that bind the enhancers and regulate their activity. This work will reveal how tissue/region-specific transcription factors and/or signals from other forebrain patterning centers regulate RFSC Fgf17 signaling.

doi:10.1016/j.ydbio.2008.05.377

Program/Abstract # 355
The role of slug in neural crest
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Neural crest (NC) cells are multipotent progenitor cells that migrate throughout the vertebrate embryo and give rise to diverse derivatives. The Snail family of transcription factors plays key roles during NC development and are important mediators of metastasis in epithelial-derived tumors. Snail family factors are among the earliest regulators expressed in newly formed NC cells and play multiple roles in their development. However, the transcriptional targets of Snail family factors in NC cells and how the activity of these factors is controlled such that correct targets are regulated at the right time remain poorly understood.We show that one mechanism which the activity of Snail family factors is controlled during NC development is at the level of protein turnover. Snail and Slug are targeted to the ubiquitin–proteasome system by an E3 ubiquitin ligase, Partner of Paired, and loss of this regulation leads to premature neural crest migration, suggesting that threshold levels of Snail/Slug protein regulate distinct targets. In order to elucidate other mechanisms via which the activity of reiterative transcription factors such as Snail and Slug can be directed to the correct developmental targets we explore the contributions that distinct protein domains play in processes regulated by these factors, including NC precursor formation, migration and the regulation of apoptosis. We dissect the role that SNAG, Slug and a C-terminal Binding Protein motif play in these processes. Also, we examine the role of apoptosis in neural crest formation. We suggest that cell death is not as prevalent in this region as previously reported and that Slug-mediated control of apoptosis may not play a major role in NC precursor cell formation.

doi:10.1016/j.ydbio.2008.05.378

Program/Abstract # 356
A regulatory network to segregate the identity of neuronal subtypes
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Spinal motor neurons (MNs) and V2-interneurons (V2-INs) are specified by two related LIM-complexes, MN-hexamer and V2-tetramer, respectively. Here we show how multiple parallel and complementary feedback loops are integrated to assign these two cell-fates accurately. While MN-hexamer-response elements (REs) are specific to MN-hexamer, V2-tetramer-REs can bind both LIM-complexes. In embryonic MNs, however, two factors cooperatively suppress the aberrant activation of V2-tetramer-REs. First, LMO4 blocks V2-tetramer assembly. Second, MN-hexamer induces a repressor Hb9, which binds V2-tetramer-REs and suppresses their activation. V2-INs use a similar approach; V2-tetramer induces a repressor Chx10, which binds MN-hexamer-REs and blocks their activation. Thus, our study uncovers a regulatory network to segregate related cell-fates, which involves reciprocal feedforward gene regulatory loops.

doi:10.1016/j.ydbio.2008.05.379

Program/Abstract # 357
MIR-124 antagonizes the anti-neural rest/scp1 pathway during embryonic development
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Neuronal gene expression is tightly regulated during embryonic development to ensure proper acquisition and maintenance of neuronal identity. The transcription factor REST suppresses premature expression of neuronal genes in neural progenitors. The phosphatase SCP1 (small C-terminal domain phosphatase 1) was previously identified as an essential co-factor of REST. In the developing nervous system, SCP1 is expressed exclusively in neural progenitors, but not in differentiated neurons. Down-regulation of SCP1 is a potentially critical step during neurogenesis, but little is known about how SCP1 expression is regulated during development. Interestingly, the 3′ UTR of SCP1 mRNA contains three evolutionarily conserved, putative binding sites for the neuron-enriched microRNA, miR-124. In situ detection revealed that miR-124 and SCP1 show a complementary expression pattern in the developing spinal cord. We show that miR-124 directly suppresses SCP1-3′-UTR, in luciferase assays and the developing spinal cord. Over-expression of miR-124 enhanced neuronal differentiation in the chick spinal cord, while miR-124 antagonism decreased expression of neuronal markers, similarly to SCP1 over-expression. In P19 cells and the developing spinal cord, miR-124 suppressed SCP1 expression and induced neurogenesis, while co-expression of a miR-124-insensitive form SCP1 (excluding its 3′ UTR) inhibited the pro-neural activity of miR-124. Our results suggest that, during CNS development, timely down-regulation of SCP1 is critical for inducing neurogenesis and miR-124 contributes to this process in part, by down-regulating SCP1-expression.

doi:10.1016/j.ydbio.2008.05.380

Program/Abstract # 358
Prrxl1 expression is upregulated upon differentiation in neuronal cells
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Prrxl1 is a paired-like homeodomain transcription factor involved in the development/maintenance of both spinal cord and peripheral