# Defining the transcription factors code directing sensory lineage diversification and connectivity

## Rendicontazione

Informazioni relative al progetto

**SENSORY NEURONS CODE**

ID dell'accordo di sovvenzione: 219333

Progetto chiuso

**Data di avvio**
2 Febbraio 2009

**Data di completamento**
1 Settembre 2010

**Finanziato da**
Specific programme "People" implementing the Seventh Framework Programme of the European Community for research, technological development and demonstration activities (2007 to 2013)

**Costo totale**
€ 178 454,93

**Contributo UE**
€ 178 454,93

**Coordinato da**
KAROLINSKA INSTITUTET
Sweden

# Final Report Summary - SENSORY NEURONS CODE (Defining the transcription factors code directing sensory lineage diversification and connectivity)

Contact with the external world is conveyed through peripheral sensory neurons that terminate in

specialised structures located in the skin, muscles and organs of the body. Neurons of the dorsal root ganglion (DRG) mediate tactile sensation, limb proprioceptive sensation and pain sensation. The mechanisms leading to the generation of different types of sensory neurons remains only partly understood.

Objective 1: Identify Cux2 as a new partner in the transcription factors network involved in emergence of neuronal diversification

Cux2 is a novel marker of DRG sensory neurons subpopulations. In particular, it is expressed in some TrkA+ neurons arising during early neurogenesis. Postnatally, Cux2 marks a specific subtype of A-delta nociceptors. Analysis of Cux2 mutant mice show that Cux2 is not required for specification of Trk+ subpopulations. However, Cux2 mutant mice are hypersensitive to mechanical stimuli. Hence, our results show that Cux2 is expressed and may participate in development of a specific subtype of myelinated TrkA+ nociceptors. Our results are soon to be published in 'Developmental Biology', indicating that the objective has been met with success.

The present project increases the knowledge of the general principles of cell type specification. Understanding development of sensory neurons subtypes are particularly important for generating large number of a particular type of sensory neuron in culture. Such cells could provide means for cell-based therapies. Being able to differentiate progenitor / stem cells into a large number of homogenous sensory neurons are of particular interest because, it also opens for a method to identify the molecular repertoire that confers the functional properties unique to the cell types. Such cells would also be amendable for large-scale drug screening efforts.

Objective 2: Defining the role of Cux2 in the establishment of specific contacts in the central nervous system

Recent findings show that neuronal identity is intimately linked to axonal behaviour. We addressed the question whether Cux2 might be involved, not only in the definition of neuronal subtype but also axonal behaviour. We induced over-expression of Cux2 by electroporation in chicken spinal cord and analyzed its impact on the expression of a large set of classical guidance molecules. We showed that Cux2 overexpression in commissural interneurons increases the expression of Neuropilin1 and induces the defasciculation as well as a re-routing of the commissural axons from contra to ipsilateral side.

How neurons interact and assemble together to form a functional network? How do abnormal development of neuronal network connect with major neuropsychiatric illnesses such as autism, schizophrenia and anxiety disorders? Recent studies imply a potential common molecular program for the control of both neuronal migration and neurite arborisation and emphasise on the role of guidance molecules in shaping axonal arborisation. I believe this work is a step toward the comprehension of this theme.

Obective 3: Identifying potential interactions between Cux and Runx factors

Data from literature in addition to our preliminary results prompted us to propose a possible interaction between the Cux and Runx factors, potentially to coordinate subtype specification and regulate the

establishment of specific points of contacts in the nervous system.

We described the pattern of expression of Runx3 and Cux2 in chicken DRG neurons. We tried to investigate the potential regulatory interactions between Runx3 and Cux2 in DRG neurons but we failed. Thus, we tried in spinal cord. We showed that Cux2 couldn't induce Runx3 but ectopic induction of Runx3 expression leads to Cux2 down-regulation. Here, we were confronted to technical difficulties that did not allow us to satisfactorily answer the questions raised.

**Ultimo aggiornamento:** 5 Luglio 2013

**Permalink:** https://cordis.europa.eu/project/id/219333/reporting/it