6. Summary

Ror2 is a membrane-bound receptor tyrosine kinase, which belongs to the family of Ror proteins. Ror2 has been implicated in chondrogenesis as shown by the severe chondrodysplasia phenotype in Ror2 knock out mice. Mutations in ROR2 have been described to be responsible for autosomal dominant brachydactyly type B and the autosomal recessive Robinow syndrome. However, protein interactions and signalling pathways in which Ror2 participates remain poorly understood to date.

In this study the cytoplasmatic part of Ror2 was used to perform yeast two hybrid- and yeast three hybrid assays. Screening was performed against a cDNA library obtained from mouse embryos stage E9.5 to E10.5. In both screens 23 potential Ror2 interaction partners have been identified, two of them have been further investigated. In this study Dlxin-1 is the most frequently identified interaction partner of Ror2. The interaction between Ror2 and Dlxin-1 was mapped to the distal part of Ror2. Dlxin-1 itself has recently been identified as a Dlx5 interaction partner. Since Dlx5 is known to act as a positive regulator of chondrocyte differentiation it is tempting to speculate that binding of Dlxin-1 to Ror2 can modulate subcellular localisation and transcriptional properties of Dlx and Msx proteins to fine-tune chondrocyte differentiation and maturation.

In addition, Wtip was identified as a novel potential interaction partner of Ror2. Wtip is a LIM domain containing protein with three C-terminal LIM domains. The fragment isolated in the screen showed that interaction with Ror2 is mediated through the first two LIM domains, whereas the third domain seems to be dispensable. Binding to Ror2 occurs at the distal part of Ror2 as demonstrated by retransformation studies in yeast und co-immunoprecipitation in HEK293 cells. In whole mount and section *in situ* hybridisations co-expression of Wtip and Ror2 could be shown in several tissues and organs (e.g. limb buds, kidneys, lung, heart, tooth anlagen). But more importantly co-expression of both proteins could also be demonstrated in the same cells in kidney, lung, intestine and rib condensations by antibody stainings. These results support the idea that interaction between Ror2 and Wtip could also be of relevance *in vivo*. Since Wtip has been identified only recently, it is hard to speculate about the function of an interaction between Ror2 and Wtip. However, Wtip as other members of the same subfamily of proteins, have been shown to shuttle between cytoplasm and nucleus to modulate the function of transcriptional regulators. Further experiments will have to clarify if Ror2 plays a role in this process and if Wtip is able to mediate Ror2 functions in the nucleus.