Contribution ID: **21** Type: **not specified**

Short Talk 10, Hongyi Xu - Solving the First Novel Protein Structure by Micro-Crystal Electron Diffraction

Friday 11 October 2019 09:40 (20 minutes)

Micro-crystal electron diffraction (MicroED) has shown in recent years to be a promising method for determining
macromolecular structures (1–5). It enables structural biologists to study proteins from micron-sized 3D crystals that are too small to be studied by conventional X-ray crystallography. Furthermore, MicroED can be applied to biomolecules of low molecular weight that are beyond what can so far be resolved by single particle cryo-EM (6,7). However, up to now, all protein structures determined by MicroED had already been solved previously by X-ray crystallography. Here, we present for the first time an unknown protein structure –an R2lox metalloenzyme–solved using MicroED (8). MicroED data were collected from plate-like crystals with an average size of 2 μm × 2 μm × 0.5 μm. By overcoming challenges in sample handling, cryo-EM specimen
preparation, limited data completeness and low signal-to-noise ratio, we are able to solve the structure by molecular replacement with a search model of less than 36% sequence identity. The resulting electrostatic scattering potential map at 3.0 Å resolution is of sufficient quality to allow accurate model building and refinement,
providing biologically relevant information on the enzyme. Our results demonstrate MicroED can be used for solving novel protein structures, using only standard X-ray crystallography software. These findings illustrate that electron crystallography has the potential to become a widely applicable tool for revealing new insights into protein structure and function, opening up new opportunities for structural biologists.

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Session Classification: Keynotes and Short talks 7