Poster

In search of new interactions for rhenium metal-based pharmaceutical development.

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Cancer is a prevalent disease in many countries and is one of the leading causes of death worldwide. [1] New insights into cancer treatment are needed particularly for treatment against strains which are resistant against current protocols. In the field of anti-cancer pharmaceutical research metalloorganic complexes have been shown to possess several benefits above the traditional carbon, nitrogen, and oxygen-based medicines. Metal complexes have, for example, greater steric variability, several oxidation states, and interesting electronic properties proving valuable for pharmaceutical investigation [2].

Pharmaceutical development has greatly benefitted from improvements in fragment-based drug discovery (FBDD) and advances in crystallographic technology. Recently covalent binding inhibitors has emerged from FBDD efforts and resulted in treatments of cancers thought previously untreatable [3]. Additionally, the use of metal-based compounds are becoming more frequently submitted for clinical trials.[4] One important aspect to consider in drug development is how the compound interacts with a drug target and indeed what are the chemical coordination preferences of the compound in question.

In this presentation we will discuss which interactions (both covalent and non-covalent) observed between a model protein (hen egg white lysozyme, i.e. HEWL) and rhenium(I) metal complexes [5]. The FBDD and crystallographic methodologies used to investigate these interactions as well as their implications with respect to pharmaceutical development will be described.[6] The design procedure for the promotion of coordination between the metal and the protein, the crystals of the metal containing protein and a representative s structure will be discussed as indicated in Fig. 1 below.

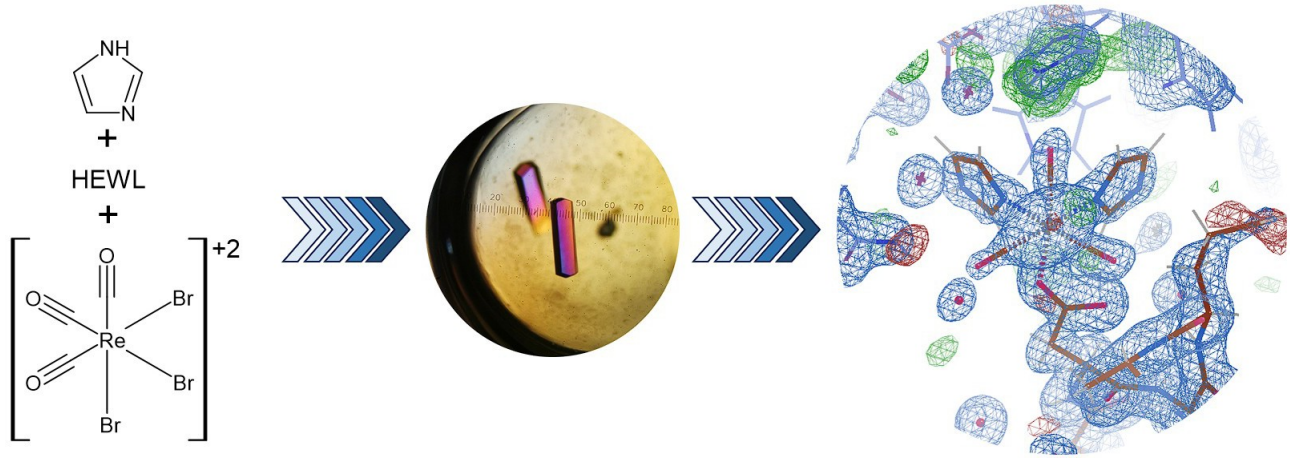

Figure 1. (Left) Schematic procedure for the synthesis of the metal bound protein complex. (Middel) Photographic image of the metal containing protein. (Right) The representative metal bounded to the protein.

[1] Frick, C., Rumgay, H., Vignat, J., Ginsburg, O., Nolte, E., Bray, F. and Soerjomataram, I. (2023). Lancet Glob Health. 11, e1700.

[2] Frei, A. (2020). *Antibiotics*, **9**, 1.

[3] Bauer, R. A. (2015). *Drug Discov Today*. **20**, 1061.

[4] Ndagi, U., Mhlongo, N., Soliman, M. (2017). *Drug Des Dev Ther*. **11**, 599.

[5] Brink, A., Jacobs, F. J. F., Helliwell, J. R. (2022). *IUCrJ*. **9**, 180.

[6] Brink, A., Helliwell, J. R. (2019). *IUCrJ*. **6**, 695.