SCIENTIFIC UPDATE BY DIR PRINCIPAL INVESTIGATOR

EXPANDING THE TOOLSET OF STRUCTURAL BIOLOGY WITH MOLECULAR MICROSCOPY

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Cryo-electron microscopy (cryo-EM) is rapidly becoming a necessity in structural biology on par with x-ray diffraction methods (x-ray) and nuclear magnetic resonance (NMR). Several publications have unequivocally established the capabilities of this technique in determining the structure of macromolecules at atomic resolution. Cryo-EM requires smaller quantities of material than other structural methods and is especially suitable for the study of hard-to-crystallize large macromolecular complexes and membrane proteins. The success of this technique has spurred a wave of interest and many structural biology groups are incorporating it into their repertoire. In addition, there is emerging interest in the application of cryo-EM technologies to perform ultrastructural analysis of cellular compartments. This rapid increase in demand for a limited number of sites endowed with appropriate/expensive equipment and expertise is creating a significant constraint.

The Research Triangle Park area is home to a strong community of structural biologists who routinely use x-ray and NMR to solve the structures of macromolecules of biomedical interest. However, by 2016 only a dozen publications by local research groups used cryo-EM and the part of these studies involving microscopy was in all cases performed in collaboration non-regional groups. For these reasons Duke, NIEHS and UNC are collaborating in the formation of the Molecular Microscopy Consortium (MMC). The mission of the consortium is to enable the use of single particle cryo-EM and other tools in molecular microscopy by research groups at partner institutions. NIEHS led this effort by establishing the first of three facilities, managed by a single team to provide a collaborative environment for the training of structural biologists. The Cryo-EM Core at NIEHS was established in June 2017 and in the first year of operation the MMC has initiated more than two dozen projects and trained collaborators in the involved process of specimen optimization and data processing. To date, ten macromolecular complexes have been solved at the MMC at high resolution (3-5 Å). Three manuscripts based on these data are submitted or in preparation, while at least another three are expected to be submitted to high quality peer-reviewed journals before the end of 2018.