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### **Molecular Editing in the Developing Brain: CRISPR wiring screens, personalized modeling, and genome therapeutics**

#### **Abstract:**

The developing brain implements a genetic blueprint that establishes neuroanatomical wiring patterns underlying cognition, sensation, and behavior. We have developed a new set of molecular tools to rapidly explore these processes directly in the developing brain of mammals. Combining technologies including genome manipulation by CRISPR/Cas9-RC and Prime Editors, subcellular proteomics, and 3D light sheet imaging, we investigate how genetic programs impact neurotypical and pathological brain wiring, model individual epilepsy patients to explore pharmacotherapy in animal avatars, and design genome therapeutics to restore genome hotspots in diseases including Huntington's, Alzheimer's, and non-CNS diseases including thalassemias. This repertoire of new molecular medicine tools enables in vivo mechanistic investigations, informs personalized medicine approaches, and sets a path toward genome therapeutics for broad classes of neurological and systemic disease.

#### **Biosketch:**

Alexandros Pouloupoulos is Associate Professor of Pharmacology & Physiology at the University of Maryland School of Medicine in Baltimore. He studied Biology at the University of Athens, and completed his PhD in Goettingen, Germany working with Nils Brose at the Max Planck Institute of Experimental Medicine. He received the 2009 Otto Hahn Medal of the Max Planck Society for outstanding doctoral research. He went on to postdoctoral training as an EMBO Fellow and HFSP Fellow with Jeffrey Macklis at Harvard University. In 2017 he was recruited to Maryland to establish an independent lab funded by the NIH High-Risk High-Reward Research program, receiving the NIH Director's New Innovator Award in 2019. His lab develops new genome editing approaches targeting the brain. More information at [poulab.org](http://poulab.org)