In-vivo studies of the development of the central nervous system

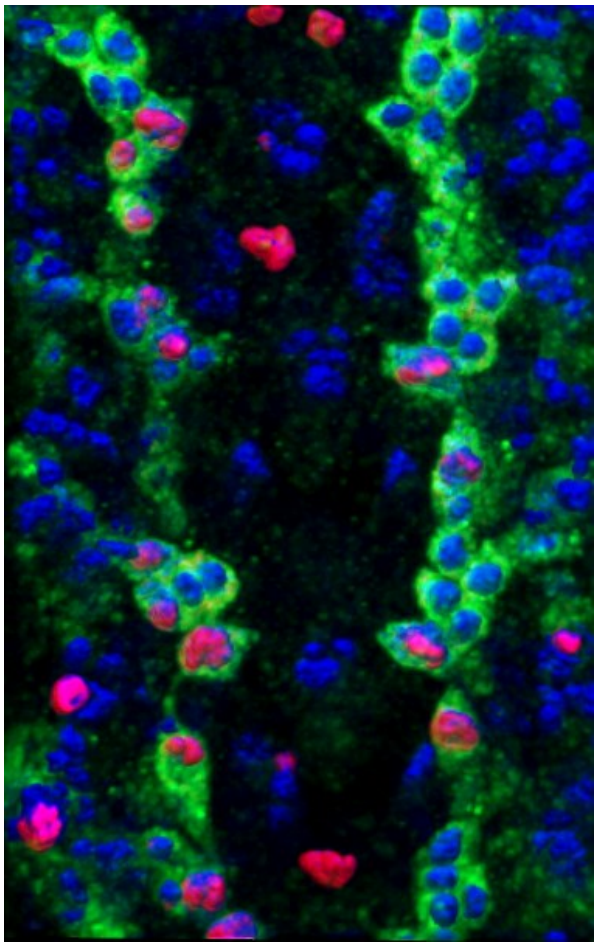
We aim to understand how the central nervous system acquires its complex organisation and structure during development, a requirement to understand nervous system function. We focus on studying the interactions between the two cell types, neurons and glia. During development, neurons trace intricate axonal patterns, neurons and glia migrate to occupy discrete positions, ultimately leading to the formation of neural networks and the functional enwrapment of axonal bundles by glia, and as these events take place, the nervous system grows. The molecular and cellular mechanisms that bring axonal patterning together with the timely and ordered adjustment of neuronal and glial cell populations during growth are still largely a mystery.

We would like to know, for instance, what are the molecular mechanisms that drive neuron-glia interactions; what are the events that determine how glial cells respond to neuronal signals to become polarised and enwrap axons; or, what controls the migration and division of glia to contact the axons in the "right" location and number, at the right time. In broader terms, is the brain built on universal molecular and cellular principles, which are analogous in all animals? What aspects of nervous system development are tightly constrained and which are responsive to the environment? What confers robustness to nervous system structure, that is, how do neurons and glia know when normal structure has been achieved and how to maintain it? By understanding nervous system structure and its regulation during growth, can we learn to direct repair?

We use Drosophila as a model system because we can address these questions swiftly, in vivo and with single cell resolution. Our approach routinely combines genetics, molecular biology and in vivo confocal microscopy in fixed specimens and in time-lapse. Our findings will have further implications in understanding the making of a brain, and its repair.

The research carried out by the group relies heavily on the daily use of imaging technology. We visualise neurons, their axonal processes and glia in vivo, on whole embryos that have been stained with antibodies. The antibodies recognise antigens (proteins) produced by the cells and they are linked either to an enzyme that upon addition of a substrate produces a coloured precipitate, or to a fluorophore that we can excite with a laser. We analyse the former with wide-field microscopy and Nomarsky optics after dissecting out the nervous system, and the latter with confocal microscopy on whole embryos. We also carry out confocal time-lapse recordings of migrating and dividing glia and extending axons, in whole living embryos whose neurons or glial are labelled with Greeen Fluorescent Protein (or Yellow YFP, or red DsRed versions of this protein). By rendering our data in 3D, and playing with opacity and transparency, we can carry out virtual sections though any plane that we may wish, and subsequently carry out rotations to visualise our cells through all perspectives.

The growing nervous system. Glia are seen here as they divide during embryonic development. Dividing glia are visualised in whole embryos with a cell division marker (red), a nuclear marker (blue) and a glial specific cytoplasmic marker (green), using laser scanning confocal microscopy. This image has been processed using Volocity 3D rendering software.



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