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The biomechanical role of the surface ectoderm and Grainyhead-like genes in neural tube closure

Viva Upgrade
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Abstract

Primary neurulation is the developmental process which forms the neural tube, the embryonic structure which goes on to form the brain and the spinal cord. A series of folding events convert the flat neural plate to a closed tube, consisting of neuroepithelium (NE, the future CNS) and a single overlying layer of surface ectoderm (SE, the future skin). As with any event during morphogenesis, cells and tissues undergo changes in shape and position during Neural Tube Closure (NTC). By definition, this means forces must be involved, the study of which is called biomechanics.

My PhD project is analysing the biomechanics of normal and abnormal NTC, focussing on the role of the SE. During normal closure of the posterior neuropore (PNP), we know that there are pro- and anti-closure forces, which must be balanced in order for successful closure to occur. In my project, I hypothesis that rostrocaudal tension in the SE may influence closure, based on cell shape and rostrocaudal actomyosin organisation. To test this, I developed a method for single border laser ablation in the intact embryo. Grainyhead-like (Grhl) mouse mutants provide an opportunity to investigate the possible link between abnormal biomechanics of the SE and failure of closure, as Grhl genes are expressed in the SE and these embryos show severe NTDs.

So far, I have found that the SE is not under high rostrocaudal tension as predicted, suggesting that the distinctive elongated cell shape at this region is not due to stretching. Furthermore, despite previous work showing abnormal SE mechanics in Grhl2 mutants, biomechanical properties of Grhl3 overexpression and hypomorphic mutants so far appear normal. Future work will focus on how SE cells may be intrinsically changing their shape during junctional remodelling, and the potential role of tissue properties (i.e. stiffness) during normal and abnormal closure.