

April 22nd, 2024 - 15:00

Seminar Room “Paoluzi”

**Chemistry of Copper-Complexes in Biology and Medicine:
Thiol oxidation and reactive oxygen species as anticancer approaches**

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Copper ions are essential for almost all living organisms and a tight control of copper binding and coordination is important as copper is potentially dangerous, often *via* its high capacity to activate dioxygen and hence catalyze the production of reactive oxygen species (ROS), such as hydroxyl radical. Several diseases have been linked to a dyshomeostasis of copper such as Wilson’s and Menkes genetic disorders, but also Alzheimer’s disease, and cancer. Thus, interfering in copper metabolism *via* small ligands is of interest as therapeutic approach.

Inorganic copper-ligand complexes (Cu-L) can be applied or formed *in situ* via chelation by L of endogenous Cu. Biological activity can consist of supplying, sequestering or transporting Cu, or by catalysing targeted chemical reactions often via dioxygen activation. Later is thought to be of high importance in development of anti-cancer drugs or for antimicrobials.

During the last years we worked on the Cu chemistry of several endogenous or exogenous ligands. This included the reactivity of several classical ligand types of Cu (thiosemicarbazones, phenanthroline, dithiocarbamate, polyamine etc.) [1] used in anticancer and antimicrobial activity. Recent advancements will be presented about mechanistic insights in the anticancer activity of Cu-complexes with α -pyridyl thiosemicarbazones [2, 3], with a particular focus on understanding the chemistry of their interaction with thiols (glutathione, cysteine, thioredoxin, metallothionein etc.) and their redox activity to oxidize thiols and produce ROS [4,5].

Related references from our group:

- [1] Santoro A, Calvo JS, Peris-Díaz MD, Krężel A, Meloni G, Faller P. *Angew Chem Int Ed Engl.*, 59, 7830-7835 (2020)
- [2] Falcone E, Ritacca AG, Hager S, Schueffl H, Vileno B, El Khoury Y, Hellwig P, Kowol CR, Heffeter P, Sicilia E, Faller P. *J Am Chem Soc.* 144, 14758-14768 (2022)
- [3] Ritacca AG, Falcone E, Doumi I, Vileno B, Faller P, Sicilia E. *Inorg Chem.*, 62, 3957-3964 (2023).
- [4] Falcone E, Stellato F, Vileno B, Bouraguba M, Lebrun V, Ilbert M, Morante S, Faller P. *Metalomics.* 15:mfad040 (2023)
- [5] Doumi I, Lang L, Vileno B, Deponte M, Faller P. *Chemistry.* 26:e202304212 (2024).