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The role of **the omega-3 fatty acid biosynthetic products resolvin D1 and resolvin E1** in maintenance of **ocular surface health**

On February 28, 2020 Marit Lippestad defended her thesis "The role of the omega-3 fatty acid biosynthetic products resolvin D1 and resolvin E1 in maintenance of ocular surface health" for the degree of PhD at Institute of Clinical Medicine, Faculty of Medicine, University of Oslo (UiO).

Ocular surface inflammatory diseases such as dry eye disease and allergic conjunctivitis are common diseases and the prevalence of these diseases are increasing. Treatment options are limited, and new management methods are warranted.

Omega-3 fatty acid biosynthetic products named resolvins may actively stop inflammation. Resolvins have shown promising results as treatment of inflammatory diseases in the eye, including dry eye disease and allergic conjunctivitis. Before resolvins are used

in treatment of ocular inflammatory disorders, the mechanism of action of the resolvins in healthy, non-diseased patients should be understood.

The aim of this project was to determine how the resolvins Resolvin D1 and Resolvin E1 work in healthy conjunctival goblet cells. Conjunctival goblet cells were studied since disruption in secretion of the goblet cell mucin MUC5AC is associated with both dry eye disease and allergic conjunctivitis. MUC5AC also plays an important role in ocular surface health

as it lubricates the ocular surface and removes pathogens and allergens from the tear film, thus preventing inflammation.

Goblet cell function was studied in cultured rat and human conjunctival goblet cells. We identified the receptors for resolvin E1 in goblet cells using RT-PCR, western blot and immunohistochemistry. The calcium concentration in the cytosol of goblet cells and the amount of mucin secretion were measured after treatment with specific signaling pathway inhibitors added before stimulation with either resolvin D1 or resolvin E1. Our studies showed that the resolvins activate multiple signaling pathways to stimulate goblet cell mucin secretion. We believe that resolvins are important both in maintenance of ocular surface health and prevention of disease. Thus, resolvins may be potential new treatments of ocular inflammatory diseases.

All the work for the PhD was performed at Schepens Eye Research Institute/Massachusetts Eye and Ear, Department of Ophthalmology, Harvard Medical School under the supervision by Professor Darlene A. Dartt.

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