Project ID: 131

Senior Division

Biochemistry

Marianthe Dresios
Carlsbad High School
Gr. 11

Integrated Chemistry and Cell-Free Synthetic Biology for Advanced Diagnostics

AWARDS:

CSEF Qualified

Although diagnostics represent a more than $40 billion market globally, there is a current lack of technologies for rapid biomarker sensing without the use of external power or costly laboratory based infrastructure. Additionally, the complexity and diversity of human diseases necessitates the development of reconfigurable technologies for detecting multiple biomarker classes, such as metabolites (ex. glucose), peptides (ex. neurodegeneration markers), or gases (ex. CO2). My project goal is to integrate the biocompatibility and encapsulation ability of metal-organic framework (MOF) materials with the rapid responsiveness, adaptability, and signal amplification properties of cell-free protein synthesis (CFPS) to develop a novel, configurable diagnostic technology for sensing various analytes without external power or complex infrastructure. MOFs will be used to encapsulate analyte-specific enzymes and DNA encoding for a light-generating protein; in the presence of the analyte, activation of the enzymatic reaction lowers the pH within the MOF, leading to its dissolution and release of DNA. A CFPS system will use the released DNA template to generate a protein-based light signal in a coupled transcription translation system without need for cell viability. The technology is scalable and can be lyophilized for long-term storage, transport, and use upon reconstitution. Given its modularity, it can be adapted for sensing different analytes, even beyond diagnostics, such as for changes in biological and/or chemical reactors; it can also be used to combine bioanalyte sensing with response via therapeutic protein production through CFPS. Such modularity enables incorporation of evolving advances in chemistry, materials, and biology toward even broader applications.

Project ID: 132

Senior Division

Biochemistry

Vibha Yadav Ganji
Del Norte High School
Gr. 10

Vidha Yadav Ganji
Del Norte High School
Gr. 10

Targeting the Ribonucleoprotein Complex Assembly as Therapy for Heroin Use Disorder (HUD)

AWARDS:

American Chemical Society - San Diego - 2nd Place
CSEF Qualified

Heroin Use Disorder (HUD) represents a significant public health challenge, affecting approximately one million individuals in the United States. Extensive research has illuminated the neuro-epigenetic alterations induced by chronic heroin abuse, particularly within the Nucleus Accumbens (NaC), a pivotal brain region in reward processing. Our study aimed to elucidate theinvolvement of ribonucleoprotein (RNP) complex assembly, a crucial homeostatic mechanism in RNA metabolism, in shaping thelong-term neuroadaptations observed in HUD patients. Through post-mortem analysis of NaC tissue from heroin overdose victims, we identified differential expression of key genes involved in RNP assembly, notably PANK3 (pantothenate kinase 3) and RFK (riboflavin kinase). While PANK3 is recognized for its role in coenzyme A biosynthesis, its relevance to chronic heroin abuse remains unexplored. Similarly, RFK, responsible for riboflavin phosphorylation, has received limited attention in the context of HUD. Our findings revealed significant overexpression of both PANK3 and RFK in post-mortem NaC tissue, implicating their potential involvement in HUD neuropathology. Additionally, repurposing antidepressants as inhibitors of RFK, coupled with derivatives of Vitamin B as inhibitors of PANK3, as well as further modified versions of existing molecules has shown promise in ameliorating heroin withdrawal symptoms. Toxicity studies were also conducted to minimize any hazards observed in the molecules. This study sheds light on the intricate molecular mechanisms underlying HUD pathology and underscores the significance of RNP complex assembly in mediating long-term neuroadaptations in the NaC. Targeting key genes within this pathway, such as PANK3 and RFK, holds potential for novel therapeutic interventions to mitigate the detrimental effects of chronic heroin abuse. In conclusion, our findings provide valuable insights into potential therapeutic targets for HUD management. Further research in this direction is warranted to develop more effective interventions to address HUD and its associated comorbidities, thereby alleviating the burden on affected individuals and society at large.

Project ID: 133
Senior Division
Biochemistry

Chloe Wang
Canyon Crest Academy
Gr. 11

Virtual Screening and Hit Confirmation of Orthosteric MEK Inhibitors for the Treatment of Pediatric Central Nervous System Tumors

Background: Central nervous system (CNS) tumors are the most common type of solid cancers in children and have the highest mortality rate. Accumulated evidence has revealed that RAS-RAF-MEK-ERK Pathway is frequently activated in these tumors, therefore targeting this pathway becomes a promising approach to fight pediatric tumors.

Procedure: A virtual screening (VS) of a kinase library was performed with MEK1 kinase. The ATP binding pocket was used to identify orthosteric inhibitors. The hits from VS were tested against MEK1 kinase in a biochemical assay.

Results: Virtual screening gave ~50 compounds with good docking score (< -11). 26 VS hits were selected in the MEK1 ADP-Glo kinase assay at 10 and 100 µM. 3 compounds demonstrated greater than 50% inhibition at 10 µM and dose-dependent activity. They were identified as confirmed hits.

Conclusion: 3 of 26 virtual screening hits were confirmed in the ADP-Glo kinase assay. They can serve as the starting point for the development of MEK1 orthosteric inhibitors for the treatment of pediatric CNS tumors. VS with AutoDock Vina could be used as an effective method to identify hits from a focused library for kinase targets.