UNIVERSITY OF WARSAW | CeNT CENTRE OF NEW TECHNOLOGIES

invites to a seminar by

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Towards deciphering the molecular mechanism regulating Wnt ligand trafficking

8th of February 2018 at 12 p.m.

Venue: Centre of New Technologies, Banacha 2C,
Lecture Hall 0142 (Ground floor)

Host: Marta B. Wiśniewska

After secretion, developmental signals must travel relatively long distances to form a concentration gradient that the responding tissue uses to acquire positional information. The role of signal transport and endocytic trafficking in this process is the subject of intense debate. Wnt proteins regulate developmental processes, tissue regeneration and stem cell maintenance. It has been postulated that Wnt/ β -catenin signalling form concentration gradients across responsive tissues. However, little is known about the transport mechanism for these lipid-modified signalling proteins in vertebrates.

We show that Wnt8a is transported on short, actin-based filopodia to contact responding cells and activate Wnt/β-signalling during zebrafish early development (1). We define these cell protrusions as Wnt cytonemes, based on the description of signalling filopodia in Drosophila. Enhanced formation of cytonemes increases the effective signalling range of Wnt by facilitating spreading. Consistently, reduction in Wnt cytonemes leads to a restricted distribution of the ligand and a limited signalling range. Using a numerical simulation, we provide evidence that such a short-range transport system for Wnt has long-range signalling function during tissue development.

After contact by Wnt cytonemes, a multi-protein complex at the plasma membrane assembles clustering membrane-bound receptors and intracellular signal transducers into the Wnt-signalosome. Our imaging studies in live zebrafish embryos show that the signalosome is a highly dynamic structure, which is continuously assembled and disassembled by a Dvl2-mediated endocytic process (3). We show that this endocytic process is not only essential for ligand-receptor internalization but also for signaling.

We conclude that a cytoneme-based transport system for Wnt and subsequent endocytosis is important for Wnt/β-catenin signaling and controls anteroposterior patterning of the neural plate during vertebrate gastrulation.

(1) Stanganello et al., 2015; (2) Brinkmann et la., 2016; (3) Hagemann, et al., 2014