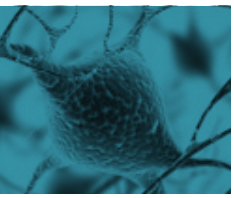

FUNDED PROJECTS

NanoStroke \\ ROLE OF DANGER SIGNALS IN STROKE AND THERAPEUTIC TARGETING BY NANOBODIES.

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In acute stroke, the size of the initial brain lesion can further increase over the first hours and days after the ischemic event. This 'infarct growth' is a significant clinical problem because it is related to worsening of neurological deficits and poor functional outcome. Recent lines of evidence directly link local inflammatory and immune reactions with the degree of stroke-associated brain damage and secondary infarct growth. What exactly triggers this inflammatory response and how the immune reaction amplifies damage is unknown. Likely candidates for immune activation are danger signals such as adenosine triphosphate (ATP), nicotinamide adenine dinucleotide (NAD), and high-mobility group box 1 protein (HMGB1) that are released from dying cerebral tissue after stroke.

In this project, we will investigate the pathophysiological role of danger signals in acute and subacute stroke. We will take a therapeutic approach using specific nanobodies to perturb danger signal receptors in vitro and in vivo. We will design different versions of nanobody complexes to achieve an optimal function and avoid the immunogenicity and toxicity characteristic of classical antibodies. These modifications will be critical for clinical application in the future. As a step towards a novel treatment option for patients, we will test if nanobody suppression of inflammatory cell activation under ischemic conditions can be extended to the human system using in vitro and ex vivo preparations.
The consortium consists of Anna Planas, Barcelona, Christoph Kleinschnitz and Guido Stoll, Würzburg, Carlos Matute, Bilbao, Andrea la Sala, Rome and Friedrich Koch-Nolte and Tim Magnus, Hamburg.

COORDINATOR | TIM MAGNUS

PROJECT **PARTNERS:**

Tim Magnus
University Medical Center Hamburg-Eppendorf, Hamburg, Germany

Christoph Kleinschnitz
University of Würzburg, Würzburg, Germany

Anna Planas
Instituto de Investigaciones Biomédicas de Barcelona, Barcelona, Spain

Carlos Matute
Universidad del País Vasco, Leioa, Spain

Andrea La Sala
IRCCS San Raffaele Pisana, Rome, Italy