Contribution ID: **111** Type: **E-Poster**

Specific Recognition of Methylated Lysines by Fluorescent Calixarenes in Protein Crystal Structures

Arginines (Arg) and Lysines (Lys) on protein surfaces undergo several post-translational events, such as acetylation, ubiquitination, and methylation. Lysine or arginine residues can undergo different extents of methylation (mono-, di- and, for lysine, also trimethylation). These modifications affect protein-protein or protein-substrate interactions and can act as the trigger of different cellular pathways. The involvement of protein methylation in disease is driving the development of new molecules both for detection of these post-translational modifications and/or for specific delivery of therapeutic drugs.[1]. Calixarenes are aromatic macrocycles with well-defined cavities that can easily host Arg or Lys residues [2]. Functionalization with different ionic groups at the upper and/or lower rims is an important step to confer metal coordination abilities and water solubility, which make them potential candidates for protein labeling [3]. Water soluble sulfonate calixarenes have a strong affinity towards methylated side chains. It has been demonstrated that a sulfonated calix[4]arene binds a specific dimethylated Lys residue of lysozyme [4] and recent studies have shown that it can be used to isolate methylated peptides from complex biological samples [5]. We will describe the synthesis and characterization by X-ray diffraction of the complexes formed by the octanionic-sulfonate calix[4]arene (sclx4mc) and lanthanide (terbium or gadolinium) ions and their interactions with a methylated lysozyme protein. The effects of pH and stoichiometry on the protein-calixarene-Ln complex formation will also be analysed.

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Session Classification: E-Poster Session

Track Classification: Crystallographic and Spectroscopic Advanced Tools Applied to Pharmaceuticals