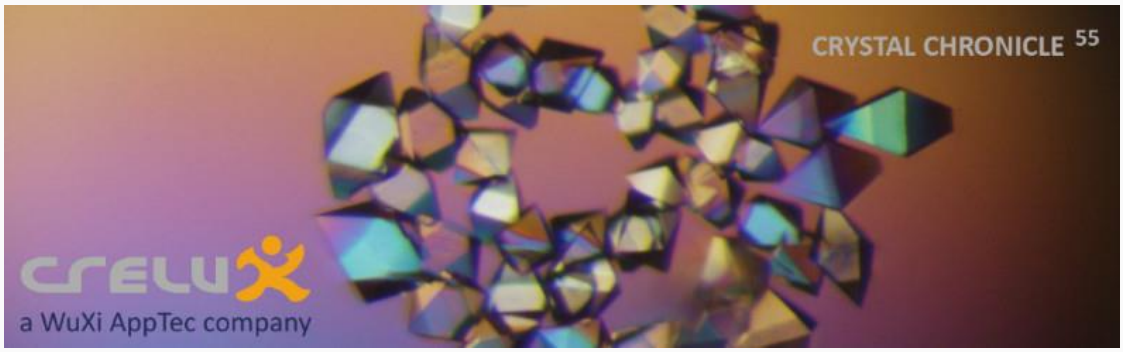
Contents #55: AMPK De Novo Structure * XPRESS PORTFOLIO



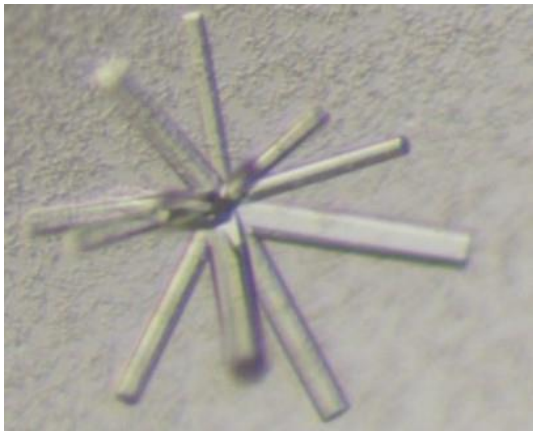
De novo structure of AMPK, a multidomain protein, solved at CRELUX

Structures of various AMPK complexes established

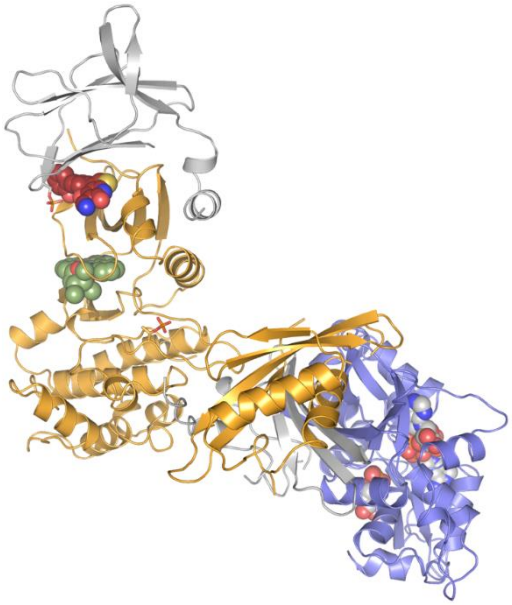
AMPK (AMP-activated protein kinase) is a key regulator of cellular energy homeostasis. The activity of the Ser-/Thr- kinase subunit (α1, α2) is mediated by two other proteins, a carbohydrate-binding module (β1, β2) and nucleotide binding sensor (γ1, γ2, γ3). Together, they form a heterotrimeric αNβNγN complex conserved from yeast to humans.

With diligently designed constructs and proprietary expression systems, CRELUX has produced all 12 human AMPK isoforms. We developed a unique purification strategy to deliver monodisperse, stoichiometric, and functional AMPK samples. The quality of the purified complex reflected on the crystallizability and subsequent structure determination of the complex in the presence of allosteric activator, kinase inhibitor, and AMPs.

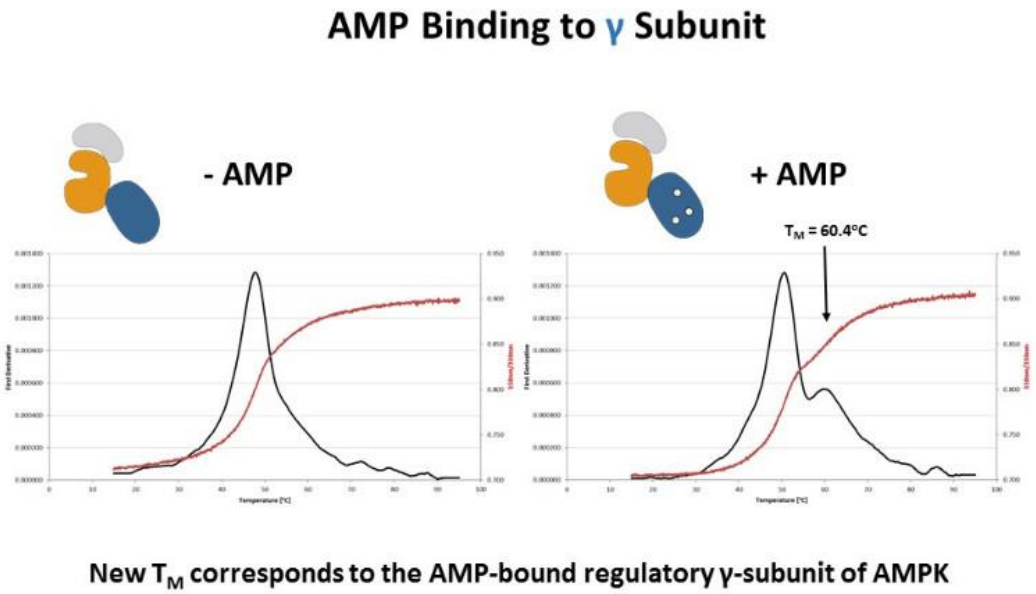
We offer tailor-made AMPK samples for assays, compound screening, FBDD, or X-ray structure determination. CRELUX is equipped with state-of-the-art technologies and tools for comprehensive biophysical characterization, as well as for automated crystallization screens and data collection.



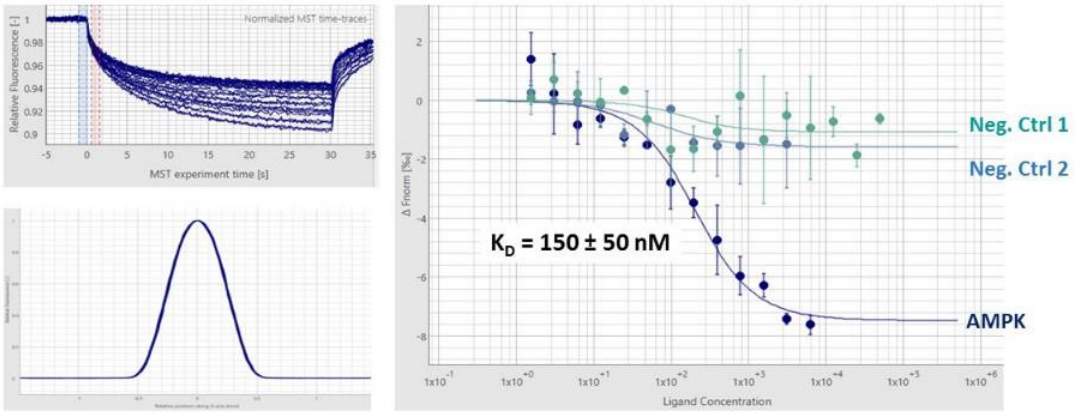
Crystals of different AMPK complexes grown at CRELUX.



The unpublished structure above shows an allosteric activator bound to a human AMPK isoform at 2.9 Angstroms resolution.



New T_M corresponds to the AMP-bound regulatory γ-subunit of AMPK



Compound binding to AMPK determined via MST

XPRESS Portfolio is constantly growing

Crystal grade protein is prepared and crystals are grown according to established protocols. This results in quick turn around times of typically 8 weeks.

Our XPRESS portfolio is constantly growing - AMPK has now been added to our list. For our XPRESS targets protein production and crystallization protocols are established and thus you benefit from short timelines and high success rates of obtaining your co-crystal structure. For several isoforms of AMPK which are not yet established we provide so-called XPEDITE services. Having in house expertise for related isoforms or alternatively access to reliable published data, we can offer new targets under establishment at preferred conditions, similarly to the XPRESS model. After having successfully completed structure analyses of the first structure, subsequent complex structures are available at quick turnaround times as known from the XPRESS service. Simply send us your ligand(s) of choice, do an optional biophysical validation and get your complex structure within usually 8 weeks.

Meet us at

BioEurope Spring, March 20-22, 2017, Barcelona, Spain
Drug Discovery Chemistry, April 23-27, 2017, San Diego, CA, USA

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