6. SUMMARY

The cytokine IL-16 is a CD4 ligand with proinflamatory, immunoregulatory and antiretroviral properties. Like many other cytokines, IL-16 is synthesised as a precursor protein (pro-IL-16) and processed by caspase-3. Pro-IL-16 is a 67 kDa protein expressed in cells of the immune system. Part of the amino terminal region comprises conserved SH3-binding domains and the C-terminal region contains three PDZ domains, one fragment of which forms the secreted IL-16. The aim of this work was to identify additional interaction partners of pro-IL-16, knowledge of which would allow the functions of pro-IL-16 and IL-16 to be further elucidated.

Using YTH-screening, the closely related F-actin binding proteins HS1, Abp1, Lasp1 and cortactin were shown to interact with the proline rich region of pro-IL-16. The interaction between pro-IL-16 and a further binding partner, the microtubulin binding protein Hook3, was not investigated further. The interaction of HS1, Abp1, Lasp1 and cortactin with pro-IL-16 was verified using YTH specificity tests and co-immunoprecipitation experiments confirmed the interaction between HS1 and pro-IL-16. By substituting proline with alanine in both PXXP-motifs of the pro-IL-16 proline-rich region and by cloning SH3 deletion mutants, it was possible using *in vitro* binding assays to confirm the binding of the HS1 protein SH3 domain to the N-terminal PXXP motif of pro-IL-16. The binding of endogenous IL-16 to HS1 was also confirmed by immunoprecipitation. The colocalisation of HS1 and pro-IL-16 and molecular complexes of the cytoskeleton was demonstrated by immunofluorescence microscopy.

Because the interacting partners identified, HS1, Abp1, Lasp1 and cortactin, are F-actin binding proteins involved in the modulation of actin assembly, the possible involvement of pro-IL-16 in the organisation of the immunological synapse is under investigation.