SUMMARY

Pumilio family members function as posttranscriptional regulators of gene expression in many organisms. Their PUF RNA-binding domain recognizes PBE (***P**umilio **B**inding **E**lement*) motifs in 3'UnTranslated regions (3'UTR) of mRNAs and recruits protein cofactors, such as nanos protein, in the fruit fly germ cells. The resulting ribonucleoprotein complexes, dependent on their composition, direct individual mRNAs towards degradation, storage in P-bodies or specific localization. However the precise mechanism of cooperation between pumilio proteins and their protein cofactors in that regulation is still to be defined. This dissertation describes a novel mRNA which is under PUMILIO1 and PUMILIO2 protein repression in human cells - *SIAH1*. This mRNA encodes an E3 ubiquitin ligase acting as a tumor suppressor. According to preliminary *in vitro* results the PUF domain of PUMILIO2 specifically interacts with PBE-like motifs in the 3'UTR of *SIAH1* mRNA, while NANOS proteins stabilize this interaction within ribonucleoprotein effector complex. Here, in *vitro* studies were confirmed by using luciferase reporter constructs encoding 3'UTR of *SIAH1* mRNA fused to luciferase ORF and by overexpression of PUMILIO and NANOS proteins in human cells. Moreover, by using RNAi technology it was shown that both PUMILIO were necessary for that regulation. Interestingly, although both PUMILIO were required, PBE-like motifs were needed only for PUMILIO2 to control repression of *SIAH1* mRNA while PUMILIO1 protein was insensitive, as shown by site directed mutagenesis. Possibly, PUMILIO1 recognizes different motifs or uses a different mechanism than PUMILIO2 to control *SIAH1* mRNA repression. To the best of our knowledge, this is the first example showing that PUMILIO1 and PUMILIO2 may use different scenarios to repress a specific mRNA. Evolutionary conserved NIM region of NANOS proteins recently described as necessary for recruitment of deadenylation CCR4-NOT complex is important only for NANOS3, in *SIAH1* mRNA regulation. Mutations of *NANOS* genes previously shown as associated with human infertility caused derepression of *SIAH1* mRNA, as demonstrated by luciferase assays. Thus, detrimental effect of mutated NANOS proteins on human germ cells could be caused by their inability to control mRNAs which are necessary for germ cell development. In anti-PUMILIO2 immunoprecipitates several miRNAs with potential binding sites in *SIAH1* 3'UTR where identified. They may act in *SIAH1* mRNA regulation together with PUMILIO and NANOS. Importantly, here it was shown for the first time that diverse mechanisms of posttranscriptional gene regulation by PUMILIO as well as NANOS paralogues are in place to control individual mRNAs. Hence, ability to form six different types of PUMILIO/NANOS complexes reflects an amazing versatility of those protein partners in posttranscriptional gene expression regulation. These results provide an interesting issue for future studies.