We received 24 nominations and selected five students. The V-CBI program aims to maintain a 50/50 ratio of trainees between chemistry and biological departments. The V-CBI proudly introduces these new trainees to training grant this year:

Lee Cantrell (Biochemistry, PI Kevin Schey) Throughout life, fiber cells are continuously differentiated to the outer cortex of the lens. These cells are not degraded – providing an intrinsic temporal gradient from the outer cortex to the inner nucleus. As fiber cells mature and compacted towards the nucleus they undergo loss of de novo protein synthesis, loss of organelles, extensive protein modification and cell morphology changes. It is the goal of the Schey lab to use mass spectrometry (MS) instrumentation to answer questions about lens biochemical changes and inherited pathologies – especially those related to age-related cataract formation. I look to employ LC-MS/MS, imaging mass spectrometry, RT-qPCR, and bioinformatic tools to provide a systems level analysis of these phenomena in various populations. In addition to characterizing distinct cell populations, I will identify novel biomarkers in the development of age-related cataracts.

Amanda Cao (Chemistry, PI Lauren Buchanan) **Characterization of α-Synuclein folding dynamics with 2D Infrared Spectroscopy and Interactomics.** Parkinson's disease is a neurodegenerative disease hallmarked by the loss of dopaminergic neurons and the accumulation of aggregated α-Synuclein (αSyn) into intracellular Lewy bodies and Lewy neurites. While the insoluble fibrils are found in deposits, it has been shown that intermediate oligomeric species are more cytotoxic. Two-dimensional infrared (2D IR) spectroscopy is an ultrafast vibrational spectroscopy that has the spectral and temporal resolution to observe changes in secondary structure during protein misfolding. Site specific incorporation of unnatural amino acids with IR probes such as, p-cyanophenyalanine and p-azidophenylalanine (pAzF) allow for monitoring residue specific changes. In addition to being an IR probe, pAzF will be utilized as a Click handle for derivatization with biotin for streptavidin pulldowns of αSyn and its interacting partners that will be followed by analysis with high resolution mass spectrometry (MS). My project involves incorporating 2D IR and MS in a time dependent manner to elucidate structural features of oligomeric species in the misfolding of αSyn.

Kathryn Kapp (Chemistry, PI Renã A. S. Robinson) Sepsis is a life-threatening disease caused by a dysregulated host response to infection. Previous studies have shown that African Americans have a higher risk of infection-related hospitalization and once infection occurs, are, on average, ten years younger than their white counterparts when they present to the emergency department with sepsis. Previous studies have also identified proteomic differences related to lipid metabolism, inflammation, coagulation, and the acute phase response between community-acquired pneumonia (CAP) patients who developed sepsis and those who did not. Therefore, in collaboration with Dr. Octavia Palmer from the University of Pittsburgh, we will assay blood plasma samples from the Protocolized Care for Early Septic Shock (ProCESS)

cohort using mass spectrometry and an integrated 'omics approach. These samples are from African American and Caucasian patients who were diagnosed with CAP, urinary tract infections, or intra-abdominal wounds and who then developed sepsis. Samples were collected at emergency department admission and at 24 hours post-admission. This study will further examine the roles that inflammatory, age-related, and lipid metabolism signaling pathways play in sepsis and will ultimately help elucidate the roles of race, age, and source of infection on the incidence of sepsis.

Robert Mann (Biochemistry, PI Manuel Ascano) **Chemical and Computational Interrogation of Viral RNA Genomic Structures.** There are over 200 viruses known to cause disease or death in humans, and over 75% contain RNA genomes. Inimitably flexible, RNA polynucleotides are inherently capable of forming both secondary and tertiary structures. Recent work with in-cell 2'-Selective Hydroxyl Acetylation and Primer Extension (icSHAPE) determined that viruses (HIV, DenV, ZikV, IAV, and others) contain structurally defined regions that affect their life cycle, and ultimately, the outcome of infection. I hypothesize that the structures of viral RNA dictate the nature and extent of interaction with viral and cellular RNA binding proteins during the earliest stages of infection. Importantly, I anticipate that the transition from a packed viral genome to its deployed state is a structurally dynamic event that is essential to establishing the first intracellular host-pathogen interactions. I aim to explain and relate the structural changes of the CHIKV genome during this event using icSHAPE, VIR-CLASP, and computational structural prediction algorithms. This triumvirate of chemical biology, high-throughput sequencing, and computational structural methods will enable a more comprehensive understanding how RNA structure leads to efficient viral replication.

Eli McDonald (Chemistry, PI Lars Plate) **Structure guided investigation of CFTR proteostasis pathology.** Cystic Fibrosis (CF) is a genetic disease resulting in the malformation of the Cystic Fibrosis Transmembrane conductance Regulator (CFTR). CFTR is a membrane anion channel that misfolds in the endoplasmic reticulum (ER) and is marked for degradation by cellular proteostasis machinery before it may be trafficked to apical membrane of epithelial cells in patients. The only clinically approved, etiologically targeted treatment paradigm for CF currently entails the modulation of CFTR folding through small molecules called correctors. My research project involves both the kinetics contribution of the proteostasis machinery, such as chaperones, to the CFTR folding process in vivo as well as the thermodynamic stability of the CFTR structure evaluated in silico. I am exploring the implication of different CFTR mutations and the effects of the corrector drugs using time resolved proteomics and molecular dynamics simulations.

The major requirements of the program are *Fundamentals of Chemical Biology* (CPB 8320), register two semesters for *Graduate Seminar in Chemical Biology* (CPB 8310), one cross-disciplinary course (chemistry or one from a Basic Science department or CPB/IGP programs), *Rigor and Reproducibility* (PHARM 8328), and participation/membership in the Chemical Biology Association of Students (CBAS) program.