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# Andrés E Dulcey

*National Institute of Health, USA*

## Discovery, optimization and characterization of CNS-Penetrant Allosteric Inhibitors of c-Abl Kinase

The loss of different neuronal populations leading to neuronal dysfunction, cytoskeletal alterations and abnormal protein phosphorylation are the main hallmarks of neurodegenerative diseases. In particular, the neuropathological hallmarks of Alzheimer's disease (AD) are neuronal loss in regions related to memory and cognition, neurotransmitter depletion, synaptic alteration and the deposition of abnormal protein aggregates. Currently, there is no effective treatment for AD, creating a need for new therapeutic treatments that can treat or prevent AD and other neurodegenerative diseases. c-Abl tyrosine kinase is a ubiquitous non-receptor tyrosine kinase involved in signal transduction. In addition to its classic function in leukemia pathogenesis, c-Abl is also thought to play a role in neuronal development, neurogenesis, neuronal migration, axonal extension, and synaptic plasticity, whereby deregulation of c-Abl could be related to early neuronal dysfunction and cytoskeletal alterations. Here we describe the chemical and pharmacological characterization of novel brain-penetrant allosteric inhibitors of c-Abl tyrosine kinase activity, with proof of principle towards their applicability as a potential treatment for neurodegenerative disorders.

### Speaker Biography

Andrés E Dulcey was born in Cali, Colombia. After completing a Bachelor of Science in Chemistry from the Ohio State University, he joined the laboratory of Professor Virgil Percec at the University of Pennsylvania. His doctoral research focused on the design, synthesis and structural characterization of biologically-inspired libraries of amphiphilic compounds which self-assemble into functional, helical, porous channels. After completion of his doctoral degree, he joined the National Institutes of Health (NIH), first as a Postdoctoral Fellow and then as a Research Scientist, where he has spent over 10 years working in different modalities of medicinal chemistry. Currently, he is at the National center for advancing translational sciences at the NIH, where he works as a Research Scientist at the forefront of translation, advancing programs in target identification and validation, assay development and screening, probe development and lead optimization, and drug repurposing, with the goal of furthering the understanding of biochemical pathways and aiding the development of new medicines.

**e:** dulceyan@mail.nih.gov

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