Dr Paola Bezzi

Investigating the role of astrocytes in behavioural impairments associated with Phelan McDermid syndrome

Mutations in the SHANK3 gene are one of the most common diagnosed causes for autism. However, we still know surprisingly little about the consequences arising from mutations in this gene. Since their original discovery, SHANK3 mutations have most commonly been studied in neurons. However, recent evidence suggests that astrocytes, a largely overlooked brain cell, may also play a key role in the development of autism. Astrocytes provide critical metabolic and trophic support to neurons and have recently been found as key players in the formation and maturation of neuronal circuits. Therefore, astrocyte dysfunction, resulting from SHANK3 mutation, may lead to problems in neuronal circuit formation and maturation, which will ultimately lead to behavioural and cognitive abnormalities.

This project has the aim of tackling these questions using an array of innovative models that include genetically engineered mouse models, as well as human brain organoids capable of closely mimicking human cellular physiology.

Understanding which brain cells are key players in autism, and how SHANK3 mutations impact normal function during disease pathophysiology will allow us to discover and design successful therapies for neurodevelopmental disorders.