Neuroscience data talk

David Vijatovic and Verena Hübschmann (NDT)

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Host:

David Vijatovic (PhD student, Sweeney group)Title and abstract:Dissecting swim-to-walk transition and its neural basis during Xenopus frog metamorphosisTo parse the neural basis of motor behavior, we capitalize on the unique swim-to-walk transition of the Xenopus frog metamorphosis. This transition enables us to dissect the spinal circuitry for tail versus limb-based movement. We combine a robust behavioral assay with molecular cell-type profiling in wild-type, and then loss-of-function mutant, tadpoles to evaluate how neuronal diversity scales with and contributes to the increase in movement complexity over this transition.To characterize movement complexity, we devised a high-speed behavioral set-up that tracks individual body parts of the frog. Using the SLEAP software, we quantified intra- and inter-body part movement and created locomotor profiles that we correlated with the cell-type composition of the spinal circuit.To assess spinal cell types at swim and limb stages, we profiled the expression of transcription factors that define motor neurons (MNs) and V1 interneurons (V1s), an inhibitory class modulating MN firing. At free-swimming tadpole stages, MNs and V1s double in number and diversify in their transcriptional profile, acquiring subpopulations resembling the mouse hypaxial and preganglionic motor columns and V1 clades. At metamorphosis, spinal neuron diversity then peaks with the formation of limb motor columns and an increase in V1 number and diversity that largely matches the neonate mouse.We then asked how loss of cell-type diversity would alter the frogs motor repertoire. Using CRISPR/Cas9, we selectively knocked out three candidate master regulator genes: FoxP1, Hoxc9, and Engrailed-1. By comparing the behavior of mutant versus wild-type animals, we unravel each cell subtypes contribution to tail and limb motor function.Our work maps MN and V1 molecular properties onto the tail and limb-based behavior of frog metamorphosis, defining how transcriptional diversity scales with movement complexity. We also demonstrate the conservation of MN and V1 molecular organization between the frog, the most ancient tetrapod, and mouse, a four-limbed mammal.Verena Hbschmann (PhD student, Siegert Group)Title and abstract:Human microglia contribute to viral-mediated inflammation and impact neuronal activity in retinal organoidsViral infection-induced inflammation during pregnancy has been associated to malformation of the fetal brain and to long-term behavioral consequences in adulthood such as schizophrenia. Microglia respond to inflammatory signals and at the same time are actively involved in neuronal development. Yet, little is known about how an inflammatory environment affects microglia during human embryonic development and which consequences this has on neuronal circuit formation and function. Human induced pluripotent stem cells (hiPSC) provide a unique opportunity to generate brain region-specific models and to study their neuronal organization

and connectivity.Recently, we have shown that we can differentiate hiPSC into functional microglia-like cells (iMG) and retinal organoids (RO) 1,2. Using both models allows us to overcome the limitation that organoids commonly lack microglia and to generate microglia-assembled retinal organoids (iMG-RO).Here, we show that iMG successfully integrate into RO and colonize synaptic layers. However, iMG presence has no immediate impact on the neuronal activity at baseline condition as determined with calcium imaging. To simulate a viral-mediated inflammatory environment, we add poly(I:C) to iMG-RO. As anticipated, iMG become activated leading to an inflammatory signature. Interestingly, it also alters the calcium amplitude but not the frequency within neurons. To identify whether we can rescue the poly(I:C)-mediated effects, we apply the anti-inflammatory drug Ibuprofen, which can be taken during the first half of pregnancy. This treatment dampens iMG activation and mitigates inflammatory gene upregulation in RO. Remarkably, only in the presence of iMG in RO, Ibuprofen treatment rescues the increased calcium amplitude suggesting that microglia are critical involved in resolving this effect. This provides first insights into how inflammation during pregnancy might lead to neurological phenotypes in human.Bartalska, K., Hbschmann, V., Korkut-Demirba, M., Cubero, R.J.A., Venturino, A., Rssler, K., Czech, T., and Siegert, S. (2022). A systematic characterization of microglia-like cell occurrence during retinal organoid differentiation. IScience 25, 104580.Hbschmann, V., Korkut-Demirba, M, and Siegert, S. (2022). Assessing human iPSC-derived microglia identity and function by immunostaining, phagocytosis, calcium activity, and inflammation assay. StarProtocol 3, 4, 101866.

Tuesday, May 2, 2023 04:00pm - 05:00pm

Heinzel Seminar Room, Ground Floor, Office Bldg West

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