



Grand Prize
winner

Andrija Sente

Category: Cell & Molecular Biology

Essay title: *Gatekeepers of the brain – Hidden mechanisms of type-A GABA receptor signaling and assembly*

Biography

Andrija Sente received an undergraduate degree from the University of Cambridge and conducted his PhD and postdoctoral research at the MRC Laboratory of Molecular Biology. His research utilized cryogenic electron microscopy to study the structures and assembly of type-A GABA receptors. He currently works as a Research Scientist at an artificial intelligence company in London.

Abstract

Type-A gamma aminobutyric acid receptors (GABAARs) mediate the majority of inhibitory neurotransmission in the central nervous system and are targeted by psychoactive medicines such as anxiolytics or general anesthetics. The receptor is a pentamer formed from a pool of 19 subunits, yet how these subunits come together to define receptor structure and function remains largely unknown. We used cryo-EM to image receptors assembled from different subunit combinations. Our findings reveal that certain subunit sets can form multiple structurally and functionally distinct receptor subtypes, which can coexist within the same cell. Additionally, we resolved the structure of a receptor prior to oligomerization, to provide mechanistic insights into the assembly process. These results advance our understanding of GABAAR assembly and highlight opportunities for pharmacological interventions.