Wah Chiu
Baylor College of Medicine

National Center for Macromolecular Imaging (NCMI)
(National Center for Research Resources, NIH)

Center for Protein Folding Machinery
(Nanomedicine Development Center, NIH Roadmap)
Research Missions at NCMI

• Develop and apply Cryo-EM for structure determinations of Molecular Nano-Machines in solution states towards atomic resolution; and of Whole Cells at molecular resolution

• Share our experimental and computational technology freely with the global academic community
Electron Cryo-Microscope at NCMI
NCMI Computer Clusters
Pipeline in Cryo-EM for Nano-Machine

biochemical preparation → cryo-em sample preparation → imaging → data collection

→ image processing → reconstruction → structural analysis → model
NCMI Collaborators and Users
Subnanometer Resolution Cryo-EM Structures Determined at NCMI

Rotavirus

P22 phage

Acrosomal bundle

RyR1

P22 procapsid

RDV

PSS7

HSV-1

CPV

Epsilon 15

GroEL
Cryo-EM: A tool for Nano-Objects

Nanotubes
Lon Wilson, Rice U

Nanowire
Rick Smalley, Rice U

DPPC-Au Hollow Sphere
Zasadzinski, UCSB

Membrane-copolymer
Ka Yee Lee U Chicago

Nanoshell
Naomi Halas, Rice U

Virus-like Particle and Au Core
Lia Stanciu, Purdue University
Cryo-Electron Tomography of Platelet

Jose Lopez
U Washington
NIH Nanomedicine Development Center

http://proteinfoldingcenter.org

PI: Wah Chiu
Protein Folding Machinery Center

Investigators

UCSF
Lawrence Berkeley Nat’l Laboratory
BCM
MD Anderson Cancer Center

Stanford University

M. I. T.
Protein Folding is a Key Step in Gene Expression
A Large Fraction of Cellular Proteins Transits Through Chaperones During their Biogenesis
Defects in Protein Folding lead to Human Disease

Amyloid Deposits: Prions, Alzheimers

Mutations: Cancer, Metabolic Diseases

Denaturing Stress: Ischemia, Stroke
Our Nanomedicine Center Goals

• Engineer chaperonin variants optimized to fold proteins of biomedical importance *in vitro*.

• Engineer chaperonin variants that promote folding/unfolding of specific proteins *in vivo*.

• Engineer an “adaptor” molecule to turn “on” or “off” substrate targeted to the chaperonin.

• Design a versatile nano-cage based on the chaperonin platform to encapsulate and release ligands of choice.

• Develop and disseminate a pipeline of measurement and simulation tools for characterizations of nanomachines.

• Develop an educational curriculum on nanomedicine.
Multi-Disciplinary Approach to Design New Chaperonin and Substrate

Chaperonin & Substrate Design

Cryo-EM X-ray Diffraction

Simulation Modeling In Silico Design

Single Molecule Imaging

In Silico Design
Protein Folding Machinery Center

- Continuously seeking for clinical partners for exploring our unique capability for treating diseases related to protein misfolds

- Actively engaging in bridging translational and biophysical/computational research