



# John B. Thomas

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**“Our long-term goal is to understand how nerve cells are assembled into circuits during development to produce a functional nervous system.”**

Growing nerve cells are great communicators, extending long projections called axons, which hook up with other specific nerve cells to form functional circuits within the developing nervous system. At the tip of each growing axon is the growth cone, which steers the axon to its target cells by responding to cues in the extracellular environment.

Capitalizing on the advanced genetics of the fruit fly *Drosophila*, John Thomas's lab has identified key molecules in the axon's navigation system that govern a basic event common to all nervous systems: making axons grow from one side of the brain to the other. Crosstalk between the two sides of the nervous system is essential for many behaviors, from simple coordinated locomotion to the integration of higher cognitive functions, and its importance is underscored by the large number of nerve cells that project their axons across the midline to the opposite side.

Using a set of axon-targeted reporter molecules, Thomas has identified a number of axon guidance molecules, including a receptor called Derailed and its ligand, Wnt5, which together control how axons cross the midline of the nervous system.

Axons, it turns out, do not cross the midline randomly. Instead, they choose specific routes, or tracts. In *Drosophila*, crossing axons choose one of two tracts. The Derailed receptor is expressed on the growth cones of all nerve cells that cross in one of the tracts. Wnt5 is secreted by nerve cells that cross in the other tract, and by binding to Derailed, it acts as a repellent to keep the Derailed-expressing axons from wandering off the beaten tract.

Both Derailed and Wnt5 belong to larger families of related molecules, and Thomas has found that their relatives control additional axon guidance events. Recent studies have revealed that in mammals, the molecule that corresponds to Derailed is also a receptor for Wnt proteins and that it too is involved in guiding axons. What that means is these guidance molecules are deeply rooted in who we are, whether we are a fly on the wall or a human being wielding a flyswatter.

For more information, please visit [salk.edu/faculty/thomas.html](http://salk.edu/faculty/thomas.html)



**Left to right:**

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