Antibodies as Chaperones in Crystallisation: Parameters for Success

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Antibodies as Chaperones in Crystallisation: Parameters for Success. Crystallization Chaperones including Antibodies, Nanobodies and Aptamers have been shown effective in promoting the crystallisation of otherwise uncrystallisable targets. A prominent example is the nanobody used to stabilize the GPCR-G-protein complex in the 2012 Nobel Prize-winning work *Nature* 2011).

Here at AstraZeneca we have pursued the use of Antibody Fragments though a bioinformatics driven approach to enable crystal systems for Drug Discovery. Recent work has been successful for the Oncology target Mcl1 Myeloid Cell Leukemia 1; an anti-apoptotic protein from the Bcl-2 enabling Structure Based Design for a DNA encoded library hit. This talk describes the process by which the chaperone molecules were obtained and, using examples from this and other projects, how their biophysical properties such affinity, epitope and thermal stability correlate with their propensity to crystallise. The talk will also cover a comparison of our ligand bound Mcl1-Antibody complex with examples of Mcl1 ligand bound structures from the literature