



UNIVERSITÀ  
DI TRENTO

Department of  
Cellular, Computational and Integrative Biology - CIBIO

# PhD Colloquia 2022

An opportunity to address, explore and exchange information on scientific topics with scientists.



**Povo 1, Room B109  
Via Sommarive 9, Povo (TN)**



**Friday, 10<sup>th</sup> June 2022 - h 14:30**

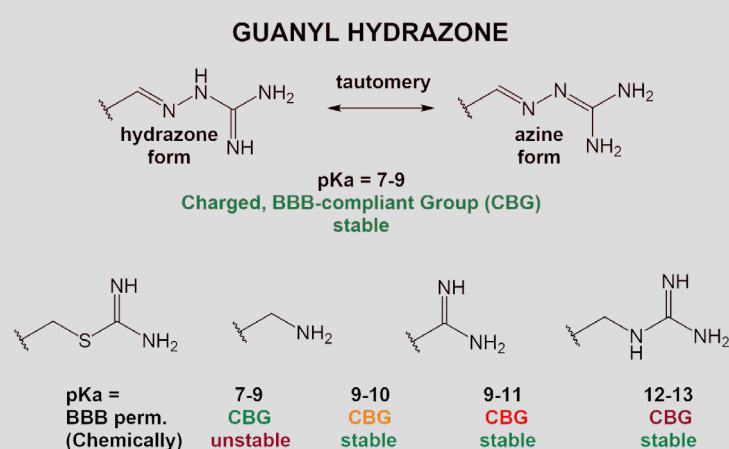
## PIERFAUSTO SENECCI

Department of Chemistry  
University of Milan, Milan (IT)



### Guanyl Hydrazones as BBB-Compliant charged groups in CNS drug discovery

Guanyl hydrazones (GHs, Figure 1, top) are synthetically accessible derivatives of biologically active hits and leads which possess suitable physico-chemical properties and a good “druggability” profile, particularly for CNS-targeted compounds. Their pKa is lower than other basic ionizable groups, such as amines, amidines and guanidines; their stability is higher than isothioureas (Figure 1, bottom).



Thus, neutral and stable GH species at physiological pH should cross the BBB and access their target site. Their presence in approved drugs and candidates validates their usefulness; in particular, I will present relevant data on the rational design, synthesis and bioprofiling of in vivo active GHs rationally designed either as ion channel antagonists (ASICs – cerebral ischemia, multiple sclerosis) or as pharmacological chaperones to stabilize protein complexes (retromer – ALS, AD).

