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Prof Renae Ryan

School of Medical Sciences
Faculty of Medicine and Health
The University of Sydney, Australia

Renae Ryan is a Professor of Biochemical Pharmacology at the University of Sydney, Australia. She received her PhD from the University of Sydney in 2004 and completed postdoctoral work with at Columbia University and the National Institutes of Health (NINDS). Renae returned to the University of Sydney in 2007 where she leads a research team that investigates the molecular mechanisms of neurotransmitter and amino acid transporters and their role in neurological diseases, such as episodic ataxia, and cancer. She has received several awards for scientific excellence, mentoring and outreach including the 2023 Nancy Millis Medal from the Australian Academy of Science and a NSW Tall Poppy Award in 2011. Renae is a globally respected leader and advocate for gender equity, diversity and inclusion, and a sought-after supervisor, mentor, and role model for women in science.

The twisted link between a dual function glutamate transporter and Episodic Ataxia

Excitatory Amino Acid Transporters (EAATs) regulate excitatory neurotransmission by transporting glutamate into cells, mostly glia, to terminate neurotransmission and to avoid neurotoxicity. EAATs also conduct chloride ions (Cl-) via a channel-like process that is thermodynamically uncoupled from transport. The molecular mechanisms that allow these dual-function transporters to carry out two seemingly contradictory roles, and the physiological role of Cl- conductance of the EAATs, are not clear. I will describe the cryo-electron microscopy structure of a glutamate transporter homologue in an open-channel state, revealing an aqueous-accessible Cl- permeation pathway that is formed during the transport cycle and discuss the impact of a series of mutations in EAAT1 that have been identified in patients with the neurological disease episodic ataxia type 6 (EA6). By studying EAAT1 function and using a Drosophila melanogaster model of locomotor behaviour, our results indicate that mutations that lead to functional glutamate transport but either increased OR decreased Cl- channel activity contribute to the pathology of EA6, highlighting the importance of Cl- homeostasis in glial cells for proper central nervous system function. Our findings provide insight into the mechanism by which glutamate transporters support their dual functions and provides a framework for the rational development of therapeutics that can differentially modulate substrate transport or channel properties for the treatment of neurological disorders caused by EAAT dysfunction, such as Episodic Ataxia.