# Stem Cell Biology and Developmental Biology

Stem cell research is a rapidly expanding discipline, focused on understanding how undifferentiated cells, stem cells, can differentiate to become various specialized cell types. Rapid progress is made in our understanding of both embryonic and adult stem cells, and the molecular mechanisms underpinning their differentiation to various fates. In a longer perspective, stem cell research will have considerable impact on regenerative medicine.

At Karolinska Institutet, a Strategic Research Center has been in operation since 2003. The aim of this center, called CEDB (Center of Excellence in Developmental Biology) is to conduct research in stem cell biology and developmental biology at the international frontline. CEDB is composed of 13 different research groups, see homepage www.cedb.se, which are at the forefront in different research areas, and which possess complementary expertise, providing synergy and fosters interdisciplinary approaches. CEDB was recently internationally evaluated and received a ranking at the highest level, with the comments "This group of scientists has established itself as one of the best concentrations of developmental neurobiologists in Europe". CEDB has a strong international network of collaborations, and have for example co-organized a course in Developmental Biology with NUS in 2004.


CEDB has a total staff of approximately 100 scientists, including more than 40 PhD students and 40 postdocs. The Center offers a stimulating and close-knit intellectual environment with weekly intra-center seminars and a strong experimental "tool box" for research in stem cell and developmental biology.

Some of the prioritized research areas in CEDB are cell fate decisions in the neural crest, the role of neurotrophin receptors in cell differentiation, and the role of the Notch signaling pathway. Below, a brief description about three PhD projects in these areas is shown:

## Examples of three potential PhD projects:

***1. Sensory neurons***

The dorsal root ganglion is derived from the neural crest, which is technically and conceptually an attractive model system in which to address cell fate commitment. Cell fate decisions and phenotypic differentiation result from the integration of distinct sets of intrinsic transcriptional programs with signaling pathways activated by extrinsic cues provided by local organizing centers. Induction of the neural crest in the neural plate and segregation of postmigratory neural crest into different lineages are under strict spatio-temporal control by signals from adjacent somites and the spinal cord. The goal of this PhD program is to elucidate when and how instructive cues such as RA, FGFs, BMPs and Wnts emanating from these tissues integrate to establish functionally different subtypes of sensory neurons (pain, touch, cold, heat, etc) by directing subtype-specific gene transcriptional programs.

***2. The p75 neutrophin receptor***

This PhD project concerns the role of signaling by the p75 neurotrophin receptor (p75ntr) in stem cell proliferation and differentiation. p75ntr is highly expressed in ES cells, and in asub-population of SVZ neural stem cells with high neurogenic potential. We have discovered a new intracellular interactor of p75ntr whose overexpression and knock-down has effects on differentiation of PC12 cells and SVZ precursors, and one important goal of this PhD program is to elucidate the role of this new p75ntr interactor.

***3. The Notch signaling pathway***

The aim of this PhD project is to further elucidate the role of the Notch signaling pathway at the molecular level and in ES cell differentiation. Notch signalling plays an important role in many cell fate decisions, and in most cases acts to maintain an undifferentiated state. In this project, we wish to explore how this occurs in mouse ES cells, and how different levels of Notch signalling (by gain-of function or loss-of-function approaches) relate to the transcriptome. We also wish to explore the molecular basis of the DNA-binding protein CSL (RBP-Jk) as a repressor when not activated by Notch.

## For more information on the Stem Cell Biology projects, please contact:

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