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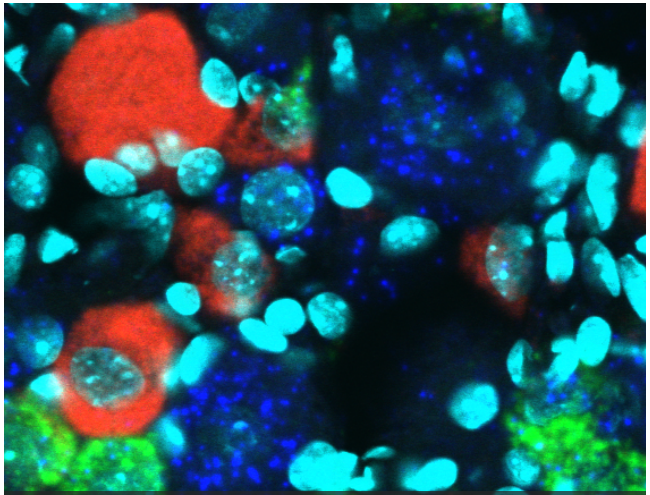
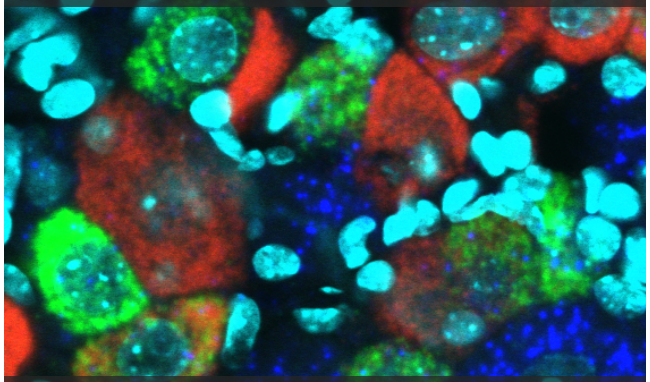


EXPLORING THE ROLE OF THE EXTRACELLULAR MATRIX IN PAIN USING EHLERS-DANLOS SYNDROMES AS A MODEL

ROBIN VROMAN



2024

GHENT UNIVERSITY

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KEY PUBLICATIONS

1. Vroman R, *et al*. Animal Models of Ehlers-Danlos Syndromes: Phenotype, Pathogenesis, and Translational Potential. Front Genet. 2021 Oct 12;12:726474.

2. Vroman R, *et al*. Analysis of matrisome expression patterns in murine and human dorsal root ganglia. Front Mol Neurosci. 2023 Aug 17;16:1232447.

3. Vroman R, *et al.* Reduced capsaicin-induced mechanical allodynia and neuronal responses in the dorsal root ganglion in the presence of protein tyrosine phosphatase non-receptor type 6 overexpression. 2024. (in press)

4. Syx D, Miller RE, Obeidat AM, Tran PB, **Vroman R,** et al. Pain-related behaviors and abnormal cutaneous innervation in a murine model of classical Ehlers-Danlos syndrome. Pain. 2020 Oct;161(10):2274-2283.

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SUMMARY

This thesis explores the relationship between the extracellular matrix (ECM) and pain using Ehlers-Danlos Syndromes (EDS) as a model. EDS, characterized by defects in ECM molecules related to collagen biosynthesis and fibrillogenesis, provides a unique opportunity to examine ECM abnormalities and pain. This work comprises multiple publications, each contributing to our understanding of the ECM-pain connection. To further understand (or investigate) this link, three research objectives were formulated:

1. A Comprehensive overview of animal models of EDS

Given the limited number of patients and the challenges in obtaining crucial nervous tissue samples, studying pain mechanisms in EDS remains a considerable challenge. Hence, we will focus on studying pain in animal models of EDS. In **manuscript 1**, we provide a comprehensive overview of the available EDS animal models. This enabled us to dive deeper into the ECM-pain questions using a fitting murine model for EDS.

2. Elucidating the role of the ECM in human and murine DRG

Subsequently we focused on defining the previously unexplored matrisome composition in human and murine dorsal root ganglion. By using a combination of different transcriptomic techniques, we studied expression patterns of matrisome genes in both species, and provided insights into cellular interactions within the DRG, and how they are altered in pain states. The findings of this study are included in **manuscript 2**.

3. Examining pain-related behavior and neuro-anatomy in a murine model of classical EDS

Finally, I acquired the skills to assess pain-related behavior and assess neuroanatomic changes in mice, and applied these to murine models. In **manuscript 3**, we used pain-related behavioral assays a murine model to study the role of a phosphatase (Shp1) that acts on an ion channel (Trpv1) expressed in sensory neurons. In **manuscript 4** we demonstrated for the first time a pain-related phenotype in a model for classical EDS as well as altered skin innervation.

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2014-2017	Bachelor of Science (BSc), Ghent University: Bachelor of Biochemistry and Biotechnology
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