Aim of this work

For many processes in our body, including the growth of nerve cells in embryonic development, the migration of cells upon injury or the replacement of old tissue, cells have to be able to change their shape. This is achieved by the actin cytoskeleton and regulated by growth and breakdown of actin fibres. An important protein involved in regulating the growth of actin fibres is called VASP (Vasodilator Stimulated Phosphoprotein). It inhibits a process known as capping, that would otherwise terminate the growth of fibres. An investigation of the function of VASP is of major interest for the understandiung of actin dynamics.

VASP is also involved in infections with the pathogenic bacterium *Listeria monocytogenes*, which may be introduced by decaying food, especially fowl. These infections can be lethal, especially for immunocompromised people. The protein ActA is presented on the surface of *Listeria*. it contains the amino acid sequence motif SFEFPPPPTEDEL, which is bound by VASP. This allows *Listeria* to recruit the cell's actin machinery to its back pole and thus propel itself through the cell.

VASP is involved in a network of protein-protein interactions, mediated by its N-terminal EVH1 domain, a central proline rich region and an F-actin binding domain. The C-terminus of VASP is formed by a coiled coil domain. VASP interacts with proline rich sequence motifs as present in ActA via its N-terminal EVH1 domain (amino acids 1-115). It recognizes sequences containing the sequence motif FPxϕP. This motif occurs in the cellular proteins zyxin and vinculin, as well as in ActA. Therefore new ligands for the VASP EVH1 domain should be developed that allow the targeted modulation of interactions of this domain with its ligands. Ligands of this type would be useful in investigations of the actin cytoskeleton and as drugs in Listeriosis treatment.

For a better understanding of ligand specificities of the VASP EVH1 domain the investigation of the structure and binding properties of other EVH1 domains will be helpful. Hence attention turned to the recently described family of Spred proteins which conatin an N-terminal EVH1 domain. Like VASP the Spred proteins are localised in the cytosol. They are involved in the regulation of the Ras/Raf signal transduction pathway.

Sequence comparison with other known EVH1 domains showed important differences in regions relating to protein ligand interactions. The structure of the human Spred2 EVH1 domain was to be determined, and conclusions drawn on its ligand specificity.

The properties of the C-terminal coiled coil EVH2 domain of VASP are important for the function of the EVH1 domain and its interactions with other proteins due to the oligomerisation mediated by the EVH2 domain (amino acids 336-380). The degree of oligomerisation (dimer, trimer, tetramer) as well as the relative orientation of monomers (parallel, antiparallel) are of interest. Therefore the oligomerisation behaviour and the strucure of the EVH2 domain were investigated