Reiterative AP2a activity controls sequential steps in the neural crest gene regulatory network.

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Résumé

The neural crest (NC) emerges from combinatorial inductive events occurring within its progenitor domain, the neural border (NB). Several transcription factors act early at the NB, but the initiating molecular events remain elusive. Recent data from basal vertebrates suggest that ap2 might have been critical for NC emergence; however, the role of AP2 factors at the NB remains unclear. We show here that AP2a initiates NB patterning and is sufficient to elicit a NB-like pattern in neuralized ectoderm. In contrast, the other early regulators do not participate in ap2a initiation at the NB, but cooperate to further establish a robust NB pattern. The NC regulatory network uses a multistep cascade of secreted inducers and transcription factors, first at the NB and then within the NC progenitors. Here we report that AP2a acts at two distinct steps of this cascade. As the earliest known NB specifier, AP2a mediates Wnt signals to initiate the NB and activate pax3; as a NC specifier, AP2a regulates further NC development independent of and downstream of NB patterning. Our findings reconcile conflicting observations from various vertebrate organisms. AP2a provides a paradigm for the reiterated use of multifunctional molecules, thereby facilitating emergence of the NC in vertebrates.

Tissue-specific expression of Sarcoplasmic/Endoplasmic Reticulum Calcium ATPases (ATP2A/SERCA) 1, 2, 3 during Xenopus laevis development.


Résumé

Calcium-ATPase pumps are critical in most cells, to sequester calcium into intracytoplasmic stores and regulate general calcium signalling. In addition, cell-specific needs for calcium signals have been described and employ a diversity of calcium ATPases in adult tissues and oocytes. A major family of such calcium pumps is ATP2A/SERCA family, for Sarcoplasmic/Endoplasmic Reticulum Calcium ATPases. Although largely studied in adults, the developmental expression of the atp2a/serca genes remains unknown. Here, we provide genome organisation in Xenopuslaevis and tropicalis and phylogeny of atp2a/serca genes in craniates. We detail embryonic expression for the three X. laevis atp2a/serca genes. We found that the three atp2a/serca genes are strongly conserved among vertebrates and display complementary and tissue-specific expression in embryos. These expression patterns present variations when compared to the data reported in adults. Atp2a1/serca1 is expressed as soon as the end of gastrulation in a subset of the myod-positive cells, and later
labels prospective slow muscle cells in the superficial part of the somite. In contrast, atp2a2/serca2 is found in a larger subset of cells, but is not ubiquitous as reported in adults. Notably, atp2a2/serca2 is prominently expressed in the neural-related tissues, i.e. the neural plate, cement gland, but is excluded from premigratory neural crest. Finally, atp2a3/serca3 expression is restricted to the ectoderm throughout development.

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Frédérique Maczkowiak, Stéphanie Matéos, Estee Wang, Daniel Roche, Richard Harland, Anne H Monsoro-Burq (2009 Sep 16)
The Pax3 and Pax7 paralogs cooperate in neural and neural crest patterning using distinct molecular mechanisms, in Xenopus laevis embryos.
Developmental biology : 381-96 : DOI : 10.1016/j.ydbio.2010.01.022

Résumé

Pax3 and Pax7 paralogous genes have functionally diverged in vertebrate evolution, creating opportunity for a new distribution of roles between the two genes and the evolution of novel functions. Here we focus on the regulation and function of Pax7 in the brain and neural crest of amphibian embryos, which display a different pax7 expression pattern, compared to the other vertebrates already described. Pax7 expression is restricted to the midbrain, hindbrain and anterior spinal cord, and Pax7 activity is important for maintaining the fates of these regions, by restricting otx2 expression anteriorly. In contrast, pax3 displays broader expression along the entire neuraxis and Pax3 function is important for posterior brain patterning without acting on otx2 expression. Moreover, while both genes are essential for neural crest patterning, we show that they do so using two distinct mechanisms: Pax3 acts within the ectoderm which will be induced into neural crest, while Pax7 is essential for the inducing activity of the paraxial mesoderm towards the prospective neural crest.

Dazap2 is required for FGF-mediated posterior neural patterning, independent of Wnt and Cdx function.
Developmental biology : 26-36 : DOI : 10.1016/j.ydbio.2009.06.019

Résumé

The organization of the embryonic neural plate requires coordination of multiple signal transduction pathways, including fibroblast growth factors (FGFs), bone morphogenetic proteins (BMPs), and WNTs. Many studies have suggested that a critical component of this process is the patterning of posterior neural tissues by an FGF-caudal signaling cascade. Here, we have identified a novel player, Dazap2, and show that it is required in vivo for posterior neural fate. Loss of Dazap2 in embryos resulted in diminished expression of hoxb9 with a concurrent increase in the anterior marker otx2. Furthermore, we found that Dazap2 is required for FGF dependent posterior patterning; surprisingly, this is independent of Cdx
activity. Furthermore, in contrast to FGF activity, Dazap2 induction of hoxb9 is not blocked by loss of canonical Wnt signaling. Functionally, we found that increasing Dazap2 levels alters neural patterning and induces posterior neural markers. This activity overcomes the anteriorizing effects of noggin, and is downstream of FGF receptor activation. Our results strongly suggest that Dazap2 is a novel and essential branch of FGF-induced neural patterning.