Biomedicine, Institute Seminar, 7th of April 2015, 12:00-13:00, Physiology lecture hall.

Mette Madsen, associate professor, Institute of Biomedicine, Biochemistry division

"Learn how years of research in endocytic receptors lead to identification of a novel biomarker in melanoma cancer"

If melanoma cancer is detected at an early stage, where it is still localized to the skin, the patient holds a good prognosis. Patients with early stage melanoma cancer are usually cured by surgical resection of the melanocytic lesion. However, if melanoma cancer spreads beyond the local lymph node, the prognosis is poor and only about 10 % of the patients diagnosed with metastatic melanoma with distant metastases survive. Unfortunately, no biomarkers have been established than can identify the most aggressive primary melanoma tumors, predict metastazation, and point towards the need of adjuvant treatment.

Aggressive melanoma cells are characterized by increased proliferative activity, improved anti-apoptotic machinery, as well as enhanced metastatic potential. Based on years of research in the field of endocytic membrane receptors and knowledge about the functional potential of receptor proteins like megalin, we recently hypothesized that acquired expression of megalin by melanocytic lesions/melanoma tumors confers or improves cancerous characteristics. The ongoing aim of our research group is to identify novel cancer biomarkers with the potential to improve early diagnosis and prognosis as well as the identification of new therapeutic targets.

Megalin is a cell surface receptor capable of binding an extensive number of different ligands, including nutrients and signalling molecules. Megalin is best known for its role in the kidney, where it mediates reabsorption of various ligands from the glomerular ultrafiltrate. It has also been widely studied in relation to embryonic development, especially of the brain. We discovered that megalin is frequently expressed in melanomas and melanoma metastases and rarely in benign counterparts. Our functional analyses indicated that melanoma megalin is probably involved in uptake and trafficking of ligands, like it is in other tissues, which could include trafficking of nutrients, signaling molecules or even signalling receptors.

Groundbreaking, our results indicated that sustained megalin expression in melanoma cells is crucial for cell maintenance, as siRNA-mediated reduction in melanoma cell expression of megalin significantly decreased melanoma cell proliferation and in particular survival rates. Our recent study has thus established a platform for acknowledging megalin as a potential new biomarker and therapeutic target in cancer, specifically in melanoma.