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Abstracts

Cell motility and guidance

Program/Abstract # 284

The role of Neuropilin-1-VEGF signaling in neural crest cell invasion

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During vertebrate development, neural crest cells (NCCs), a highly invasive, pluripotent stem-cell like population, delaminate from the neural tube and follow stereotypical migratory routes to reach specific targets. In the head, discrete NCC migratory streams travel through different microenvironments to the branchial arches, yet signaling mechanisms that produce the migration pattern are still unclear. NCCs travel in loosely connected streams with constant contact between cells making this an excellent model system to study cell-cell and cell-microenvironment communication. Here we test the function of a putative NCC guidance cue, neuropilin-1. We previously showed that when neuropilin-1 expression is knocked down in NCCs, they fail to fully invade the 2nd branchial arch. Motility and directionality of these non-invading NCCs is rescued by transplantation into the hindbrain (rhombomere 4) of younger host embryos. Interestingly, we found that the ectoderm of the growing tissue adjacent to rhombomere 4, which becomes branchial arch 2, expresses a ligand for neuropilin-1, vascular endothelial growth factor (VEGF). In vitro culture experiments show that cranial NCCs are actively attracted to branchial arch 2 tissue as well as to VEGF-soaked beads. Furthermore, both VEGF-soaked beads and transplanted VEGF-expressing cells attract NCCs in vivo. Our results provide evidence for a role for neuropilin-1-VEGF interactions in rhombomere 4 neural NCC invasion in vivo. We suggest that neuropilin-1 may be critical to NCC homing into the branchial arches by maintaining an active motility state and responding to VEGF in the local microenvironment.

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Program/Abstract # 285

Towards an automated cell morphometric analysis to determine variation within neural crest cell migratory streams

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Neural crest cell (NCC) derivatives are critical to the vertebrate body plan and rely on the proper migration and targeting of progenitor cells. Measurements of NCC parameters along the migratory route would help us better understand how cells acquire direction and sustain guidance, yet it is time consuming to visually mark and measure individual cell properties from large sets of migratory stream data. Here, we present a novel approach that combines automated throughput analysis with visual detection to measure multiple NCC features with respect to distance along and to stereotypical, digitally recorded NCC migratory routes. Avian NCCs, transfected with H2B-mRFP and Gap43-EGFP, were imaged at 8, 16, and 24 h post injection. Individual NCCs were identified by visual and automated detection and cell morphometric parameters were measured and compared to NCC positions along the migratory route. Preliminary analyses showed NCCs emerged from the neural tube without orientation, but rapidly became aligned within the first 120 μm along the migratory route. Interestingly, lead NCCs and NCCs far from the migratory route were significantly less oriented to the migratory direction, while mid-stream NCCs were consistently oriented along the direction of migration. Our results suggest a model where NCCs acquire directed migration after interaction with local micro-environments and highlight the potential for throughput cell morphometric analysis to analyze large data sets of cell migration.

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Program/Abstract # 286

Directed vs. random: Does cadherin-11's extracellular cleavage fragment act as a chemoattractant to cranial neural crest cells?

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Multiple features within the embryo can influence the orientation of cell migration during morphogenetic movements. Physical constrain, remodeling of the ECM, and the establishment of chemical gradients have all been shown to play a role in these processes. In this work, we show that the production of an extracellular cleavage fragment (NTF) of Cadherin-11, a cell adhesion molecule present in the cranial neural crest promotes cell migration in vivo. In tissue culture, the NTF can bind to select molecules at the cell surface. Binding to these cell-surface receptors could promote intracellular signaling events, and may be used to establish a chemical gradient that helps orient CNC cells during their large-scale migration. We are currently using the open-sourced ImageJ software to track the migration of *Xenopus* CNC cells ex vivo. With this data, we are establishing methods to measure the directionality of