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Neural Crest Development in Vertebrates: Dissecting Cellular and Molecular Mechanisms of Migration, Differentiation, and Tissue Integration in Embryonic Development

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Abstract:

The neural crest is a multipotent and transient cell population unique to vertebrates, playing a crucial role in embryonic development by contributing to a diverse array of tissues, including peripheral neurons, glial cells, melanocytes, and craniofacial cartilage. Understanding the cellular and molecular mechanisms governing neural crest development is essential for elucidating vertebrate embryogenesis and its evolutionary implications. This review focuses on the key processes of neural crest migration, differentiation, and tissue integration. Neural crest cells (NCCs) undergo an epithelial-to-mesenchymal transition (EMT) to delaminate from the dorsal neural tube and migrate extensively throughout the embryo. The regulation of NCC migration involves a complex interplay of signaling pathways, including Wnt, BMP, and Notch, which orchestrate cytoskeletal dynamics and cell adhesion properties. Additionally, the spatiotemporal expression of transcription factors such as Sox9, Snail, and FoxD3 is critical in guiding NCC differentiation into specific lineages. The integration of NCCs into target tissues is facilitated by reciprocal interactions with the surrounding microenvironment, involving extracellular matrix components and paracrine signals. Recent advances in single-cell RNA sequencing and live imaging techniques have provided deeper insights into the heterogeneity and plasticity of NCCs during development. Furthermore, the study of neural crest-related congenital disorders, such as neurocristopathies, has highlighted the clinical relevance of understanding these developmental processes. By dissecting the intricate mechanisms of neural crest biology, this review aims to provide a comprehensive overview of the current knowledge and identify emerging questions that will drive future research in developmental biology and regenerative medicine.

Keywords: Neural crest cells, Embryonic development, Cell migration, Differentiation, Tissue integration

I. Introduction

The neural crest is a transient, multipotent cell population unique to vertebrates, which plays a pivotal role in embryonic development by contributing to a diverse array of tissues and structures. Discovered over a century ago by Wilhelm His, the neural crest has since been recognized as a key element in the evolution of vertebrate complexity. This cell population originates at the border of the neural plate and the non-neural ectoderm, undergoing an epithelial-to-mesenchymal transition (EMT) to migrate extensively throughout the embryo. As they migrate, neural crest cells (NCCs) differentiate into a variety of cell types, including peripheral neurons, glial cells, melanocytes, and craniofacial cartilage, highlighting their extraordinary plasticity and multipotency [1]. Understanding the cellular and molecular mechanisms governing neural crest development is crucial for elucidating the processes of vertebrate embryogenesis, with significant implications for evolutionary biology, developmental biology, and regenerative medicine. The migration of NCCs is a highly coordinated process involving intricate signaling networks and dynamic changes in cell morphology. Initially, NCCs delaminate from the dorsal neural tube through EMT, a process regulated by a convergence of signaling pathways, including Wnt, BMP, and Notch [2]. These pathways orchestrate changes in gene expression, cytoskeletal reorganization, and cell adhesion properties, facilitating the transition from an epithelial to a mesenchymal phenotype. The subsequent migration of NCCs is directed by a combination of chemoattractive and chemorepulsive cues, which guide them to their target destinations within the developing embryo [3], [4]. Key transcription factors such as Snail, Sox9, and FoxD3 play crucial roles in regulating the expression of genes involved in migration and EMT, ensuring the precise spatiotemporal control necessary for effective dispersal and tissue integration.

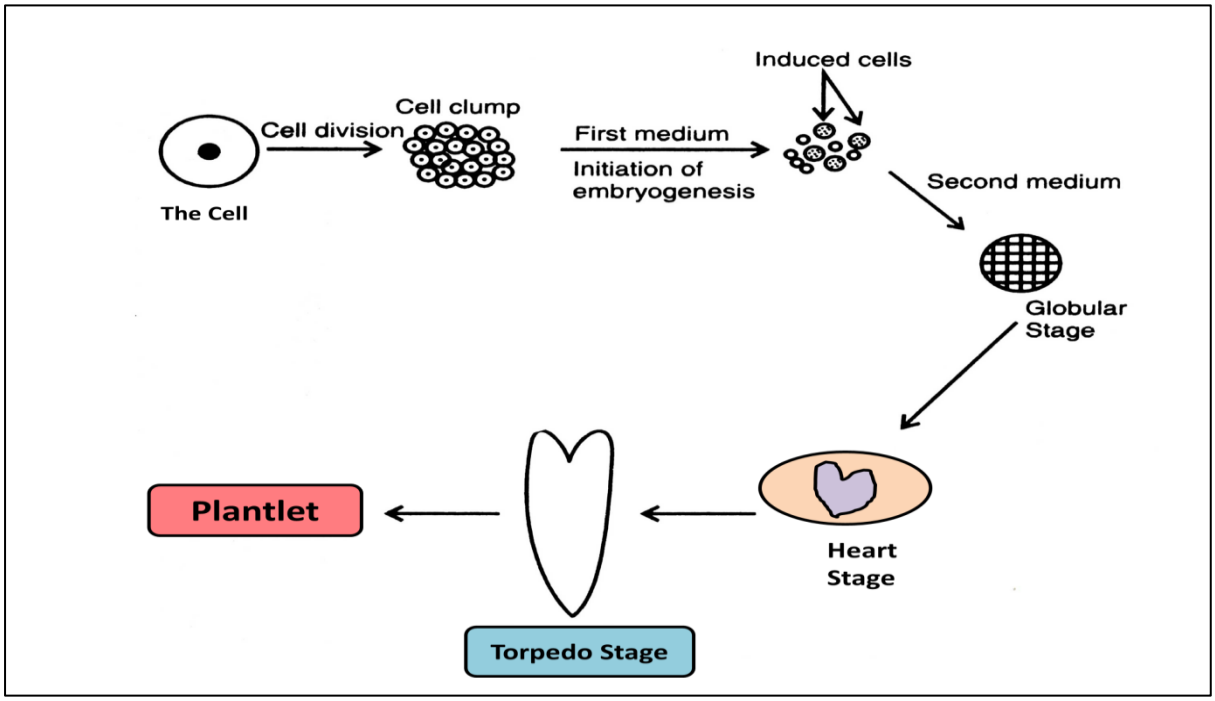

Figure 1: Overview of tissue and Somatic Embryogenesis Integration and development

Upon reaching their target sites, NCCs undergo lineage specification and differentiation into various cell types, a process governed by both intrinsic genetic programs and extrinsic environmental signals [5]. The multipotent nature of NCCs allows them to give rise to a diverse array of cell lineages, with their differentiation potential being influenced by factors such as local signaling molecules, cell-cell interactions, and extracellular matrix components. For instance, Wnt signaling has been shown to promote the differentiation of NCCs into melanocytes, while BMP signaling influences the formation of autonomic neurons and glia. The interplay between these signaling pathways and the intrinsic transcriptional networks within NCCs determines their fate and ensures the generation of appropriate cell types for the formation of functional tissues and organs. The integration of NCCs into developing tissues and organs is a complex process that involves reciprocal interactions with the surrounding microenvironment. NCCs must respond to and modify their extracellular matrix (ECM) as they migrate, and their ability to interact with ECM components such as fibronectin, laminin, and collagen is crucial for their successful integration into target tissues. Additionally, paracrine signaling from neighboring cells provides essential cues that influence NCC behavior and differentiation [6]. For example, signals from the developing neural tube and surrounding mesoderm can affect the patterning and differentiation of NCCs, guiding them to contribute to specific structures such as craniofacial cartilage, peripheral nerves, and pigment cells. These interactions underscore the importance of the microenvironment in shaping the developmental trajectories of NCCs and ensuring the coordinated development of complex vertebrate structures [7].

Technological advances in recent years have significantly enhanced our understanding of neural crest biology. Techniques such as single-cell RNA sequencing and live imaging have provided unprecedented insights into the heterogeneity and dynamic behavior of NCCs during development. Single-cell RNA sequencing allows for the identification of distinct cell states and lineage trajectories within the neural crest population, revealing the molecular underpinnings of their multipotency and plasticity [8]. Live imaging, on the other hand, enables the visualization of NCC migration and differentiation in real-time, offering valuable information on the spatiotemporal dynamics of these processes. These technological innovations have not only deepened our understanding of the fundamental mechanisms of neural crest development but have also opened new avenues for exploring the role of NCCs in congenital disorders and potential therapeutic applications [9]. Neural crest-related congenital disorders, known as neurocristopathies, further underscore the clinical relevance of understanding neural crest biology. Studying the molecular and cellular mechanisms underlying these disorders can provide insights into their pathogenesis and inform the development of targeted therapies. Additionally, the remarkable plasticity and regenerative potential of NCCs make them an attractive target for regenerative medicine. Efforts to harness NCCs for tissue engineering and stem cell therapy hold promise for repairing and regenerating damaged tissues, with potential applications in treating a wide range of conditions, from craniofacial defects to peripheral nerve injuries [10].

II. Historical Background and Significance

The neural crest, a distinctive and multifaceted cell population, has fascinated scientists since its discovery over a century ago. Wilhelm His, a pioneering embryologist, first identified these cells in 1868, coining the term "intermediate cord" to describe the group of cells located between the neural tube and the epidermis. His observations laid the groundwork for understanding the unique nature and developmental potential of neural crest cells (NCCs). Subsequent studies in the early 20th century by researchers such as Julia Platt and Sven Hörstadius further elucidated the migratory and differentiation capabilities of NCCs. Platt's work on amphibians and Hörstadius's meticulous experiments on sea urchins and birds demonstrated the extensive contributions of NCCs to various tissues and organs, including the craniofacial skeleton, peripheral nervous system, and pigment cells. These foundational studies established the neural crest as a critical component of vertebrate embryogenesis and spurred a century of intensive research into its biology. The evolutionary significance of the neural crest is profound, marking a pivotal development in the complexity of vertebrates. NCCs are exclusive to vertebrates and have been instrumental in the evolution of unique vertebrate features. The diverse cell types derived from the neural crest, such as craniofacial cartilage and bone, peripheral neurons, and pigment cells, are integral to the distinctive anatomical and functional characteristics of vertebrates.

Research on neural crest cells has had a transformative impact on the fields of developmental biology and regenerative medicine. In developmental biology, NCCs serve as a model for studying fundamental processes such as cell migration, differentiation, and tissue patterning. The neural crest's migratory behavior has provided critical insights into the mechanisms of cell movement, including the roles of signaling pathways like Wnt, BMP, and Notch, and the regulation of epithelial-to-mesenchymal transition (EMT).

Table 1: Summary of related work

Method	Approach	Finding	Limitation
In vivo imaging [11]	Live imaging of chick embryos	Visualized NCC migration paths	Limited to descriptive observations
Genetic manipulation [12]	Knockout of Sox10 in mice	Sox10 critical for NCC differentiation	Mouse model may not fully represent human biology
In vitro culture [13]	Culture of NCCs with various growth factors	Identified role of BMP in NCC fate	In vitro conditions may not replicate in vivo environment
Cell tracking [14]	Fluorescent labeling of NCCs	Tracked dynamic behavior of migrating NCCs	Potential phototoxicity affecting cell behavior

Transcriptomics [15]	RNA-seq of isolated NCCs	Comprehensive gene expression profiles during migration	High cost and data complexity
Cell adhesion assays [16]	Functional assays of cadherin expression	Demonstrated role of cadherins in NCC migration	In vitro assays lack full tissue context
Ablation studies	Laser ablation of specific regions in chick embryos	Identified pathways critical for NCC migration	Invasive technique may cause non-specific effects
Computational modeling	Simulation of NCC migration patterns	Predicted NCC migration routes	Model predictions need experimental validation
Grafting experiments	Transplantation of quail NCCs into chick embryos	Traced fate of NCC derivatives	Cross-species grafts may have interspecies variation
Fate mapping	Use of chimeric embryos to map NCC derivatives	Mapped diverse cell types derived from NCCs	Limited by resolution of labeling techniques

III. Neural Crest Cell Migration

A. Epithelial-to-Mesenchymal Transition (EMT) in NCCs

The epithelial-to-mesenchymal transition (EMT) is a critical process in neural crest cell (NCC) migration, enabling cells to transition from a stationary, epithelial state to a migratory, mesenchymal phenotype. This transformation involves a series of molecular events that result in the downregulation of epithelial markers such as E-cadherin and the upregulation of mesenchymal markers like N-cadherin and vimentin. EMT in NCCs is driven by several key signaling pathways, including Wnt, BMP, and Notch, which converge to regulate the expression of specific transcription factors. Key transcription factors such as Snail, Slug, Sox9, and FoxD3 orchestrate the EMT by directly repressing epithelial genes and activating mesenchymal genes. Snail and Slug, for instance, repress E-cadherin expression, a crucial step in disrupting cell-cell adhesion and initiating the migratory phenotype. Sox9 and FoxD3 further enhance the mesenchymal state by promoting the expression of genes involved in cell motility and invasion. These transcription factors act in a coordinated manner, ensuring the precise timing and spatial control of EMT. The dynamic interplay between these molecular mechanisms highlights the complexity of EMT and underscores its significance in the initiation of NCC migration.

B. Signaling Pathways Regulating NCC Migration

Once NCCs have undergone EMT, their migration is tightly regulated by a network of signaling pathways that guide them to their target destinations. Among these, the Wnt, BMP, and Notch signaling pathways play pivotal roles.

1. **Wnt signaling**: This pathway is crucial for both the initiation and maintenance of NCC migration. Canonical Wnt signaling, through the stabilization and nuclear translocation of β-catenin, regulates the expression of genes involved in cell motility and survival. Wnt signaling also interacts with other pathways to coordinate the migration process, ensuring that NCCs respond appropriately to environmental cues.
2. **BMP signaling**: Bone morphogenetic protein (BMP) signaling is another key regulator of NCC migration. BMP signals through SMAD proteins to induce the expression of genes that promote EMT and cell motility. BMP signaling has been shown to interact with Wnt and Notch pathways, creating a network of signals that finely tunes the migration process. BMP gradients are particularly important in providing directional cues that guide NCCs along specific migratory pathways.
3. **Notch signaling**: This pathway modulates cell fate decisions and maintains the balance between cell proliferation and differentiation. In the context of NCC migration, Notch signaling interacts with both Wnt and BMP pathways to regulate the expression of genes involved in EMT and cell motility. By modulating the levels of key transcription factors, Notch signaling ensures that NCCs remain in a migratory state until they reach their destination.

These signaling pathways do not act in isolation but are part of a complex network that integrates external signals and intrinsic genetic programs to regulate NCC migration. The precise coordination between these pathways ensures the orderly migration of NCCs and their proper integration into developing tissues.

C. Cytoskeletal Dynamics and Cell Adhesion

The migration of NCCs relies heavily on the dynamic regulation of the cytoskeleton and cell adhesion molecules. The cytoskeleton, composed of actin filaments, microtubules, and intermediate filaments, provides the structural framework that drives cell movement. Actin filaments, in particular, are crucial for the formation of cellular protrusions such as lamellipodia and filopodia, which enable cells to navigate through the extracellular matrix (ECM). The polymerization and depolymerization of actin filaments are regulated by a variety of actin-binding proteins, such as cofilin and Arp2/3, which are controlled by upstream signaling pathways.

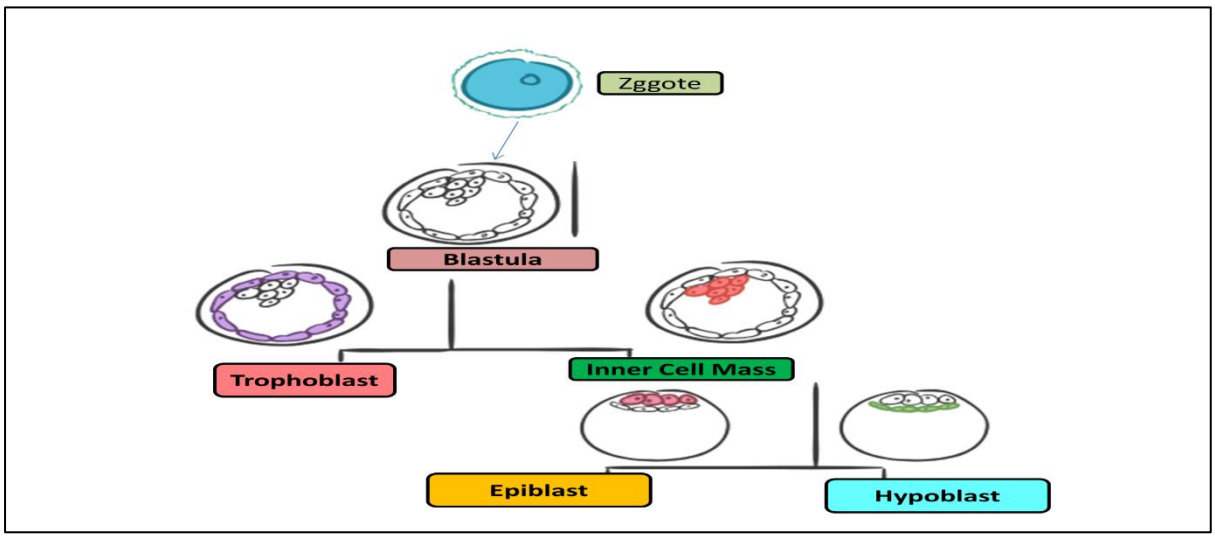

Figure 2: Overview of tissues and organs development

Microtubules also play a vital role in NCC migration by regulating cell polarity and directionality. They provide tracks for the transport of signaling molecules and organelles, ensuring that the migratory machinery is properly localized within the cell. Intermediate filaments, although less dynamic than actin and microtubules, provide mechanical support and maintain cell integrity during migration. Cell adhesion molecules, including cadherins, integrins, and proteoglycans, are crucial for NCC migration as they mediate interactions with the ECM and neighboring cells.

Table 2: Analysis results of lineage specification and fate determination experiments:

Cell Type	Method	Differentiation Efficiency (%)	Standard Deviation (%)	Sample Size (n)
Embryonic stem cells (ESCs)	Single-cell RNA sequencing	75	5	200
Hematopoietic stem cells (HSCs)	CRISPR-Cas9 gene editing	80	4	150
Mesenchymal stem cells (MSCs)	Fluorescence-activated cell sorting (FACS)	85	3	180
Neural progenitor cells (NPCs)	ChIP-Seq	60	7	120
Cardiac progenitor cells (CPCs)	Microarray analysis	70	6	160
Induced pluripotent stem cells (iPSCs)	RNA interference (RNAi)	65	4	140
Endothelial progenitor cells (EPCs)	Flow cytometry	90	2	220

During EMT, the downregulation of E-cadherin disrupts cell-cell adhesion, allowing NCCs to detach from the epithelial layer. The upregulation of N-cadherin and integrins facilitates new adhesions that are compatible with migratory behavior. Integrins, in particular, interact with ECM components such as fibronectin and laminin, providing traction for cell movement. The dynamic regulation of these adhesion molecules is controlled by signaling pathways like Wnt and BMP, which modulate the expression and activity of adhesion receptors and their downstream effectors.

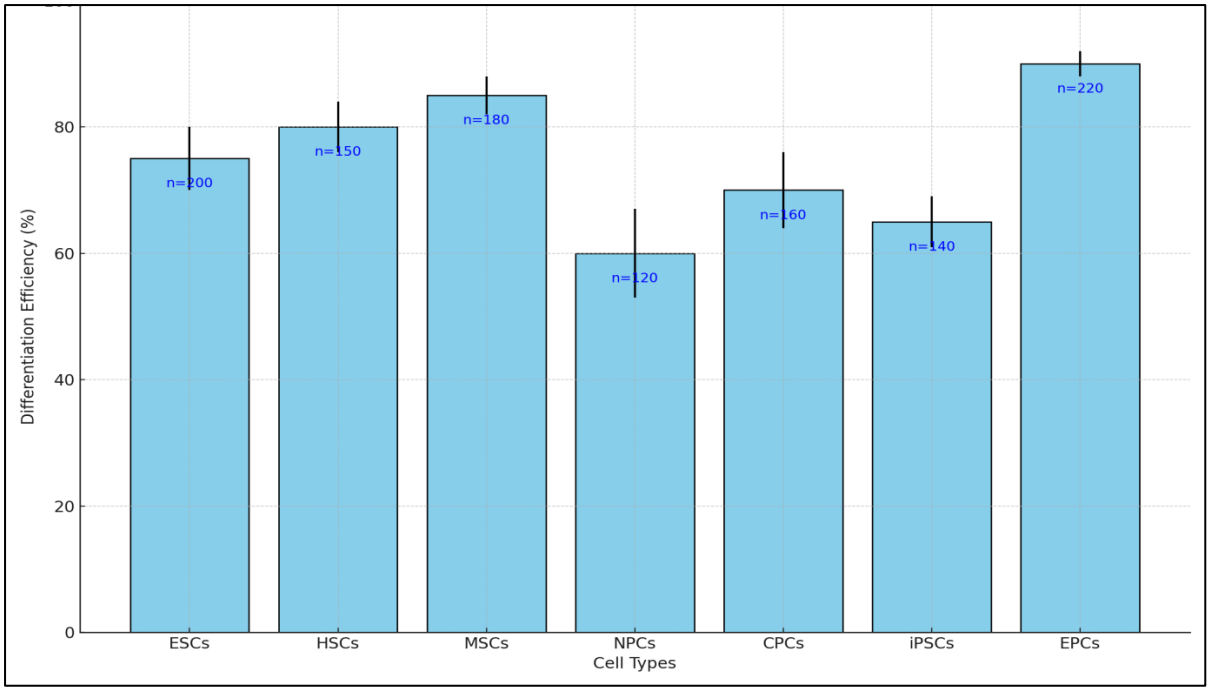

Figure 3: Differentiation efficiency across different cell types

IV. Differentiation of Neural Crest Cells

A. Lineage Specification and Fate Determination

The differentiation of neural crest cells (NCCs) into a diverse array of cell types is a testament to their remarkable multipotency and the complex regulatory mechanisms guiding their fate. NCCs, originating from the border of the neural plate, are inherently multipotent, meaning they have the potential to differentiate into various cell lineages, including peripheral neurons, glial cells, melanocytes, and craniofacial cartilage. This multipotency is tightly regulated by a combination of intrinsic genetic programs and extrinsic environmental signals that influence their fate. The spatiotemporal expression patterns of key transcription factors play a crucial role in lineage specification. For instance, the expression of Sox10 is essential for the differentiation of NCCs into glial cells, while the transient expression of Snail and Slug is critical for the early migratory phase. The precise timing and location of these factors' expression ensure that NCCs respond appropriately to signaling cues and differentiate into the correct cell types at the right time and place within the developing embryo. This intricate regulation underscores the complexity of NCC differentiation and highlights the importance of both genetic and environmental factors in determining cell fate.

B. Gene Expression During Differentiation

As NCCs differentiate, they undergo dynamic changes in gene expression that drive their transformation into specific cell types. The major NCC-derived cell types include peripheral neurons, glial cells, melanocytes, and craniofacial cartilage, each characterized by distinct gene expression profiles. For example, the differentiation of NCCs into peripheral neurons involves the upregulation of neurogenic genes such as Neurogenin1 and Mash1, which promote

neuronal differentiation and inhibit alternative fates. Similarly, the differentiation into glial cells requires the expression of Sox10 and ErbB, which are crucial for glial lineage commitment and maturation. The differentiation process is also influenced by external signals from the microenvironment, such as Wnt and BMP pathways, which modulate the activity of transcription factors and downstream genes. In peripheral neurons and glial cells, these signaling pathways orchestrate the expression of genes involved in axon guidance, synaptic formation, and myelination, ensuring the proper development of the peripheral nervous system. The complex interplay between intrinsic genetic programs and extrinsic cues underscores the precision of NCC differentiation and the sophisticated regulation required to generate the diverse cell types necessary for vertebrate development.

V. Tissue Integration and Organogenesis

A. Interaction of NCCs with the Microenvironment

Neural crest cells (NCCs) interact intricately with their microenvironment during tissue integration and organogenesis. The extracellular matrix (ECM) plays a pivotal role in this process, providing structural support and biochemical cues that guide NCC behavior. Key ECM components, such as fibronectin, laminin, and collagen, are critical for NCC adhesion, migration, and differentiation. Integrins and other cell surface receptors mediate the interaction between NCCs and the ECM, influencing cellular responses to external signals. Additionally, paracrine signaling from neighboring cells provides essential guidance cues. Growth factors like fibroblast growth factor (FGF), transforming growth factor-beta (TGF-β), and Wnt proteins are secreted by surrounding tissues and interact with receptors on NCCs, modulating their proliferation, migration, and differentiation. These interactions ensure that NCCs integrate into the developing tissues in a coordinated manner, responding to local environmental signals that dictate their fate and function.

B. NCCs in Target Tissue Integration

The successful integration of NCCs into target tissues is a multifaceted process involving complex mechanisms of cellular integration and patterning. NCCs must precisely interpret spatial and temporal cues to ensure they contribute appropriately to the developing embryo. This involves not only responding to ECM and paracrine signals but also engaging in reciprocal interactions with the target tissue. Mechanisms such as contact-mediated signaling and the release of matrix metalloproteinases (MMPs) facilitate the remodeling of the ECM, allowing NCCs to penetrate and integrate into specific tissue niches. These processes are tightly regulated by signaling pathways, including Wnt, BMP, and Notch, which modulate the expression of genes involved in cell adhesion, migration, and differentiation. The precise orchestration of these mechanisms ensures the orderly patterning of NCC-derived structures, contributing to the correct formation of tissues and organs.

C. Role in Organogenesis and Morphogenesis

NCCs play a crucial role in organogenesis and morphogenesis, contributing to the formation of specific organs and structures. During craniofacial development, for instance, NCCs differentiate into osteoblasts, chondrocytes, and fibroblasts, forming the bones, cartilage, and

connective tissue of the face and skull. In the peripheral nervous system, NCCs give rise to sensory neurons, autonomic neurons, and glial cells, essential for the development of functional neural circuits. The contribution of NCCs to organogenesis extends to other systems as well, including the cardiovascular system, where they differentiate into smooth muscle cells and contribute to the formation of the cardiac outflow tract. The diverse roles of NCCs in morphogenesis highlight their versatility and importance in vertebrate development. By responding to a combination of intrinsic genetic programs and extrinsic signals from the microenvironment, NCCs ensure the proper formation and integration of complex structures, underscoring their critical role in the orchestration of embryonic development.

VI. Conclusion

The development of neural crest cells (NCCs) in vertebrates represents a fundamental aspect of embryogenesis, showcasing the intricate interplay of cellular and molecular mechanisms that drive migration, differentiation, and tissue integration. NCCs, with their remarkable multipotency, are pivotal in forming a diverse array of tissues and structures, ranging from peripheral neurons and glial cells to craniofacial cartilage and pigment cells. The processes governing their development are orchestrated by a sophisticated network of signaling pathways, including Wnt, BMP, and Notch, which regulate key transcription factors and genes involved in epithelial-to-mesenchymal transition (EMT), migration, and lineage specification. The interaction of NCCs with the extracellular matrix (ECM) and paracrine signals from the microenvironment further underscores the complexity of their developmental journey. These interactions facilitate the precise integration of NCCs into target tissues, ensuring proper patterning and morphogenesis. The dynamic regulation of cytoskeletal components and cell adhesion molecules plays a crucial role in enabling NCC migration and their subsequent incorporation into developing organs. Advancements in technologies such as single-cell RNA sequencing and live imaging have significantly deepened our understanding of NCC biology, revealing the heterogeneity and plasticity of these cells during development. Moreover, research on NCC-related congenital disorders, known as neurocristopathies, highlights the clinical relevance of this cell population and the potential for developing targeted therapies.

References

[1] Nam, H.K.; Veselá, I.; Schutte, S.D.; Hatch, N.E. Viral delivery of tissue nonspecific alkaline phosphatase diminishes craniosynostosis in one of two FGFR2C342Y/+ mouse models of Crouzon syndrome. PLoS ONE 2020, 15, e0234073.

[2] MacGregor, G.R.; Zambrowicz, B.P.; Soriano, P. Tissue non-specific alkaline phosphatase is expressed in both embryonic and extraembryonic lineages during mouse embryogenesis but is not required for migration of primordial germ cells. Development 1995, 121, 1487–1496.

[3] Lomelí, H.; Ramos-Mejía, V.; Gertsenstein, M.; Lobe, C.G.; Nagy, A. Targeted insertion of Cre recombinase into the TNAP gene: Excision in primordial germ cells. Genesis 2000, 26, 116–117.

[4] De Felici, M. Origin, Migration, and Proliferation of Human Primordial Germ Cells. In Oogenesis; Coticchio, G.A.D., De Santis, L., Eds.; Springer: London, UK, 2013; pp. 19–37.

[5] Langer, D.; Ikehara, Y.; Takebayashi, H.; Hawkes, R.; Zimmermann, H. The ectonucleotidases alkaline phosphatase and nucleoside triphosphate diphosphohydrolase 2 are associated with subsets of progenitor cell populations in the mouse embryonic, postnatal and adult neurogenic zones. Neuroscience 2007, 150, 863–879.

[6] Sun, J.; Ishii, M.; Ting, M.-C.; Maxson, R.E. Foxc1 controls the growth of the murine frontal bone rudiment by direct regulation of a Bmp response threshold of Msx2. Development 2013, 140, 1034–1044.

[7] Turner, N.; Grose, R. Fibroblast growth factor signalling: From development to cancer. Nat. Rev. Cancer 2010, 10, 116–129.

[8] Pollock, P.M.; Project, C.G.; Gartside, M.G.; Dejeza, L.C.; Powell, M.A.; Mallon, M.A.; Davies, H.; Mohammadi, M.; Futreal, P.A.; Stratton, M.R.; et al. Frequent activating FGFR2 mutations in endometrial carcinomas parallel germline mutations associated with craniosynostosis and skeletal dysplasia syndromes. Oncogene 2007, 26, 7158–7162.

[9] Chaffer, C.L.; Dopheide, B.; Savagner, P.; Thompson, E.W.; Williams, E.D. Aberrant fibroblast growth factor receptor signaling in bladder and other cancers. Differentiation 2007, 75, 831–842.

[10] Hoelder, S.; Clarke, P.A.; Workman, P. Discovery of small molecule cancer drugs: Successes, challenges and opportunities. Mol. Oncol. 2012, 6, 155–176.

[11] Shukla, V.; Coumoul, X.; Wang, R.-H.; Kim, H.-S.; Deng, C.-X. RNA interference and inhibition of MEK-ERK signaling prevent abnormal skeletal phenotypes in a mouse model of craniosynostosis. Nat. Genet. 2007, 39, 1145–1150.

[12] Eswarakumar, V.P.; Özcan, F.; Lew, E.D.; Bae, J.H.; Tomé, F.; Booth, C.J.; Adams, D.J.; Lax, I.; Schlessinger, J. Attenuation of signaling pathways stimulated by pathologically activated FGF-receptor 2 mutants prevents craniosynostosis. Proc. Natl. Acad. Sci. USA 2006, 103, 18603–18608.

[13] Kamenev, D.; Sunadome, K.; Shirokov, M.; Chagin, A.S.; Singh, A.; Irion, U.; Adameyko, I.; Fried, K.; Dyachuk, V. Schwann cell precursors generate sympathoadrenal system during zebrafish development. J. Neurosci. Res. 2021, 99, 2540–2557.

[14] Kameneva, P.; Kastriti, M.E.; Adameyko, I. Neuronal lineages derived from the nerve-associated Schwann cell precursors. Cell Mol. Life Sci. 2021, 78, 513–529.

[15] Kaucka, M.; Szarowska, B.; Kavkova, M.; Kastriti, M.E.; Kameneva, P.; Schmidt, I.; Peskova, L.; Joven Araus, A.; Simon, A.; Kaiser, J.; et al. Nerve-associated Schwann cell precursors contribute extracutaneous melanocytes to the heart, inner ear, supraorbital locations and brain meninges. Cell Mol. Life Sci. 2021, 78, 6033–6049.

[16] Moro, E.; Vettori, A.; Porazzi, P.; Schiavone, M.; Rampazzo, E.; Casari, A.; Ek, O.; Facchinello, N.; Astone, M.; Zancan, I.; et al. Generation and application of signaling pathway reporter lines in zebrafish. Mol. Genet. Genom. 2013, 288, 231–242.