

PROJECT 1**DoS:** Marco BacigaluppiTitle: Cerebral thrombus analysis in large vessel stroke to unravel pathogenesis of ischemiaCurriculum: Neuroscience and Experimental NeurologyResidency Program: Neurology

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<https://www.unisr.it/offerta-formativa/medicina-chirurgia/post-lauream/dottorato-medicina-molecolare0/director-of-studies/bacigaluppi-marco>**Project description** (*Number of characters, including spaces: 2.000 - 3.000*):

Stroke represents the third cause of mortality and the first cause of disability. An essential issue in stroke treatment and secondary prevention is to understand the underlying pathophysiology to set up adequate therapeutic strategies. The pathogenic mechanisms underlying ischemic stroke are extremely heterogeneous, and human cerebral thrombi can originate from different sources, such as from cardioembolism, unstable atherosclerotic plaque, paraneoplastic hypercoagulable states, venous paradox thromboembolism. Unfortunately, in the etiologic workup of stroke patients, up to one third – despite an extensive diagnostic workup - the cause of a stroke cannot be identified. Therefore, the etiology remains classified as cryptogenic.

Recent advances in endovascular treatments in large vessel ischemic stroke have provided the opportunity to retrieve occlusive cerebral thrombi. Indeed, the analysis of the retrieved thrombi could lead to the optimization and personalization of preventive and acute stroke therapies.

This project hypothesizes that a detailed study of structural, inflammatory, and molecular features of cerebral thrombi could lead to important insights into thrombus pathophysiology and etiology. Indeed, diverse thrombotic sources bear different pathophysiological mechanisms conditioning thrombus composition features. Inflammation in this context is emerging as an essential trigger and constituent of thrombosis. The delicate interplay between innate immunity and coagulation - named thromboinflammation, can be triggered by diverse stimuli (e.g., infection, arrhythmia, aging) and lead rapidly to detrimental pathologic processes, sustaining immunologic disease, venous and arterial thrombosis.

This project will thus aim to analyze several features of retrieved cerebral thrombi, including imaging, histology, molecular biology, and cellular characteristics of human cerebral thrombi, as well as to model lytic and composition features. The ultimate goal is to provide new insight into the pathophysiology of stroke that can lead to the design of new therapeutic and diagnostic strategies.

Skills to be acquired by the student:

The Ph.D. Student is expected throughout the studies to learn and deepen knowledge in the management of clinical data, capacity to analyze clinical and imaging data with sophisticated statistical models. Moreover, laboratory skills ranging from histological staining, molecular biology assays, ELISA, and in particular cytofluorimetry will be acquired. Laboratory assays and to assay thrombus composition and formation will have to be learned. The Ph.D. will also be required to develop skills in multidimensional data analysis and graphical representation (RNA seq, cytofluorimetry, multiple histological staining).

References (max. 3)

- Insights from thrombi retrieved in stroke due to large vessel occlusion. Bacigaluppi M, Semerano A, Gullotta GS, Strambo D. J Cereb Blood Flow Metab. 2019 Aug;39(8):1433-1451.
- Engelmann B, Massberg S. Thrombosis as an intravascular effector of innate immunity. Nat Rev Immunol. 2013;13:34-45
- Staessens, S., Fitzgerald, S., Andersson, T., Clarençon, F., Denorme, F., Gounis, M., ... De Meyer, S. Histological stroke clot analysis after thrombectomy: Technical aspects and recommendations. International Journal of Stroke. 2019