

Structure of EVH1, a Novel Proline-Rich Ligand-Binding Module Involved in Cytoskeletal Dynamics and Neural Function

S. Almo and A. Federov (Albert Einstein College of Medicine) and F. Gertler (MIT)

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Diverse cellular processes such as cell motility, neuronal growth cone migration, focal adhesion formation and cytokinesis depend on regulated, coordinated site-specific assembly of multiprotein complexes that ultimately govern the dynamics of the actin cytoskeleton. A large repertoire of protein–protein interaction modules, including SH2, SH3, WW, pleckstrin homology (PH) and phosphotyrosine-binding (PTB) domains, mediate the formation and targeting of these assemblies and integrate them into the overall physiology of the cell. Vasodilator-stimulated phosphoprotein (VASP), enabled gene product from *Drosophila* (Ena), mammalian enabled (Mena) and Ena/VASP-Like protein (EVL) belong to a family of proteins, the ‘Ena/VASP’ family, that localize to focal adhesions and to sites of actin filament dynamics such as lamellipodia and neuronal growth cone filopodia. Genetic studies have identified roles for Mena and Ena in axon guidance and for VASP in the regulation of platelet aggregation, while assays in cell-free systems have demonstrated that Ena/VASP proteins are required for the actin-based motility of the bacterial pathogen *Listeria monocytogenes*.

The Ena-VASP homology (EVH1) domain is a protein interaction module that specifically recognizes proline-rich sequences in its binding partners and directs the localization and formation of multicomponent assemblies involved in actin-based motile processes and neural development. The structure of the complex between an EVH1 domain and the target peptide sequence EFPPPPT, solved based on MAD data collected on resource beamline X9B, identifies the interactions responsible for recognition and distinguishes it from other proline binding modules, including SH3 and WW domains.