Thu 14. September 2017
Time: 11:00 h

Institute of Biochemistry and Molecular Medicine
IBMM, Gertrud Woker Strasse 5, 3012 Bern

Everybody is welcome

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Dr. Laura Soucek, PhD is ICREA Research Professor and Principal Investigator Mouse Models of Cancer Therapies Laboratory at Vall d'Hebron Institute of Oncology (VHIO), Barcelona, Spain.

This lecture is hosted by Prof. Roch-Philippe Charles (IBMM)

NCCR TransCure Lecture in Biology

by Dr. Laura Soucek

Targeting the undruggable: inhibiting Myc in cancer

Deregulation of the MYC oncoprotein promotes tumorigenesis in most, if not all, cancers and is often associated with poor prognosis. However, targeting MYC has long been considered impossible based on the assumption that it would cause catastrophic side effects in normal tissues. Despite this general preconceived notion, we showed that MYC inhibition exerts extraordinary therapeutic impact in various genetic mouse models of cancer, and causes only mild, well-tolerated and reversible side effects. For these studies we employed the systemic and conditional expression of a dominant negative of MYC, called Omomyc, which we designed and validated, and that can inhibit MYC transactivation function both *in vitro* and *in vivo*. To date, Omomyc has only been considered a proof of principle, with any potential clinical application limited to gene therapy. Now, though, we have evidence that the 11 kDa Omomyc polypeptide spontaneously transduces into cancer cells, demonstrating unexpected cell-penetrating ability and the potential to become a clinically viable drug. Once inside the nuclei, the polypeptide effectively blocks MYC binding to its target DNA sites, interfering with MYC transcriptional regulation and halting cell proliferation. Moreover, intranasal (i.n.) administration of the Omomyc polypeptide in mice results in its rapid and persistent distribution to lungs, as well as to other organs (i.e. intestine, liver, kidneys and brain). Importantly, i.n. treatment of mice bearing either Non-Small-Cell-Lung-Cancer (NSCLC) or glioblastoma (GBM) with the *Omomyc cell-penetrating peptide* (Omomyc^{CPP}) significantly reduces tumor burden compared to their control counterparts. An intravenous formulation of the same peptide can achieve systemic distribution and demonstrates efficacy in various other types of tumors as well, increasing the potential applications of this therapeutic. In summary, our data indicate that this novel generation of polypeptides represents a new opportunity to potentially inhibit MYC pharmacologically in a variety of malignant diseases.

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