

Collective migration in tissues

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The Minisymposium on “Cell Migration in Tissues” focused on analysis of dynamic collective cell migration in several model systems and was cochaired by Alissa M. Weaver (Vanderbilt University Medical Center) and Celeste M. Nelson (Princeton University). The program highlighted both the physical forces exerted during migration and the signaling pathways involved in the process.

Celeste Nelson (Princeton University) presented results suggesting that cells migrate collectively through fibrous extracellular matrix (ECM) by exerting tensile forces at the leading edge of the cohort. Three-dimensional traction force microscopy was used to quantify the physical forces exerted by normal and malignant mammary epithelial cells undergoing collective migration through collagen gels (Gjorevski *et al.*, 2015). The forces and displacements were surprisingly dynamic, with the cohort periodically relaxing as it migrated forward.

Jessica Konen (Marcus laboratory, Emory University) described a new technique called spatiotemporal genomic analysis, which was used to select rare populations of leader cells from three-dimensional (3D) lung cancer spheroids and compare their gene expression patterns to that of follower cells. Leader cells were found to express higher levels of genes related to cell adhesion and vascular sprouting. These gene expression changes persisted in purified cultures.

Elijah Shamir (Ewald laboratory, Johns Hopkins University) showed that in 3D culture of mammary epithelial organoids, the myoepithelial layer was required to prevent invasion and dissemination of Twist1-expressing luminal epithelial cells. Surprisingly, Twist1-induced invasion required the expression of E-cadherin, and knocking down expression of this cell–cell adhesion protein prevented dissemination downstream of Twist1 (Shamir *et al.*, 2014).

Joshua Bloomekatz (Yelon laboratory, University of California, San Diego) showed a critical role for platelet-derived growth factor (PDGF) in the movement of cardiomyocytes during cardiac fusion. A

forward genetic screen was used to identify a mutation called *re-fuse-to-fuse*, which causes inhibition of cardiac fusion and the subsequent formation of a bifurcated ventricle. This mutation was found to disrupt splicing of *pdgfra*, leading to expression of a truncated form of the PDGF receptor. Expression of PDGF ligands in relatively medial locations suggested a model in which PDGF signaling coordinates the movement of cardiomyocytes toward the midline during cardiac fusion.

Bong Hwan Sung (Weaver laboratory, Vanderbilt University) showed that directionally persistent migration of cancer cells is promoted by autocrine secretion of exosomes, late endosome–derived extracellular vesicles (Sung *et al.*, 2015). Exosomes were shown to contain ECM proteins as cargo and to be secreted at sites of nascent adhesions. Accordingly, exosome secretion promoted adhesion assembly, migrational polarity, and the stability of lamellipodia.

David Matus (Stony Brook University) used an RNA interference screen to identify a transcriptional program that maintains invasive anchor cells in a cell cycle–arrested state during uterine–vulval attachment in *Caenorhabditis elegans*. Nuclear hormone receptor *nhr-67* (TLX) expression leads to up-regulation of cyclin-dependent kinase inhibitor *cki-1*, causing cell cycle arrest in G1 (Matus *et al.*, 2015). Cells that lack *nhr-67* are proliferative and noninvasive, failing to express matrix or form invadopodia.

The Minisymposium concluded with three lightning talks. **Micah Webster** (Fan laboratory, Carnegie Institution for Science) showed a role for “ghost fibers,” ECM remnants of damaged muscle fibers, in organizing skeletal muscle progenitor migration, division, and fusion during regeneration in mice (Webster *et al.*, 2016). **Rebecca Green** (Oegema laboratory, University of California, San Diego) developed a four-dimensional high-content imaging approach to screen for developmentally important genes within *C. elegans* embryos. **Yutaka Matsubayashi** (Stramer laboratory, King’s College London) showed that formation of the basement membrane in the *Drosophila* embryo requires rapid anterior–posterior dispersal of macrophages (hemocytes), which first appear in the head of the embryo.

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