CeNT CENTRE OF NEW TECHNOLOGIES

UNIVERSITY OF WARSAW

invites to a seminar by

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Inflammatory signaling from the endocytic pathway

30th March 2017 at 1:00 p.m.

Venue: Centre of New Technologies, Banacha 2c,
Lecture Hall 0142 (ground floor)

Host: Prof. Joanna Kargul

Endocytosis was first viewed simply as a mechanism of signal termination through the downregulation and degradation of surface receptors. However, more recent data indicate that endosomal compartments and their resident proteins play an important role in transmitting intracellular signals by transporting ligand-receptor complexes and affecting their activity inside the cell.

Cytokine receptors from the TNFR (tumor necrosis factor receptor) superfamily signal via the NF-κB pathway which induces a proinflammatory and stress response of the cells. However, endocytic trafficking of the TNFR receptors and its impact on signaling remain poorly investigated. We have recently uncovered a role of ESCRT-dependent sorting of cytokine receptors as an important factor limiting constitutive NF-κB signaling. Depletion of selected ESCRT components potently activates both the canonical and noncanonical NF-κB pathways without cytokine stimulation, inducing proinflammatory transcriptional response in cultured human cells, zebrafish embryos and fly fat bodies. These effects depend on cytokine receptors, such as lymphotoxin β receptor (LTβR) and TNFRI. ESCRT-dependent defects in their trafficking can induce receptor oligomerization and signaling in a ligand-independent manner. We propose that ESCRTs constitutively control levels and distribution of ligand-free cytokine receptors to restrict their signaling. This may represent a general mechanism to prevent spurious NF-κB activation. Moreover, we demonstrate that cytokine receptors from the TNFR superfamily can elicit inflammatory signals intracellularly when localized to endosomes.