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MatriSVDs

Multidimensional interrogation of microvascular matrisome abnormalities in cerebral small vessel diseases

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One quarter of ischemic stroke, the vast majority of spontaneous intracerebral hemorrhage and about one third of dementia cases world-wide are caused by diseases affecting these small brain vessels, also called cerebral small vessel diseases (cSVDs). cSVD is an heterogeneous group of diseases and currently there is no understanding of what goes wrong and therefore these diseases lack an effective treatment. Cells that make up the vessel wall are embedded in a complex mesh of proteins called the matrisome. Altered levels of matrisome proteins can lead to small vessel lesions, the underpinning of cSVDs. Our hypothesis is that matrisome changes in small brain vessels take center stage in cSVDs. This project aims at addressing the 3 following questions: 1) What drive these matrisome changes in cSVDs? 2) How do changes in the levels/activity of HTRA1, a matrisome protein and key player in cSVDs, contribute to disease manifestations and death of contractile vascular cells and 3) conversely, can some matrisome modifications have a protective role, preventing the occurrence of disease manifestations? Altogether, the information obtained from our study can be used to get an inspiration for future studies to develop therapeutics - either directly to interfere or correct the disease pathway or to stimulate existing protective pathways.