

CONFERENCE du Prof. **Andreas VILLUNGER**

Invitation: Groupe Anim'Pharma

Mardi 23 mai 2023 à 11h30
FACULTE de PHARMACIE – Salle des Actes
4 Avenue de l' Observatoire 75006 Paris



The PIDDosome and Caspase-2 in cell cycle control and beyond

The death fold domain-containing protein PIDD1 has recently attracted renewed attention as a regulator of the orphan cell death-related protease, Caspase-2. Caspase-2 can activate p53 to promote cell cycle arrest in response to centrosome aberrations, and its activation requires formation of the PIDDosome multi-protein complex containing multimers of PIDD1 and the adapter RAIDD/CRADD at its core. However, PIDD1 appears to be able to engage with multiple client proteins to promote an even broader range of biological responses, such as NF- κ B activation, translation, DNA synthesis or cell death. PIDD1 shows features of inteins, a class of self-cleaving proteins, to create different polypeptides from a common precursor protein that allow it to serve these diverse functions. In this presentation, I will discuss recent experimental advances that highlight the potential pathophysiological roles of this unique death fold protein to highlight its drug-target potential.

About Andreas Villunger:

Dr Andreas Villunger is full professor of Developmental Immunology at Medical University of Innsbruck (MUI) and Director of the Institute for Developmental Immunology (Biocenter MUI,¹ Innsbruck, AUSTRIA). Dr Villunger is also adjunct-PI at the Center for Molecular Medicine (CeMM)² of the Austrian Academy of Science, within the Ludwig Boltzman Institute for Rare and Undiagnosed Diseases (LBI-RUD, Vienna, AUSTRIA). Villunger Lab³ explore the cross talk between core cell death pathways and the cell cycle machinery. The team focus on understanding signaling events that define thresholds for cell death or survival after mitotic errors. Dr Villunger has a strong track record in generating and analyzing genetically modified mouse models and has first characterized the physiological functions of the BH3-only proteins PUMA and Noxa. He also explored the role of BH3-only proteins in different models of lymphatic malignancies, including E μ Myc and γ -irradiation driven lymphomas, thereby demonstrating that pro-death genes can unexpectedly also exert tumour-promoting functions. He also has investigated the role of a multi-protein signaling complex, dubbed the PIDDosome, that drives p53 activation upon cytokinesis failure, a process that can prime cells for transformation but may also be the desired outcome during normal organ development, as exemplified in the liver or heart.

Groupe Anim'Pharma (Faculté de Pharmacie) :

Lucie Chevillard (OTeN), Khair Alhareth (UTCBS), Isabelle Broutin (CiTCoM), Romain Duval (MERIT), Luc Demange (CiTCoM-PNAS), Yves Jacquot (CiTCoM-ERL), Nesrine Aissaoui (CiTCoM), Thierry Fournier (3PHM), Véronique Baud (OncokappaB), Marie Verbanck (BioSTM), Guillaume Ulmann (PRETRRAM), Catherine Boisson-Vidal (IThEM).

¹ <https://biocenter.i-med.ac.at/>

² <https://cemm.at/research/adjunct-pis/andreas-villunger-cemmlbi-rud/>

³ www.villungerlab.com