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MicroED: Conception, Practice and Future Opportunities

Tamir Gonen is a membrane biophysicist and an expert in electron crystallography and cryo EM. Gonen is a professor of Biological Chemistry and Physiology at the David Geffen School of Medicine of the University of California, Los Angeles and an Investigator of the Howard Hughes Medical Institute and a Member of the Royal Society of New Zealand. In 2011 while leading a lab at the HHMI Janelia Research Campus he began developing Microcrystal Electron Diffraction (MicroED) as a new method for structural biology. With this method Dr Gonen has pushed the boundaries of cryoEM and determined several previously unknown structures at resolutions better than 1Å. Gonen authored more than 100 publications and several of his past trainees are now faculty around the world at top universities.

Abstract: My laboratory studies the structures of membrane proteins that are important in maintaining homeostasis in the brain. Understanding structure (and hence function) requires scientists to build an atomic resolution map of every atom in the protein of interest, that is, an atomic structural model of the protein of interest captured in various functional states. In 2013 we unveiled the method Microcrystal Electron Diffraction (MicroED) and demonstrated that it is feasible to determine high-resolution protein structures by electron crystallography of three-dimensional crystals in an electron cryo-microscope (CryoEM). The CryoEM is used in diffraction mode for structural analysis of proteins of interest using vanishingly small crystals. The crystals are often a billion times smaller in volume than what is normally used for other structural biology methods like x-ray crystallography. In this seminar I will describe the basics of this method, from concept to data collection, analysis and structure determination, and illustrate how samples that were previously unattainable can now be studied by MicroED. I will conclude by highlighting how this new method is helping us understand major brain diseases like Parkinson's disease; helping us discover and design new drugs; shedding new light on chemical synthesis and small molecule chemistry; and showing us unprecedented level of details with sub atomic resolutions.

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