Neuromedin U, new potential regulator of colorectal cancer metastasis mechanisms.

Colorectal cancer is the third most lethal invasive cancer in Poland. Therapy choice, metastasis and tumor recurrence are critical processes influencing the CRC treatment. The most successful therapeutic approach in colorectal cancer (CRC) is the resection of the tumor during the early stages of disease. However, even when diagnosed early, new putative CRC progression markers are still needed to help with prediction of clinically latent versus invasive tumors and qualify patients for more aggressive adjuvant therapy. CRC subtypes were identified but their ability to metastasis need to be further investigated.

While we were searching for new players and mechanisms of metastasis initiation depended on a key regulator of epithelial to mesenchymal transition (EMT), transcription factor Snail, neuromedin U (NMU) was detected as one of the most upregulated gene involved in cellular motility modulation but not associated previously with early stages of CRC metastasis. Increased expression was detected in more invasive cells therefore, **in the current project we propose that neuromedin U is involved in active regulation of colorectal cancer progression and may have a potential as a new marker of the process.**

To verify above hypothesis we have to consider NMU effect not only on CRC cells but also on tumor microenvironment cells expressing NMU receptors such as macrophages and endothelial cells.
NMU is a small secretory peptide synthetized as a precursor. Two G-coupled receptors (GPCRs), NMUR1 and NMUR2, are expressed on cancer cells but also, between others, on macrophages and endothelial cells, known to be active modulators of tumor microenvironment. Cancer niche modulation by CRC cells is a known phenomenon. However NMU produced and released by cancer cells, although associated before with cancer progression, has never been studied in the context of its effect on tumor niche.
In this proposal we plan also to verify whether NMU has a potential as a new biomarker of colorectal cancer progression initiation as its overexpression was already proposed in breast and endometrial cancers as a prognostic marker of poor outcome.

Analysis of NMU expression, signaling induction, release and extracellular abundance in CRC cells, tissues and surrounding cells, will shed more light on the potential function of this molecule as a regulator, potential target for therapy and the marker of the early stages of colorectal cancer metastatic process.