

Fluid biomarkers of extracellular matrix remodelling across neurological diseases

Akademisk avhandling

Som för avläggande av medicinsk doktorsexamen vid Sahlgrenska akademien,
Göteborgs universitet kommer att offentligen försvaras i hörsal **Arvid Carlsson**,
Medicinaregatan 3, den **5 mars 2021**, klockan **9:00**

av **Karolina Minta**

Fakultetsopponent: Prof. Dr. **Andreas Faissner**, Ruhr-Universität, Bochum, Germany

Avhandlingen baseras på följande delarbeten

- I. **Minta K**, Cullen NC, Al Nimer F, Thelin EP, Piehl F, Clarin M, Tullberg M, Jeppsson A, Portelius E, Zetterberg H, Blennow K, Andreasson U. *Dynamics of extracellular matrix proteins in cerebrospinal fluid and serum and their relation to clinical outcome in human traumatic brain injury*. Clin Chem Lab Med 2019, 57:1565-1573
- II. **Minta K**, Brinkmalm G, Thelin EP, Al Nimer F, Piehl F, Tullberg M, Jeppsson A, Portelius E, Zetterberg H, Blennow K, Andreasson U. *Cerebrospinal fluid brevican and neurocan fragment patterns in human traumatic brain injury*. Clin Chim Acta 2020,512(2021):74-83
- III. **Minta K**, Brinkmalm G, Al Nimer F, Thelin EP, Piehl F, Tullberg M, Jeppsson A, Portelius E, Zetterberg H, Blennow K, Andreasson U. *Dynamics of cerebrospinal fluid levels of matrix metalloproteinases in human traumatic brain injury*. Scientific Reports 2020, 10(1):18075
- IV. **Minta K**, Jeppsson A, Brinkmalm G, Portelius E, Zetterberg H, Blennow K, Tullberg M, Andreasson U. *Lumbar and ventricular CSF concentrations of extracellular matrix proteins before and after shunt surgery in idiopathic normal pressure hydrocephalus*. Manuscript
- V. **Minta K**, Brinkmalm G, Portelius E, Johansson P, Svensson J, Kettunen P, Wallin A, Zetterberg H, Blennow K, Andreasson U. *Brevican and neurocan peptides as potential cerebrospinal fluid biomarkers for differentiation between vascular dementia and Alzheimer's disease*. J Alzheimer's Dis 2021, doi: 10.3233/JAD-201039, in press
- VI. **Minta K**, Portelius E, Janelidze S, Hansson O, Zetterberg H, Blennow K, Andreasson U. *Cerebrospinal fluid concentrations of extracellular matrix proteins in Alzheimer's disease*. J Alzheimer's Dis 2019, 69(4):1213-1220
- VII. Fernström E*, **Minta K***, Andreasson U, Sandelius Å, Wasling P, Brinkmalm A, Höglund K, Blennow K, Nyman J, Zetterberg H, Kalm M. *Cerebrospinal fluid markers of extracellular matrix remodelling, synaptic plasticity and neuroinflammation before and after cranial radiotherapy*. J Intern Med 2018, 284:211-225

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Abstract

Neurological diseases constitute a major health and socioeconomic issue. Despite an enormous amount of research going on globally, the prevalence and mortality of neurological disorders are still rising. This has placed a big pressure on health-care systems for biomarker development to be able to detect early stages of the disease and to predict clinical outcomes in patients. The fact that biochemical changes in the brain can be reflected in blood or cerebrospinal fluid paves the way for the fluid biomarkers to become beneficial, cost-effective, and easily accessible tools in neuroscience. The ambition of this thesis was to investigate if measurements of extracellular matrix proteins in human body fluids have a potential to characterise neurological conditions. The findings presented in this thesis suggest that several extracellular matrix proteins may serve as novel cerebrospinal fluid biomarkers for outcome prediction following traumatic brain injury. In addition, they showed a novel diagnostic biomarker potential to differentiate vascular dementia from Alzheimer's disease, the two most common types of dementia with largely overlapping symptoms. Moreover, their levels in cerebrospinal fluid may represent complex biochemical changes of the brain's extracellular matrix in patients with idiopathic normal pressure hydrocephalus and in patients who received cranial radiotherapy. These findings may lead to a better understanding of the role of extracellular matrix remodelling across neurological diseases and may contribute to the management and development of future therapies.

Keywords: Alzheimer's disease, biomarker, extracellular matrix, idiopathic normal pressure hydrocephalus, immunoassay, mass spectrometry, radiation-induced brain injury, traumatic brain injury, vascular dementia.

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