Neurocristopathies: How New Discoveries in Neural Crest Research Changed our Understanding

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Introduction

Neural Crest Cells (NCC) have long been recognized as the fourth layer of developing vertebrate embryos. The neural crest is a transient cell population that is probably heterogeneous but multipotent, giving rise to melanocytes, Schwann cells, sympathetic, parasympathetic and enteric neurons, enteric glia, endocrine cells, fibroblasts, muscle, bone, cartilage and meninges, among others cell types [1]. The disorders that stem from neural crest dysfunction, called Neurocristopathies (NCP) [2], are still only partially understood. Despite the great advances in our understanding of NCC formation and development, the causal link leading to NCP has remained elusive. In a recent review dealing with NCP [2] we provided a thorough analysis of 66 NCP associated with a dozen “Cell Signaling Pathways”, 4 different “families of Transcription Factors” and a wide diversity of “cellular processes”. In over 5 model organisms (mouse, chicken, frog, fish and others, it has been demonstrated that NCP are linked to NCC faults during essential developmental processes. We also discussed the incorporation of new diseases or syndromes based on the defects of neural crest-derived tissues and organs that have also been unveiled very recently. In the light of recent discoveries we also included RASopathies, Ciliopathies, Ribosomopathies and defective epigenetic mechanisms as responsible for four newly established NCP categories.

Developmental Insight

Our recent review of NCP [2] also contributed to the understanding of the role of NCP in the development of different organs. A group of newly found neural crest derivatives were catalogued and described. Moreover, the recent advances in the field of neural crest developmental studies added to the review provide the basis for the proposal of a new general classification of NCP. This new classification, based on the axial origin of the neural crest derivatives, is more comprehensive and easier to understand and represents a guide to identify the possible origin of an NCP.

The Making of Hematopoietic Precursors

Our NCP review [2] also took into account an old proposal that considers hematopoietic precursors as derived from a common intermediate progenitor, the NCCs. This idea arose in part from the observation that hematopoietic precursors and their lymphoid progenitors are supported by the finding that the adult bone marrow microenvironmental niches are composed of various stromal cells, sympathetic non- myelinating glial Schwann cells and sympathetic nerve fibers. Since NCCs contribute to the development of all three, they are present in the human adult bone marrow to generate or regulate hematopoietic precursors [3,4]. The myelinating and non-
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