

**ISTITUTO PASTEUR ITALIA**

**Fondazione Cenci Bolognetti**

**Lunedì 17 Luglio 2023**

**h 11:00**

**Prof. Amedeo Caflisch**

*University of Zürich  
Switzerland*

*Terrà il seguente seminario:*

***Structure-based medicinal chemistry  
optimization of a potent and selective  
METTL3 inhibitor***

*N6-methyladenosine (m6A) is the most frequent of the 160 RNA modifications reported so far. Accumulating evidence suggests that the METTL3/METTL14 protein complex, part of the m6A regulation machinery, is a key player in a variety of diseases including several types of cancer, type 2 diabetes, and viral infections.*

*The talk will focus on a protein crystallography-based medicinal chemistry optimization of a METTL3 hit compound that has resulted in a 1400-fold potency improvement and an IC50 of 5 nM for the lead compound 22 (also called UZH2). The series has favorable ADME properties as physicochemical characteristics were taken into account during hit optimization. UZH2 shows target engagement in cells and is able to reduce the m6A/A level of polyadenylated RNA in MOLM-13 (acute myeloid leukemia) and PC-3 (prostate cancer) cell lines.*

***Il seminario si terrà nell'Aula A "Raffaele Giuliano" del Dipartimento di Chimica e  
Tecnologie del Farmaco (CU019)***



**SAPIENZA**  
UNIVERSITÀ DI ROMA

*Per informazioni rivolgersi a:  
Prof. Antonello Mai  
antonello.mai@uniroma1.it  
+39 06.49913392*



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FONDAZIONE CENCI BOLOGNETTI

**LA RICERCA IN PERSONA**