**Titel des Projekts**

Characterization of Semaphorin 3F as a biomarker of myocardial dysfunction in post-cardiac arrest syndrome

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**Zusammenfassung des Projekts**

Out-of-hospital cardiac arrest (OHCA) presents a considerable health burden worldwide and is one of the main causes of death in Europe [1]. After successful resuscitation many patients develop the post-cardiac arrest syndrome (PCAS) that comprises a systemic inflammatory response, encephalopathy and hemodynamic instability due to myocardial dysfunction and impaired vasoregulation [2]. PCAS is a consequence of whole body ischemia/reperfusion (I/R) injury after successful resuscitation when spontaneous circulation returns after cardiac arrest (CA) [3]. The heart is very susceptible to I/R and as a result a state of reduced systolic heart function called post cardiac arrest myocardial dysfunction (PCAMD) often occurs [3]. PCAMD contributes to hemodynamic instability and poor prognosis in the first three days after ROSC [4–7]. Despite the clinical importance of PCAMD, its pathophysiology is incompletely understood and specific therapeutic strategies are lacking.

Semaphorin (Sema) 3F is an extracellular protein and was discovered as an inhibitor of tumour growth but recent studies indicate that Sema3F regulates inflammation [2] and vascular integrity following I/R [8]. The applicants have recently shown that Sema3F protein concentrations are elevated in blood of OHCA patients in the post-resuscitation period [2].

The aim of this project is to explore whether Sema3F plasma levels are associated with pre-cardiac arrest conditions (e. g. comorbidities, medication), interventions during resuscitation (e. g. defibrillation) as well as post-cardiac arrest aspects (e.g. left ventricular function, hemodynamic instability) that have been found to influence PCAMD and mortality of patients with OHCA.

The applicants hypothesize that Sema3F plays a key role in the pathogenesis of PCAMD because …

1. … inflammation is a pathogenetic key feature after I/R injury [9] and Sema3F is upregulated during inflammation and promotes leukocyte recruitment [8].
2. … Sema3F is upregulated in patients with heart failure with reduced ejection fraction [unpublished data of the applicants] and PCAMD is characterized as a transient cardiomyopathy with reduced ejection fraction after ROSC [9].

The applicants conclude that circulating plasma Sema3F may be a potential novel biomarker of PCAMD. Quantification of plasma Sema3F will allow to identify OHCA patients with increased risk of hemodynamic instability and poor prognosis after ROSC. Early recognition of this high-risk subgroup may lead to individualized therapies of OHCA patients to improve their outcome.