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Overcoming two major chokepoints of protein crystallography with lanthanide complexes.

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Protein crystallography, the leading technique for protein structure determination, is limited by two main chokepoints: (a) obtaining single crystals and (b) solving the phase problem. Since 2000, our team has developed luminescent lanthanide complexes as auxiliary for structure determination of macromolecules, in particular, exploiting the high-phasing power of lanthanide elements [1-3].

Our previous works highlighted the supramolecular interactions between lanthanide complexes and proteins, and provided the required technical specifications to design compatible agents with high-throughput crystallization platforms. This unprecedented approach lead to a new terbium complex, named Tb-Xo4, which showed exceptional nucleant properties, when added to the crystallization media. Up to now this effect was tested on 12 proteins with different molecular weights and different oligomeric states (2 with unknown structure) and compared to the classical screening conditions. It was observed that, in addition to new crystallization conditions, Tb-Xo4 also improves the quality of the crystals obtained (see picture) and is a high-phasing lanthanide complex, fully compatible with conventional phasing methods.

We will present our last results using this new agent for protein crystallography which, in addition to nucleant and phasing properties, also allows an easier detection and centring of the protein crystals thanks to its luminescence. We believe that this all-in-one lanthanide complex is a new and efficient way to promote protein crystallization as well as a convenient alternative to the tedious and time-consuming work of seleno-methionine labelling or of heavy-atom incorporation.

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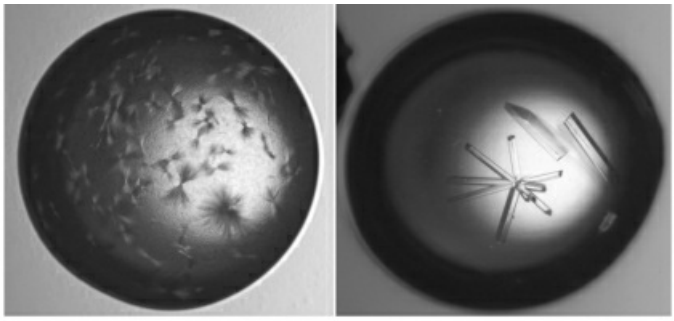

Figure Crystals of PB6 protein: classical conditions (*on left*); with Tb-Xo4 (*on right*).

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