LIMNA
Lausanne Integrative Metabolism & Nutrition Alliance

# SEMINAR

**Monday August 29, 2016 – 9h30**
Conference room AI 1153 (*) - EPFL - Lausanne


## Dr. Giovanni Sorrentino
National Laboratory CIB, Area Science Park Trieste (Italy)


## Metabolic control of YAP and TAZ by the mevalonate pathway

**Host:** Prof. Kristina Schoonjans


## Abstract:
The YAP and TAZ mediators of the Hippo pathway promote tissue proliferation, organ growth and cancer development. However, how their biological properties intersect with cellular metabolism remains unexplained. In our recent work, we show that YAP/TAZ activity is controlled by the SREBP/mevalonate pathway. Inhibition of the rate-limiting enzyme of this pathway (HMG-CoA reductase) by statins opposes YAP/TAZ nuclear localization and transcriptional responses. Mechanistically, the geranylgeranyl pyrophosphate produced by the mevalonate cascade is required for activation of Rho GTPases that, in turn, activate YAP/TAZ by inhibiting their phosphorylation and promoting their nuclear accumulation. In *Drosophila melanogaster*, inhibition of mevalonate biosynthesis and geranylgeranylation blunts the eye overgrowth induced by Yorkie, the YAP/TAZ orthologue. In tumour cells, YAP/TAZ activation is promoted by increased levels of mevalonic acid produced by SREBP transcriptional activity, which is induced by its oncogenic cofactor mutant p53. These findings reveal an additional layer of YAP/TAZ regulation by metabolic cues.


(*) IMPORTANT NOTICE: All external participants have to pass through SV Reception/Welcome Desk to be able to access to AI 1153.
Contact person to call at arrival at SV Reception Desk: Johan Auwerx 30951 /Administrative Assistant: 39522.


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