



## PROJECT

**Supervisor:**

Dr. Marco Piccoli

**Title:**

Exploring Protein Sialylation in Brugada Syndrome: Implications for  
Clinical Management and Diagnosis

**Curriculum:**

Molecular Medicine; Clinical and Experimental Medicine

Link to the personal page of the  
University or relevant hospital site  
website:

<https://unifind.unisr.it/resource/person/5163>

## Description of the Project (max 3,000 characters including spaces)

### **Background/gap of knowledge**

Brugada syndrome (BrS) is one of the main causes of sudden cardiac death, especially in people under 40 years of age without structural heart disease. The worldwide prevalence is estimated at 5-20 cases per 10,000, with the majority of patients remaining asymptomatic until a potentially fatal arrhythmic event occurs. While genetic abnormalities, particularly in the SCN5A gene, are responsible for approximately 35% of cases, the aetiology of the remaining cases is unclear. Recently, we have focused on alterations in protein sialylation in BrS, which have not been extensively studied despite their known effects on cardiac ion channel functionality.

### **Rationale and hypothesis**

Given our preliminary results showing significant changes in protein sialylation patterns in BrS patients, we hypothesize that dysregulated sialylation of the cardiac sodium channel NaV1.5 and possibly other proteins may contribute to the pathogenesis of BrS. These post-translational modifications could alter the functionality of the ion channel and thus influence cardiac excitability and arrhythmogenesis.

### **Objectives and specific aims**

1. Characterisation of differences in protein sialylation in peripheral blood mononuclear cells of BrS patients compared to healthy controls.
2. Confirmation of results using an independent cohort and validation of potential sialylation-based biomarkers.
3. To investigate the association of altered sialylation with the clinical course of BrS with the aim of finding potential diagnostic and prognostic applications.



### **Expected outcomes**

This study aims to establish altered sialylation as a new biomarker for BrS and thus significantly improve the diagnostic and prognostic possibilities for this disease. The identification of specific sialylation profiles associated with BrS could lead to the development of non-invasive testing methods, reducing the reliance on current invasive diagnostic procedures. In addition, these biomarkers could provide new insights into the risk stratification and management of asymptomatic patients, potentially leading to therapeutic decisions and preventing sudden cardiac deaths.

### **Skills that the student should acquire** (max. 600 characters including spaces):

The student must master advanced biochemical techniques including isolation of proteins, sialylation-specific enrichment and analysis by western blot and mass spectrometry. They will understand the mechanisms of post-translational modifications and their effects on protein function. The project will improve skills in experimental design, data interpretation and the use of statistical tools for the identification of biomarkers in the context of clinical research.

### **References** (max. 15)

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**APPLICATION TO ACT AS SUPERVISOR AND  
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