Our lab aims to employ design-based engineering to address the challenges in energy, environment, and health. The design-based engineering strategies focused on chemical, computational, and systems biology analyses to understand the fundamental mechanisms and to guide the design of enzymes, processes, microorganisms, and plant for various applications. While the principle can be broadly applied, our research primarily focused on increasing biorefinery waste utilization, enhancing photosynthetic terpene production, and improving enzymes based on structure dynamics.

The first research area addresses one of the most challenging issues in the use of plant materials for energy production: the conversion of highly recalcitrant lignocellulosic waste into fungible bioproducts. Over the past decades, extensive research has successfully processed cellulose and hemicellulose from plant biomass into advanced biofuels. However, current bioconversion platforms still leave up to 30% carbon as lignin-containing waste streams that must be further processed into fungible products. The utilization of this excess lignin as feedstock for renewable fuels and chemicals offers a significant opportunity to enhance the operational efficiency, lower the biofuel cost, reduce the net carbon footprint, and improve the replacement of petroleum. Funded by two major DOE EERE (Department of Energy, Office of Energy Efficiency & Renewable Energy) grants, we are leading multidisciplinary and multi-state academic-industrial coalitions to address the challenge with the advanced biological and chemical design of lignin bioconversion. Unlike cellulose, lignin evolved to sustain the land plant growth with highly recalcitrant aromatic heteropolymers, which makes the breakdown and conversion of this macromolecule particularly challenging. We integrated enzymes, electron mediators, and microorganisms to develop several bioprocessing platforms able to convert lignin into lipid for biodiesel or PHA (Polyhydroxyalkanoate) for bioplastics at improved efficiency and titer. The chemical design allowed more rapid electron transfer during redox reactions to breakdown lignin, and the new fractionation strategies enabled the innovative biomanufacturing processes to produce quality asphalt binder modifiers, carbon fibers, and such. The research area is being translated into developing biomanufacturing platforms for energy and biomedical applications.

One of the fundamental challenges in renewable energy is the efficient harnessing and transformation of sunlight energy for reducing inorganic carbon toward the production of fuels and chemicals. Our second research area is developing novel approaches to redirect carbon, electron, and energy from photosynthesis into terpene products. On one side, terpene has broad applications as chemicals, nutraceuticals, antioxidants and drugs. On the other side, the direct channeling of carbon, reducing equivalents, and energy (ATP) from photosynthesis to terpene synthesis represents one of the most energy and carbon efficient routes from sunlight to hydrocarbon fuel in living organisms. Despite the advantages, we must understand how the flow of energy, electrons, and carbon from photosynthesis to non-native sinks can be achieved to produce biofuels and specialty chemicals. I successfully competed for a DOE ARPA E (Advanced Research Project Administration- Energy) grant due to my leadership and ability to coordinate multidisciplinary expertise. We have integrated computational modeling of the metabolic bottlenecks with synthetic biology design to overcome these bottlenecks to achieve a record level of volatile terpene production in *Synechococcus elongatus* PCC 7942. The research then identified NADPH and ATP balance as additional biochemical limitations for terpene biosynthesis, leading to a broad impact in the field. The strategies and findings were translated into higher plants, where we have integrated photosynthesis improvement, carbon redirection, and product storage to achieve a record production of squalene in tobacco. Squalene has broad applications in the pharmaceutical and cosmetic industries as vaccine adjuvant, antioxidant, and such. A major impact of my work is enabling the replacement of shark-derived squalene with environmentally sustainable manufacturing using engineered tobacco. Further technology development in photosynthetic terpene production can be implemented to both address fundamental scientific questions and deliver applicable solutions for energy, biotech and biomedical applications.

The third research direction for the lab is structure dynamics-guided biocatalyst improvement. We have established that HDX mass spectrometry can be an effective platform to study enzyme dynamics. The platform is now being used to improve enzyme efficiency and stability.