CDB SEMINAR

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Wednesday, October 25

9:30~10:30 C1F CDB Auditorium

Signalling and Tissue Interactions for Anterior Morphogenesis in the Mouse

Summary

Morphogenesis of the craniofacial structures begins with the specification of the anterior-posterior polarity of the embryo prior to the onset of gastrulation. This patterning activity is reinforced by a putatively graded level of WNT signalling that is generating by the interaction of the activities of agonists in the posterior and the antagonists in the anterior germ layer tissues. By examining the phenotype of compound mutant *Dkk1;Wnt3* and *Dkk1;Gsc* mice, we demonstrate a requirement for the modulation of WNT signal at distinct times and sites during development. The manifestation of enhanced as well as novel mutant phenotypes in embryos harbouring loss of function mutations of *Dkk1* and *Wnt3* reveals a genetic interaction between the activities of these genes in head morphogenesis. Surprisingly, a reduced *Wnt3* activity over the *Dkk1*-null background may lead to an amelioration of forebrain and facial defects in the $Dkk1^{-/-};Wnt3^{+/-}$ embryo. This finding suggests that *Wnt3* plays a role at the initial phase of anterior morphogenesis and this early action has a lasting impact on craniofacial development. Analysis of the genetic interaction of *Dkk1* and *Gsc* revealed a dosage-related requirement of gene functions most likely in the prechordal mesoderm and the foregut endoderm during anterior morphogenesis. The phenotypic impact of combined loss of *Gsc* and *Dkk1* activities is consistent with a role of *Gsc* in the modulation of WNT signalling activity.

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