



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP170644

Project Title:  
Establish a New Cryo-Electron Microscopy Core Facility and Service for  
Structure Determination at UT Southwestern Medical Center

Award Mechanism:  
Core Facility Support Awards

Principal Investigator:  
Nicastro, Daniela

Entity:  
The University of Texas Southwestern Medical Center

### Lay Summary:

Understanding the causes of cancer and identifying treatments for this devastating disease require knowledge of the cellular machineries (protein complexes) that are the drivers of tumor initiation, progression and metastasis. Determining the three-dimensional structures of these machineries is essential to understanding the mechanisms of cancer, identifying drug targets and developing therapeutics. Recent revolutionary advances have rendered cryo-electron microscopy (cryo-EM) the method of choice for determining protein structures in detail, i.e. at the level of individual atoms; while cryo-electron tomography (cryo-ET) enables these molecular machines to be viewed inside cells. UT Southwestern has invested ~\$17M to acquire and house a collection of instruments capable of performing cryo-EM/ET that is unique in the United States. But instruments alone are insufficient to enable the research of a broad community. To make these resources widely available to the cancer research community, we are requesting funds for additional infrastructure to advance the Cryo-EM Core Facility (CEMF) and establish a Service for Single-Particle structure determination (SSP). Together, the CEMF and SSP will provide cancer researchers with: A) a new microscope and robotics to facilitate optimization of protein samples, dramatically increasing productivity by widening the main bottleneck in the structure determination pipeline, B) expert consulting and technical assistance in data collection and analysis, C) educational programs to raise awareness of the research opportunities afforded by these new methods and to train the next generation of cryo-EM/ET experts, D) a robust cryo-ET pipeline, and E) computational infrastructure to efficiently store and analyze cryo-EM data. The CEMF will be directed by Dr. Daniela Nicastro, a pioneer in development and application of cryo-ET, and co-directed by Dr. Xiao-chen Bai, an innovator in methods for high-resolution cryo-EM structure determination.