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Abstract:
1. Objectives: Central nervous system needs to be isolated from the body fluid to maintain its special chemical and metabolic microenvironment. This insulation of communication between the brain and the rest of the body is achieved by the blood–brain barrier (BBB). Recently, a genetically tractable model organism, *Drosophila*, has emerged as a model system to study the BBB physiology due to similarities between *Drosophila* and vertebrate BBB. The objective of the proposed research is to understand the mechanisms of cellular communication across the BBB using the *Drosophila* model system.

Our recent studies have shown that two molecules, Dally-like protein (Dlp; a *Drosophila* heparan sulfate proteoglycan) and Dawdle (an activin homologue, a potential HS-dependent factor), regulate cellular communications between glial cells outside the BBB and neuroblasts (NBs: neural stem cells) inside the BBB. These preliminary data led us to hypothesize that the BBB is not a simple structural insulator, but a dynamic regulator of brain development. We studied the mechanisms underlying the functional interactions of the nervous system with the external environment across the BBB.
2. Methods: We determined the contributions of two biological processes, (1) filopodia formation and (2) transcytotic transport, to cellular communications across the BBB. We disrupted the functions of molecules responsible for these processes by RNAi knockdown and assessed their effects on NB proliferation and brain morphology as readouts of signaling across the BBB.
3. Results: We detected no effect of inhibition of filopodia formation on NB development. On the other hand, blocking membrane trafficking in the BBB cells significantly disrupted NB proliferation and brain morphology. Our study supports a model that cellular communications across the BBB is mediated via transcytotic transport of signaling molecules, including heparan sulfate proteoglycans and activin-like ligands.