

Research visit to the Department of Biochemistry and Food Chemistry in the University of Turku

10.-14.10.2011

The aim of the research visit was to learn to use Isothermal Titration Calorimetry (ITC) device for studies of protein-small molecule interaction. ITC is a highly sophisticated thermodynamic technique for simultaneous determination of all binding parameters. ITC directly measures the heat absorbed or released in a molecular binding event. This measurement of the heat allows resolving of binding constants, reaction stoichiometry, enthalpy and entropy. Modern ITC devices, as for example ITC200 (GE Healthcare) at the Department of Biochemistry and Food Chemistry in the University of Turku, allow labeling- and immobilization-free measurements and require only small amount (sub-milliliter) of samples.

During my one week visit in the laboratory of Professor Jyrki Heino and Associate Professor Jarmo Käpylä, I learned to use the ITC for our protein-ligand studies with T-cell protein tyrosine phosphatase (TCPTP) and various small molecules. TCPTP is a negative regulator of many cancer-relevant receptor tyrosine kinases (RTKs). As TCPTP expression is not down-regulated in cancers, TCPTP is a potential target for drug development against cancer-relevant RTKs identified as TCPTP substrates. As TCPTP exhibits auto-inhibition with its C-terminal domain, potential cancer treatments should activate TCPTP. We have studied the binding of phosphatase activators to TCPTP. By combining various biochemical and molecular modeling methods, we have been able to identify the TCPTP binding site for small molecule TCPTP activator, mitoxantrone. With ITC, we wanted to study the binding of mitoxantrone, as well as some mitoxantrone-derivatives recently synthesized by our collaborators, to TCPTP.

Finding the appropriate ITC parameters for our TCPTP-small molecule study was challenging. However, the visit was successful as many runs were performed with various ligands during the week. The results from these experiments will be added to our manuscript that can soon be submitted.

I want to thank Associate Professor Jarmo Käpylä for his guidance with ITC. I also want to acknowledge ISB for financial support that made this research visit possible.

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