

Our brain is composed of billions of electrically active cells called neurons. During brain development, several millions of wirings (axons) from neurons are correctly laid. Out of these millions of axons scattered across the brain, some axons must be connect to other neurons. These specific connections are called as synapses. Only due to correct axon position and synapses, a new-born infant can smile, cry, hold on and suckle mothers nipple for milk.

Brain wiring and synapses are correctly made due to the help of star-shaped cells called astroglia. Astroglia instruct axons where to go and how to connect. Without astroglia, we will have less synapses, an improperly wired brain and we may most likely develop neurodevelopmental disorders. Hence, it is important to study how astroglia can speak and instruct neurons, its axons and synapses.

In this proposal, we will focus how astroglia can speak and instruct axon and synapse development at a molecular level. Specifically, we will focus on an important brain region called the posterior pituitary (PP). Human patients with problems in PP development will urinate a lot (20 litres per day), a condition called as diabetes insipidus. How the PP astroglia instruct the developing axons and synapse is the central theme of this proposal.

PP development is challenging to study in human fetus or mice embryos without surgery. This can be overcome by using optically transparent zebrafish larvae. Zebrafish are small freshwater fish from South Asia. Zebrafish is used as research model organism in 1000s of research laboratories in the world. Zebrafish has even helped scientists identify drugs to treat epilepsy in humans. Approximately 70% of zebrafish genes are conserved in humans. Thus, many of the genes that are responsible for zebrafish brain development are also involved in human brain development.

To study how glial cells instruct axons and synapses in zebrafish PP, we will apply latest technologies to develop genetically modified zebrafish and use advanced microscopic techniques to image PP in larval zebrafish. We expect that our studies in zebrafish, will also help understand the molecular mechanisms underlying human neurodevelopmental disorders.