



**Dr. Aurélie de Rus Jacquet
& Dr. Francesca Cicchetti**
Université Laval



Aurélie de Rus Jacquet, PhD, is a researcher in the Neurosciences program of the CHU de Québec-Université Laval Research Center, and an assistant professor in the Department of Psychiatry and Neurosciences in the Faculty of Medicine at Université Laval. She obtained her PhD in Medicinal Chemistry and Molecular Pharmacology from Purdue University (USA) in 2016, during which she undertook an ethnopharmacological approach rooted in the valorization of First Peoples' knowledge and discovered neuroprotective botanicals that attenuated Parkinson's disease-related pathology. She then joined the Howard Hughes Medical Institute to train in the use of induced pluripotent stem cells (iPSCs) in the laboratory of Dr. Randall Moon (2016–2017, Institute for Stem Cell and Regenerative Medicine, University of Washington, USA). Subsequently, she completed two postdoctoral trainings on the neurobiology of Parkinson's disease with Dr. Erin O'Shea (2017–2020, Howard Hughes Medical Institute, USA), and with Dr. Francesca Cicchetti (2020–2023, Université Laval, Canada). Her work has highlighted the role of glial cells, and astrocytes in particular, in the progression of neurodegenerative disorders such as Parkinson's and Huntington's disease.

While Dr. de Rus Jacquet is an early-career researcher, the co-PI, **Dr. Cicchetti**, is a well-established veteran of Huntington disease research whose research has been awarded the HSC Navigator three times: in 2006 and 2009 for her work on graft survival in HD, and most recently in 2019 for a project titled "Targeting the blood brain barrier to treat HD." She is now a professor at the Department of Psychiatry and Neurosciences, Faculty of Medicine of Université Laval. Dr. Cicchetti has published over 100 manuscripts in high-impact journals, and three of her recent publications have been awarded most influential papers in the field of Huntington's disease by the Huntington Study Group. She is an active member of several scientific committees and editorial boards. Her research program aims to understand the prion-like properties of abnormal proteins associated with neurodegenerative diseases and to develop therapeutic strategies that would target this aspect of the pathophysiology. More recent work focuses on elucidating the impact of Parkinson's and Huntington's disease-related proteins and toxins on the functionality of the blood-brain barrier.

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Research Project Title: *Brain rejuvenation: an innovative approach to Huntington's disease therapy*

Lay Summary: Huntington's disease (HD) is a neurodegenerative disorder caused by a single defective gene known as huntingtin (HTT). This disease is characterized by uncontrolled movements, a decline of thinking ability, as well as psychiatric problems. The life span of affected individuals is usually 10 to 30 years after the appearance of symptoms. In this disease, an abnormal form of a protein referred to as mutant Huntingtin (mHtt) accumulates in brain cells, disrupting their normal function and eventually leading to their death. Recently, the Cicchetti group utilized a model system called "parabiosis" in which mice are surgically sutured to create the joint circulatory system and has provided exciting new evidence showing reduced pathology in the diseased (HD) mice that were surgically paired to normal mice. This study demonstrated the involvement of circulating factors from healthy blood in diluting/ameliorating disease pathology. Building on this new data, we designed a project that aims to identify the beneficial elements contained in healthy blood and to understand how they ameliorate brain health. To achieve this goal, we will isolate human plasma proteins capable of migrating from the blood into the brain because they will likely be the most neuroprotective factors. We will then evaluate if these proteins improve the survival and function of neurons and non-neuronal cells in a dish but also in a mouse model of HD. This project will help us identify circulating factors in healthy plasma that may prevent the death of brain cells and that therefore could be useful in treating various disease features. Additionally, outcomes of this study may encourage the transfusion of healthy human plasma as a potential therapeutic strategy to treat HD.