The Morpheus III protein crystallization screen: At the frontier of drug discovery

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The original Morpheus screen has proven to be a very efficient protein crystallization screen in the long term for a broad variety of protein samples and the first follow-up screen, Morpheus II starts to have an impact for many research groups. The main ideas behind the formulation of Morpheus III were the same as originally to increase the chances of crystal nucleation and growth by integrating mixes of additives that can act as stabilizers, cross-linkers, etc. Follow systematic approaches to select the reagents and formulate the screen, such as the integration of ligands that are highly represented in the PDB and a 3D grid formulation. Consider pragmatic ways to facilitate structure solution. For example, the screening of cryoprotectants and flash-freezing crystals are simplified. The novelty in Morpheus III is the selection of small drug-like compounds as additives (average MW=248 Da). To some extent, the approach can be compared to fragment-based lead discovery. The primarily aim however is to obtain novel macromolecular crystals (with or without ligand observed in the structures). The final formulation of the new 96-condition crystallization screen integrates 44 compounds overall, divided into 8 mixes of additives. Each mix of additives is combined with 4 cryo-protected precipitant mixes and 3 buffer systems to form the 3D grid.

Recent Publications


Biography

Fabrice Gorrec has participated in the development of innovative technologies applied to protein crystallization over 14 years, including microplates (e.g., TOPAZ®), liquid-handlers (e.g., Dragonfly®) and initial screens (e.g., MORPHEUS™). Since 2008, he is responsible for the crystallization facility at the MRC Laboratory of Molecular Biology (MRC-LMB, Cambridge, UK) where he invented and developed the 96 condition Morpheus protein crystallization screens. He pursued his Master’s degree in Molecular Biology, Biochemistry and Biophysics from University of Rennes, France.