

Neurulation from neural plate to neural tube.

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Introduction

Embryonic development is a wondrous journey marked by a series of intricate processes that give rise to the complex structures of the human body. Among these marvels is neurulation, a pivotal event in early embryogenesis where the neural plate transforms into the neural tube, laying the foundation for the Central Nervous System (CNS) [1]. Neurulation exemplifies the elegant orchestration of cellular movements, signalling pathways, and genetic programs that shape the vertebrate nervous system. In this comprehensive exploration, we unravel the mysteries of neurulation, from its molecular underpinnings to its clinical relevance in neurodevelopmental disorders [2].

Neurulation unfolds during the third week of human gestation, following gastrulation, a process that establishes the three germ layers ectoderm, mesoderm, and endoderm. The ectoderm, the outermost layer, gives rise to both the epidermis and the neural plate, a specialized region destined to become the CNS. The neural plate emerges as a flat, elongated structure along the dorsal midline of the embryo, flanked by the neural folds, which gradually elevate and converge toward the midline [3].

The transformation of the neural plate into the neural tube is orchestrated by a complex series of morphogenetic events that involve coordinated cell shape changes, migrations, and interactions. As the neural folds rise and approach each other, the midline of the neural plate thickens to form the neural crest, a transient structure that gives rise to a diverse array of cell types, including neurons, glial cells, and craniofacial structures. Concurrently, the lateral edges of the neural plate begin to elevate, forming the neural folds, which gradually converge toward the midline [4].

The apposition and fusion of the neural folds along the dorsal midline culminate in the closure of the neural tube, a process that proceeds in a rostral-to-caudal direction. Closure begins at the future brain region (rostral neuropore) and proceeds along the entire length of the developing embryo until reaching the tail region (caudal neuropore) [5].

During neurulation, the neural tube undergoes regionalization along its anterior-posterior axis, giving rise to distinct anatomical regions of the CNS, including the forebrain, midbrain, hindbrain, and spinal cord. This patterning is regulated by a precise spatiotemporal expression of morphogens and transcription factors, such as Sonic Hedgehog

(Shh), Bone Morphogenetic Proteins (BMPs), and Homeobox (Hox) genes [6].

Neurulation is governed by a complex interplay of signalling pathways, transcription factors, and cell-cell interactions that regulate cell fate specification, proliferation, and differentiation.

Sonic Hedgehog Shh, a secreted morphogen, plays a central role in dorsoventrally patterning of the neural tube, promoting the proliferation of ventral progenitor cells while inhibiting dorsal cell fate specification. Bone Morphogenetic Proteins BMPs, members of the Transforming Growth Factor-beta (TGF- β) superfamily, exert distalizing effects on the neural tube, promoting the differentiation of dorsal cell types and inhibiting centralization [7].

Notochord and Floor Plate notochord, a rod-like structure located ventral to the developing neural tube, secretes signalling molecules that induce floor plate formation, a critical organizer of dorsoventrally patterning. A multitude of transcription factors, including members of the Pax, Sox, and Nkx families, regulate the expression of genes involved in neural tube patterning, cell proliferation, and differentiation [8].

Disruptions in neurulation can lead to a spectrum of congenital anomalies collectively known as Neural Tube Defects (NTDs), including spina bifida, anencephaly, and craniorachischisis. NTDs result from genetic mutations, environmental factors, or a combination of both, which interfere with the delicate processes of neural plate folding and neural tube closure. Folic acid supplementation during pregnancy has been shown to reduce the risk of NTDs, underscoring the importance of prenatal care and public health initiatives in preventing these devastating birth defects [9].

Neurulation stands as a testament to the exquisite precision and complexity of embryonic development, where seemingly simple cellular movements give rise to the intricate architecture of the nervous system. Through the coordinated interplay of molecular signals, transcriptional regulators, and cellular behaviours, the neural plate transforms into the neural tube, laying the foundation for the human brain and spinal cord. As our understanding of neurulation continues to deepen, so too will our ability to unravel the mysteries of neurodevelopmental disorders and devise strategies for their prevention and treatment [10].

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Received: 25-Mar-2024, Manuscript No. aacnj-24-136334; Editor assigned: 28-Mar-2024, PreQC No. aacnj-24-136334(PQ); Reviewed: 11-Apr-2024, QC No. aacnj-24-136334; Revised: 16-Apr-2024, Manuscript No. aacnj-24-136334(R); Published: 23-Apr-2024, DOI:10.35841/aacnj-7.2.198

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