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in kemijsko tehnologijo

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*VABILO NA PREDAVANJE
V OKVIRU DOKTORSKEGA ŠTUDIJA
KEMIJSKE ZNANOSTI*

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z naslovom:

**EpCAM expression and functions in cell
differentiation and tumor progression**

v četrtek, 11. aprila 2019 ob 15:00 uri
v predavalnici 1 v 1. nadstropju Fakultete
za kemijo in kemijsko tehnologijo, Večna pot 113

Vljudno vabljeni!

Abstract:

Cancer remains a global, life-threatening disease that newly affects more than 15 million people each year. Patients with cancers that have not spread from their primary site, have strongly enhanced chances to survive. Oppositely, metastasized cancers, where tumor cells have disseminated to secondary locations in the body and have given rise to metastases in life-supporting organs, have dismal survival rates. Hence, understanding biochemical and cellular processes that govern the metastatic cascade is of paramount importance to guide and improve tumor therapy efficiency.

The metastatic cascade initiates with the delamination of single or small groups of malignant cells from primary tumors. Invasive tumor cells then gain access to the blood circulation and thereby become systemic, circulation tumor cells (CTC). Eventually, CTC extravasate out of the blood stream and disseminate into secondary sites, including liver, lungs, and brain. Here, disseminated tumor cells (DTC) regain adhesive and proliferative properties, and grow out to life-threatening metastases.

One central, membrane-associated protein that is used as an anchor molecule to isolate CTC and DTC in the clinical setting, and which is involved in the regulation of cellular differentiation aspects required during the metastatic cascade, is epithelial cell adhesion molecule EpCAM. In carcinomas, EpCAM is frequently and strongly expressed. However, more recent findings, including publications from our group, pinpointed a dynamic regulation of EpCAM during the metastatic cascade, which was linked to the cellular functions of EpCAM that include the regulation of cell-cell adhesion, proliferation, and epithelial-to-mesenchymal transition (EMT). Our laboratory has studied the molecular and cellular functions of EpCAM in stem and cancer cells. Using this model antigen, we could demonstrate that regulated intramembrane proteolysis (RIP) of EpCAM by membrane-tethered proteases of the ADAM family and by the γ -secretase complex, has multiple impact on the function of EpCAM. RIP generates sub-domains of EpCAM with individual functions in the regulation of gene transcription and the activity of additional receptors such as the epidermal growth factor receptor EGFR, for which the soluble extracellular domain of EpCAM serves as ligand. Additionally, RIP of EpCAM is a means of protein disposal that, together with endocytosis, regulates the availability of the protein at the membrane.

In summary, EpCAM expression is associated with an epithelial phenotype in cancer and normal cells. During the metastatic cascade, down-regulation of EpCAM expression induces a migratory and invasive phenotype, while (re-)expression of EpCAM equips tumor cells with proliferative and adhesive capacities required in the late phases of tumor and metastases formation.