ASRC - City College of New York

Seminar in Biochemistry, Biophysics & Biodesign

SEMINAR LOCATION:

ASRC Main Auditorium
85 St. Nicholas Terrace

For non-CUNY attendees, advance registration is required; please contact Jennifer Chow at jchow@gc.cuny.edu

THE SEMINAR WILL ALSO BE AVAILABLE VIA ZOOM:

Click here for Zoom link
Meeting ID: 966 7763 1144
Passcode: asrc-ccny

HOST:
Kevin Gardner
kgardner@gc.cuny.edu

FOR MORE INFORMATION, CONTACT:
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ADVANCED SCIENCE RESEARCH CENTER
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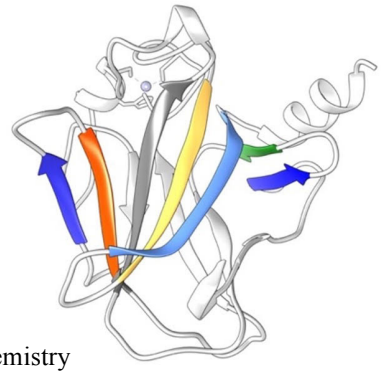
Wednesday, Oct. 18, 2023
Coffee & tea 11:30 AM
Seminar 12:00 – 1:00 PM



Melanie Cocco

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Protein Dynamics Determined from NMR Hydrogen Exchange Measurements and Hemoglobin Stability with Voxelotor

ABSTRACT The NMR spectroscopy provides a measure of protein dynamics in solution that is useful in understanding the relative stabilities of mutants, drug-bound states, or homologous proteins. Hydrogen-deuterium exchange reactions occur during a timescale specific to protein folding events and can provide details on local unfolding and/or global stability. Here we present three studies of hydrogen exchange in DNA-binding protein domains (DBDs). The cytidine repressor (CytR) is a bacterial sensor that regulates the production of enzymes needed for nucleic acid production. CytR has been identified as a target in the treatment of cholera and urinary tract infections. We compare the structure and stability of the CytR protein to the lactose repressor (LacR). Hydrogen exchange for another system, the DBD of the p53 transcription regulator reveals how the structure of this protein can be stabilized by rescue mutations that restore function of this important anti-cancer protein. A third system, a thermally stable archaeal bypass polymerase Dbh is shown by hydrogen exchange to maintain structural features in proximity to the catalytic domain at high temperatures.

Hemoglobin is the last system to be discussed. Voxelotor (aka Oxbryta) is a new drug developed to treat sickle cell disease by binding the hemoglobin tetramer and maintaining the protein in a stable soluble conformation. We examine the effect of this drug on the natural degradation of hemoglobin in solution.