

Myers, S.A., J.W. Han, Y. Lee, R.A. Firtel and C.Y. Chung (2005). A *Dictyostelium* homologue of WASP is required for polarized F-actin assembly during chemotaxis. *Mol. Biol. Cell* 16:2191-2206.

The actin cytoskeleton controls the overall structure of cells and is highly polarized in chemotaxing cells, with F-actin assembled predominantly in the anterior leading edge and to a lesser degree in the cell's posterior. Wiskott-Aldrich syndrome protein (WASP) has emerged as a central player in controlling actin polymerization. We have investigated WASP function and its regulation in chemotaxing *Dictyostelium* cells and demonstrated the specific and essential role of WASP in organizing polarized F-actin assembly in chemotaxing cells. Cells expressing very low levels of WASP show reduced F-actin levels and significant defects in polarized F-actin assembly, resulting in an inability to establish axial polarity during chemotaxis. GFP-WASP preferentially localizes at the leading edge and uropod of chemotaxing cells and the B domain of WASP is required for the localization of WASP. We demonstrated that the B domain binds to PI(4,5)P₂ and PI(3,4,5)P₃ with similar affinities. The interaction between the B domain and PI(3,4,5)P₃ plays an important role for the localization of WASP to the leading edge in chemotaxing cells. Our results suggest that the spatial and temporal control of WASP localization and activation is essential for the regulation of directional motility.