Chapter 2. Development and disease.

Our understanding of developmental mechanisms has been transformed during the 20th century by advances in genetic technology and molecular biology. The key genes regulating embryonic segmentation and the allocation of regional fate were identified in *Drosophila* [1 2 3 4 5 6 7] and are highly conserved in other segmented organisms. An additional set of genes regulating epithelial planar cell polarity (PCP) has been studied [8 9 10], although mainly during later development. The relationship between embryonic patterning and cellular polarity remains unclear. Recently, novel roles for the core PCP genes have been identified in neuronal function and disease mechanisms, both in model organisms and humans. For example, the mammalian Prickle (Pk) orthologues (Pk-1, -2 and -3) are expressed during embryonic convergent extension movements, somite formation and left-right symmetry breaking; with later functions during limb growth [11 12 13 14]. In the zebrafish, Pk orthologues are required for cell motility during gastrulation and neuronal migration [15]. Pk-associated disease syndromes include autism spectrum disorders, myoclonus epilepsy, lissencephaly and cancer metastasis [16 17 18 19 20 21 22 23 24]; similar defects are associated with other PCP mutants, including neural tube malformations in Celsr1 and Celsr3 [25 26 27]. Similarly, Testin (Tes) has a female germline function and acts as a tumour suppressor in mice and humans [28 29]. Thus, PCP gene functions regulate complex developmental processes and are associated with multiple disease syndromes. However, the PCP genes do not form a discrete group, and their associated mutant phenotypes depend on interactions between transcription factors (TFs), growth factors (GFs) and morphogens. Regulation of none of these genetic functions is independent of the others.

Summary:

Multiple morphogenetic defects and adult disease syndromes are associated with mis-regulation of PCP signalling interactions. These processes are co-ordinated between individual cells, across epithelial fields, and maintained within adult tissues.

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