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research highlights

IN BRIEF

NEUROSCIENCE

Man's microglia meets mouse

Hasselmann, J. et al. Neuron https://doi. org/10.1016/j.neuron.2019.07.002 (2019)

Microglia, immune first responders in the nervous system, are increasingly recognized as important components to the development of a number of neurological disorders. When studied in vitro however, the cells don't quite live up to their full potential—location matters. To add biological context, researchers from the University of California, Irvine have been moving human microglia in vivo.

Using MITRG mice, a humanized, immunodeficient strain, they xenotransplanted iPSC-derived human microglia into pups and over time observed human-like cell behavior and gene expression patterns after acute and chronic injuries as well as in response to betaamyloid plagues, a characteristic feature of Alzheimer's disease. The authors suggest that the chimeric mouse could be a new *in vivo* tool for studying the complexities of human microglial function and its role in neurological disease.

https://doi.org/10.1038/s41684-019-0408-5

IMAGING

Voltron lights up neurons

Abdelfattah, A.S. et al. Science **365**, 699-704 (2019)

Genetically encoded voltage indicators, or GEVIs, are a means to image fast neuronal activity in the brain. As different neurons fire, voltage-sensitive dyes detect that change and light up in response. These have been common for some time, but many can leave a little resolution to be desired. A new tool, dubbed 'Voltron' by its creators at the Howard Hughes Medical Institute, adds additional detail.

Voltron pairs a protein genetically encoded in individual neurons in vivo with a synthetic dye that is brighter and lasts longer than other fluorescent protein-based GEVIs. Writing in *Science*, the team demonstrates Voltron at work in real time in mice, larval zebrafish, and Drosophila. The tool is currently compatible with conventional and EPNlight-sheet microscopes.

https://doi.org/10.1038/s41684-019-0409-4

CANCER

Where to, tumor?

Paul, C.D. Cell Syst 9, 187-206 (2019)

Once a cancer metastasizes, many become resistant to treatment. It is therefore a high priority in cancer research to better understand the earliest stages of the metastatic process. Where metatheses end up is not entirely random—organ tropism has been documented for a number of primary cancers—but how malignant cells ultimately become established at those secondary sites has been less clear. A new paper now observes those transitions across a whole organism: an optically clear larval zebrafish.

The researchers from the NIH injected larvae with brain- and bone marrowtargeting tumor lines and followed the physical dynamics the cells encountered as they traversed the fish's circulatory system. They note that vessel architecture seemed to play a role in where cells stopped, after which cell-specific differences began to influence their entry into the different EPNtargeted tissues.

https://doi.org/10.1038/s41684-019-0410-y

NEURODEVELOPMENTAL DISORDERS

Studying stuttering mice

Han, T. et al. PNAS **116,** 17515-17524 (2019)

Human stuttering has been linked to mutations in a number of intracellular trafficking genes, including one called N-acetylglucosamine-1-phosphate transferase subunits α and β —*GNPTAB*, for short. Mice have a related gene, and while the animals don't 'speak' in the same way as people, Gnptab-mutant pups emit disrupted ultrasonic vocalizations (USV) that researchers from the NIH have found to be similar to human stuttering—essentially, the flow of the pups' USVs is interrupted by long pauses.

With their stuttering mouse model, the researchers looked more closely at the animals' brains. They discovered astrocyte deficiencies, particularly in the corpus callosum area. These cells play a variety of roles in maintaining homeostasis in the brain and are thought to contribute to a growing number of neuropathologies. Including now, stuttering. **EPN**

https://doi.org/10.1038/s41684-019-0411-x