Key Facts

This network brings together **basic scientists** and **academic clinicians** and will make use of novel animal models, state-of-the art technologies and expertly phenotyped patient cohorts to **identify key mechanisms** common to multiple **SVDs** and determine how these mechanisms contribute to individual SVDs.

SVDs@target is coordinated by Prof: Martin Dichgans (LMU) and runs from January 1, 2016 until December 31, 2021.

SVDs@target receives 5,998,300 EUR funding from EU.

Project Partners

Ludwig-Maximilians-University Munich (LMU)	**DE**
University of Vermont (UVM)	**USA**
University of Oxford (UOXF)	**UK**
University of Edinburgh (UEDIN)	**UK**
Institut national de la santé et de la recherche médicale (INSERM)	**F**
University of Utrecht (UMCU)	**NL**
University of Münster (WWU)	**DE**
University of Maastricht (UM)	**NL**
Technical University Munich (TUM-MED)	**DE**
Stroke Alliance for Europe (SAFE)	**UK**
ARTTIC Innovation GmbH (AI)	**DE**

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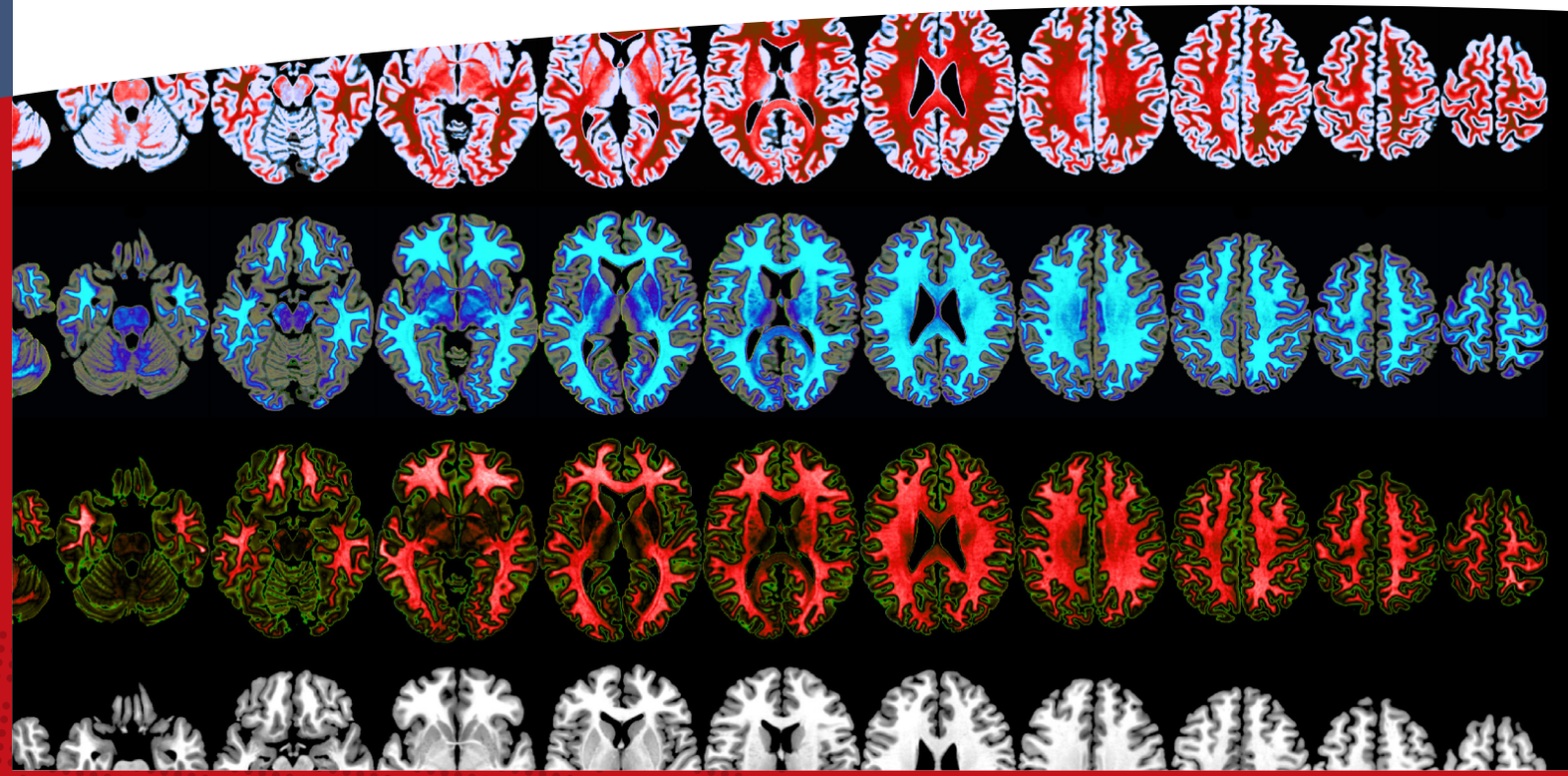

For further information visit:
www.svds-at-target.eu
Follow us on Twitter @SVDs_at_target

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Funded by the European Union

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Small vessel diseases in a mechanistic perspective:

Targets for Intervention – Affected pathways and mechanistic exploitation for prevention of stroke and dementia

Funded by the European Union

The Challenge

- **Stroke and dementia** rank among the **most pressing health issues** in Europe.
- **Cerebral small vessel diseases (SVDs)** have emerged as a central link between these two major co-morbidities.
- SVDs account for more than **30% of all strokes** and at least **40% of all dementia** cases.

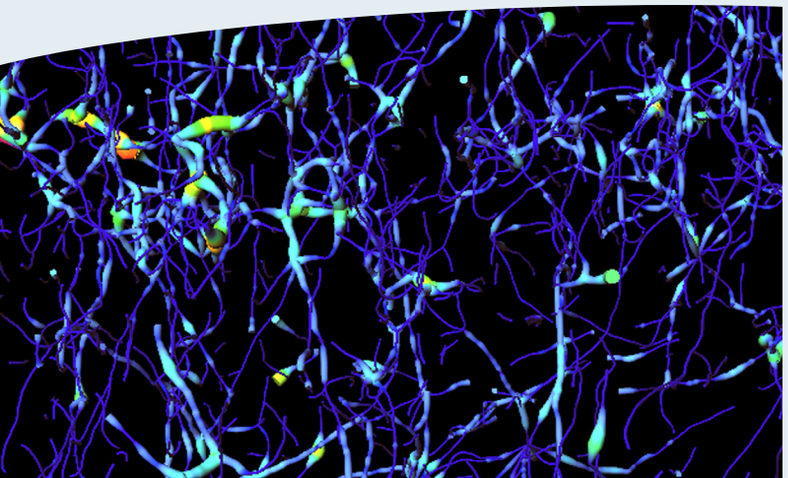
The SVDs@target project aims to investigate the underlying mechanisms.

Our Objectives

Specifically, the network aims to

- **define** common molecular, cellular, and physiological **mechanisms** underlying the regulation of blood flow, blood brain barrier and clearing functions of microvessels that are comprised in different SVDs
- **determine** how these common mechanistic defects intersect to **drive brain parenchymal damage**
- **validate** the relevance of **mechanisms** and **biomarkers** through interventions in experimental systems and in patients

With the better understanding of small vessel diseases SVDs@target will develop novel therapeutic treatments and finally contribute to the prevention of stroke and dementia.



Our Impact

SVDs@target will offer new directions for clinical research for better prevention, health promotion, and therapy development, as well as for the management of patients with stroke and dementia.

SVDs@target will improve the preventive treatment of the disease and will lead to a significant benefit at the individual and societal level.

Our first results already provide a better understanding of disease pathways leading from basic risk factors to functional deficits.

First Results

- Functional hyperemia, the blood flow response to nerve activity, is progressively impaired due to crippeled capillary-to-arteriole vasodilatory signalling in animal model of chronic hypertension and CADASIL.
- Beneficial effect of antihypertensive treatment on functional hyperemia depends on the class of antihypertensive.
- Recent studies indicate the deleterious influence of midlife hypertension on later-life cognitive function highlight the importance of adequate blood pressure control.
- In our clinical study INVESTIGATE-SVDs we confirm that blood brain barrier leakage increases with white matter hyperintensity (WMH) severity and that cerebral vascular reactivity is lower in patients with severe WMH, higher vascular pulsatility and with more visible perivascular spaces.
- The results of our clinical study ZOOM@SVDs in CADASIL represent a breakthrough in SVD research in humans. We have delivered the first MRI markers that assess small vessel malfunction directly at the level of the small vessels themselves.

Clinical Studies

Small vessel disease (SVD) is associated with vascular risk factors and it strongly increases with age however, there are also rare genetic variants of the SVD. CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) is caused by mutations in the NOTCH3 gene, represents a pure form of SVD and has successfully been used as a model.

We aim to advance our knowledge of the mechanisms of SVDs by three clinical studies:

ZOOM@SVDs, an observational MRI study at ultra-high resolution (7T) to assess microvascular function and parenchymal damage.

Study sites: **Utrecht, Munich**

INVSTIGATE-SVDs, observational MRI study at 3T to assess blood brain barrier function, microvascular function, and perivascular flow.

Study site: **Edinburgh, Maastricht, Munich**

TREAT-SVDs, an interventional study to determine the effects of different blood pressure lowering agents on microvascular function in patients with distinct SVDs.

Study sites: **Munich, Oxford, Edinburgh, Utrecht, Maastricht**