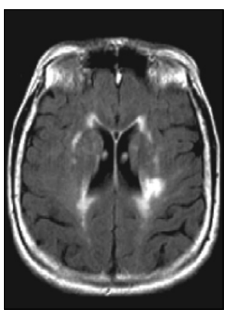
Vascular disease and neurodegeneration: advancing together

On Feb 19, 2017, immediately before the International Stroke Conference, the MarkVCID consortium held its first meeting in Houston (TX, USA). The focus of this new research consortium is on understanding small vessel disease and its contributions to vascular cognitive impairment and dementia (VCID). For too long, research in dementia has neglected the most common comorbidity in elderly patients: cerebrovascular disease. Funders are now reversing this trend and encouraging research into the role of brain vessels in neurodegeneration, and MarkVCID is a momentous initiative in that direction.

Vascular brain lesions are very common in people aged 70 years and older, and a large proportion of dementia cases might be attributed to cerebrovascular disease. Arteriolosclerosis and cerebral amyloid angiopathy (small vessel disease) are commonly found in patients who also have other brain pathologies, such as the plaques and tangles associated with neurodegenerative disease; small vessel disease might also increase the risk of Alzheimer's disease. Nevertheless, the physiological relation of small vessel disease with neurodegeneration is unclear. In an animal model of multiple brain microinfarts, these ischaemic lesions seem to trap proteins and other solutes within the parenchyma, and impair brain clearance. But whether the mechanisms behind small vessel disease and neurodegeneration act synergistically or in parallel is not known.

Despite the scarcity of physiological evidence, robust epidemiological findings provide support for an association between dementia and cerebrovascular disease. These findings indicate that the incidence of Alzheimer's disease and other dementias can be substantially reduced if vascular risk factors (eg, hypertension, obesity, and diabetes) are targeted at the population level. Vascular health and brain health are intertwined, and the advances in prevention and treatment of vascular risk factors are probably behind the decreases in dementia incidence in Europe and North America over the past three decades. In clinical practice, physicians must therefore recommend lifestyle changes and interventions to tackle these factors, but neurologists also need biomarkers of small vessel disease that reliably reflect not only the development of vascular brain lesions in a patient, but also the progression of cognitive impairment. The identification of such biomarkers is the overarching goal of the MarkVCID consortium. The consortium is composed of seven research groups based in the USA, and a group at Massachusetts General Hospital in Boston acting as a coordinating centre. Some research groups will focus on population-based cohorts at early disease stages, whereas others will make use of their expertise on established neurovascular and cognitive impairment, and the biology of small vessel disease. In the initial 2 years, each site will concentrate on the characterisation of different non-invasive biomarker candidates, from serological and CSF markers to neuroimaging, retinal, and other brain measures. After the analysis of data from this initial phase, in a second phase (years 3 to 5) the consortium will move towards the implementation of joint protocols for the validation of the most promising biomarker candidates across the sites and the various cohorts. At the end of its 5-year programme, the consortium is committed to deliver biomarkers ready to be used in phase 2 and 3 trials of interventions to stop or prevent cognitive impairment, either by refining the selection of participants or as outcome measures.

MarkVCID is one of a number of research initiatives that must jointly accomplish the main goal of the National Alzheimer's Project Act (NAPA): to prevent and effectively treat Alzheimer's disease and related dementias by 2025. Among the other initiatives, the Molecular Mechanisms of the Vascular Etiology of Alzheimer's Disease (M2OVE-AD) consortium is working to develop mathematical and animal models of vascular pathways in neurodegeneration, and thus should complement the translational research of MarkVCID at the mechanistic level. This increased support for multidisciplinary research on the vascular contributions to cognitive impairment will accelerate discoveries in two fields that have traditionally advanced in parallel; the need for them to converge is also being recognised in Europe, where stroke and dementia research come together in landmark initiatives such as the CoSTREAM consortium, SVDS@target, and METACOHORTS. Continued funding is needed to support these initiatives in achieving their goals. By 2025, these collaborations might provide neurologists with biomarkers that enable them to track vascular pathology, provide accurate prognoses, and even prescribe treatments that can stop or delay vascular cognitive impairment. ■ *The Lancet Neurology*



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For more on the **MarkVCID consortium** see https://markvcid.partners.org/drupal/

For more on **vascular cognitive impairment** see *Alzheimers Dement* 2015; **11:** 710–17

For more on **small vessel disease** see **Position Paper** *Lancet Neurol* 2013; **12:** 822–83

For more on **small vessel disease and risk of Alzheimer's disease** see **Articles** *Lancet Neurol* 2016; **15:** 934–43

For the **findings in an animal model** see *J Neurosci* 2017; **37:** 2870–77

For more on **dementia epidemiology in Europe** see **Policy View** *Lancet Neurol* 2016; **15:** 116–24

For more on **M2OVE AD** see http://sagebase.org/research-projects/m2ove-ad-consortium/

For more on **CoStream** see http://www.costream.eu/

For more on **SVDS@target** see https://www.svds-at-target.eu/

For more on **METACOHORTS** see *Alzheimers Dement* 2016; **12:** 1235–49