Collective guidance wisdom

Traditionally, cell migration studies focus on the responses of a single cell to guidance signals, but migrations during development and metastasis involve traveling clumps of cells. Pernille Rørth and colleagues (EMBL, Heidelberg, Germany) now show that a collective consciousness can direct the migration of cell clusters.

The team tracked two distinct migration phases—a quick start and a later, slower phase—by the border cell cluster in developing fly egg chambers. They found that the phases required different growth factor–induced signaling pathways; only the latter was controlled by MAPK and PLCγ.

While early signals were restricted to the front of the cluster’s leader, the later MAPK signal was uniform throughout leading cells. How this signal could direct movement puzzled the group until they considered that the cluster might be guided as a unit. Movies revealed that, in the late phase, the cluster slowed to a tumbling, shuffling motion in which the leading cell or two—ones with the most MAPK signaling—often changed identity.

The shuffling means that cells are constantly in competition for who is “seeing” growth factor best at any given moment by being closest to the ligand source and sensing it best. This group mentality, which can assess a larger environment than individual cells, may boost migration precision.

Reference: Bianco, A., et al. 2007. Nature. 448:362–365.

Fluid for a single lumen

All biological tubes consist of a single lumen. According to Michel Bagnat, Didier Stainier, and colleagues (University of California, San Francisco, CA), one way to ensure this singularity is to use fluid pressure.

Too many lumens are found in the gut of Zebrafish larvae lacking the Tcf2 transcription factor. Extra tubes remain because they fail to coalesce normally during development. Bagnat and colleagues guessed that coalescence might be controlled by genes under Tcf2’s control.

DNA microarrays revealed that the gene for an epithelial junction protein, called claudin 15, was down-regulated in tcf2 mutants. Claudins form pores between cells that allow ions to be transported across epithelia down an electrochemical gradient. Tcf2 mutant gut cells also lacked a Na+/K+ ATPase, which probably creates the gradient that drives ions through the pores.

Where ions flow, water is sure to follow, resulting in lumenal fluid build-up. In vitro, Claudin 15 plus ion flow encouraged small neighboring lumens to unite. The authors hypothesize that pressure from the fluid forces lumens to join together, but cell rearrangements must also occur.

Fluid accumulation probably promotes single lumen formation in structures such as the pancreas, which begins with multiple small lumens, and the neural tube, where fluid accumulation is tightly regulated.

Reference: Bagnat, M., et al. 2007. Nat. Cell Biol. doi:10.1038/ncb1621.

SINEs create boundaries

Transcription requires chromatin to be in the unwound, open-access state. Boundary elements create a roadblock to remodeling machinery to prevent euchromatin from improperly converting back to tightly wound heterochromatin, and vice versa. Now, Victoria Lunyak, Geoff Rosenfeld (University of California, San Diego, CA), and colleagues reveal that boundary elements can be created by the transcription of non-coding repeat sequences derived from retrotransposons.

Lunyak et al. were dissecting the unwinding and regulation of the mouse growth hormone gene (GH). They mapped histone modifications that mark the transition to unwound chromatin to a region far upstream of the gene’s enhancer—a spot containing a short interspersed nuclear element (SINE) B2 repeat. SINE B2 repeats are best known as retrotransposon-derived pseudogenes of the rRNA gene that are uniquely transcribed on opposite strands by RNA polymerases II and III.

Enhancer-blocking assays confirmed the sequence’s role as a boundary element. Deleting the short sequence, which is about the length of one nucleosome, left GH in a permanently heterochromatic state.

Most known vertebrate boundary elements recruit proteins that form the chromatin roadblock. It is unknown what triggers the bidirectional transcription of SINE B2, but boundary activity only occurred when both transcription machineries were in play. The authors also found that the boundaries were created by the double transcription, not the transcripts. Lunyak suggests that this boundary strategy might be sprinkled throughout the mouse and human genomes where SINE-type repeats exist.

Reference: Lunyak, V.V., et al. 2007. Science. 317:248–251.