Chapter 8

Conclusion
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Results obtained from the study confirm the differentiation of mouse embryonal carcinoma cells PCC4 by heat shock. Upon heat stress PCC4 cells stop dividing and terminally differentiate into endodermal lineage. It appears that cell cycle arrest along with specific HSP expression might be responsible for the differentiation.

Expression of p21 and LaminA indicates cells cycle arrest and cell plasticity, AFP, tPA and HSP 47 confirm the endodermal lineage of differentiation. Genes identified by the differential display reconfirm the process of differentiation. Cullin4A and Cullin4B randomly identified from the DD play screen might not be solely responsible for the differentiation but definitely play important role during differentiation.

Chapter 3 describes the characterization of Cul4A and Cul4B gene. Cul4A and Cul4B are very similar genes present on two different chromosomes and code for the two different proteins. Cul4B appears to function in the nucleus also as it is translocating into the nucleus with the help of NLS present in the unique N-terminus of Cul4B, whereas Cul4A is present only in the cytoplasm, especially during PCC4 cell differentiation.

In chapter 5 I have described the correlation between the Cul4B expression and β-catenin amounts. Cul4B is upregulated whereas β-catenin is downregulated during PCC4 cell differentiation. β-catenin is present abundantly in the stem and embryonal carcinoma cells and it's down regulation is an important event during the process of differentiation. This is also true in the case of PCC4 differentiation. Upregulation of Cul4B corresponding to β-Catenin down regulation is not a mere coincidence; RNAi and co-immunoprecipitation experiments suggest that β-Catenin and Cul4 are part of the same complex and changes in levels of Cul4B effect β-catenin.
Experiments done with *Drosophila* also corroborate the results obtained with mammalian cells. Larval lethality of dCul4 mutants and earlier report that Cul4A knockout mouse is embryonic lethal, suggests a conserved and important role for Cul4 during embryonic development, throughout evolution.