *S. pombe* using a combination of cellular, molecular, biochemical, genetic, and microscopic approaches. In the long term, I also plan to apply our knowledge of cytokinesis to other systems by studying orthologs of fission yeast cytokinesis proteins in cancer cells. I hope that some of these genes/proteins will become novel targets for cancer therapy and treating other human diseases.

Dr. Wu has a joint appointment in the Department of Molecular and Cellular Biochemistry, College of Medicine, OSU.