Tundra, an affordable microscopy for sample screening to high resolution structures

Dimple Karia[1], Zuzana Hlavenkova[2], Milos Malinsky[2], Vojtech Dolezal[2], Marketa Cervinkova[2], Rastislav Ostadal[2], Jeroen Bresser[1], Lingbo Yu[1], Abhay Kotecha[1]

[1]*Materials and Structural Analysis Division, Thermo Fisher Scientific, Achtseweg Noord, Eindhoven, Netherlands*
[2] *Thermo Fisher Scientific Brno s.r.o., Materials & Structural Analysis, Brno, Czech Republic*

Electron cryo-microscopy (cryo-EM) single particle analysis (SPA) method has become one of the dominating methods for high resolution structure determination of a wide variety of biological macromolecules. Such high resolution structures facilitate understanding of their functions, mechanism of action and protein ligand/drug interactions. With an increase in the popularity of cryo-EM, the need for accessibility, ease of use and improved efficiency has also increased. Tundra cryo-TEM operating at 100kV with semi-automated grid loading system and automated SPA data collection, makes EM accessible to scientists from diverse Life Science backgrounds. It enables novice users as well as users with varied level of EM experience to carry out sample optimization and obtain high resolution 3D structures to gain insights into biological macromolecules important to human health.

In this abstract, we describe how Tundra was used for sample screening of a challenging small membrane protein that represents a crucial class of drug target for various diseases (Fig1). We solved structure of a challenging homo-pentameric human $GABA_A$ (gamma-aminobutyric acid type A) receptor, an important drug target for numerous neurological disorders to 3.4 Å resolution (Fig2). In addition, we also solved high resolution structures of other important biological samples such as Adeno-Associated Virus6 that is used as viral vector in gene therapy and vaccines. These results clearly demonstrate potential of the Tundra microscope in drug discovery and how it will add great value at different stages of Cryo-EM workflow for our customers.

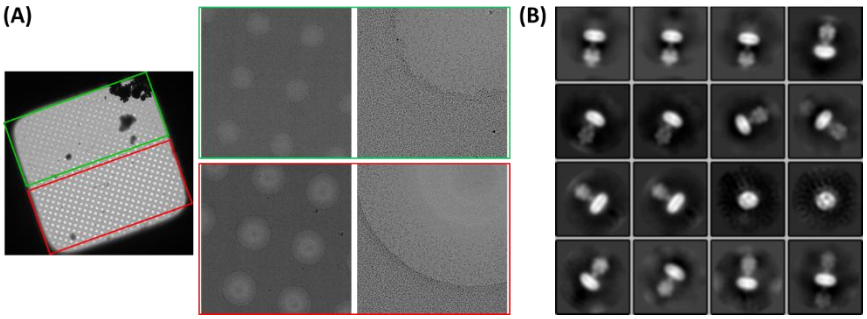

Figure 1. A. Sample screening of GPCR protein B. 2D class averages

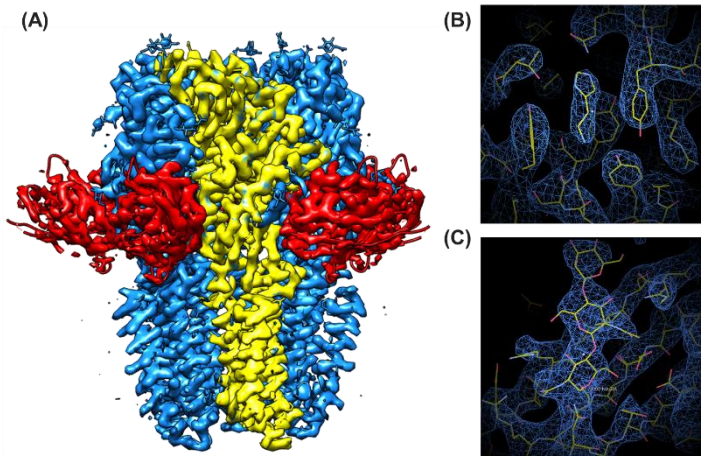

Figure 2. A. 3.4A reconstruction of $GABA_A$ receptor from Tundra. B, ligand density and C, sugars.