SJSU | DEPARTMENT OF CHEMISTRY

CHEMISTRY Departmental Seminar

Spring 2019
CHEM 285/191 Schedule
Tuesday at 4:30-5:45PM
Room Duncan Hall 250

Mar. 19th, 2018

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MS Final Oral Seminar

Light Activation of P450 Enzymes Using Ru(II)-Diimine Complexes

Due to their great selectivity and unique catalytic features, the use of enzymes is gaining increasing importance in biotechnology as an alternative approach to traditional chemical syntheses. Of particular interest is the superfamily of cytochrome P450 enzymes, which are monooxygenases capable of catalyzing regio- and stereoselective oxyfunctionalization.[1] These enzymes activate molecular dioxygen at their heme center using two reducing equivalents and insert one of the oxygen atoms into C-H bonds of various substrates. However, their dependence on redox partner proteins and NADPH cofactor are limiting their industrial applications. To overcome those challenges, our laboratory has developed a light-driven hybrid enzyme approach taking advantage of the Ru(II)-diimine photosensitizer and their unique excited state properties.[2] This methodology has resulted in efficient delivery of electrons to the heme domain and high photocatalytic activity.[3] Recently, we have been interested in expanding the scope of the light driven P450 enzymes. First, we combined the light-driven hybrid enzymes with photoredox catalysis to marry the advantages of biocatalysis selectivity with chemical catalysis and thus developed a light-driven chemoenzymatic trifluoromethylation/oxyfunctionalization synthesis.[4] Along with the GC/MS protocols, reverse-phase HPLC methods have been developed to separate, characterize and identify products. Second, we focused on the coupling efficiency in the light-driven approach, namely the electrons used in productive pathway leading to the formation of product versus the uncoupling pathway and the formation of reactive oxygen species, quantified using HPLC.[5] Third, the substrate scope has been expanded to include human drug metabolites using several P450 variants in conjunction with the newly optimized light-driven approach. The products were analyzed using HPLC and LC/MS.

References

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2. Shalan, H., Kato, M., Cheruzel, L. *Biochim. Biophys. Acta, Prot. Proteomics.* **2018**, 1866, 80-87
3. Tran, N., Nguyen, D., Dwaraknath, S., Mahadevan, S., Chavez, G., Nguyen, A., Dao, T., Mullen, S., Nguyen, T., Cheruzel, L. *J. Am. Chem. Soc.* **2013**, 135, 14484−14487.
4. Sosa, V., Melkie, M., Sulca, C., Li, J., Tang, L., Li, J., Faris, J., Foley, B., Banh, T., Kato, M., Cheruzel, L. *ACS Catal.* **2018**, 8 (3), 2225–2229.
5. Kato, M., Melkie, M., Li, J., Foley, B., Cheruzel, L. **2019**, *in preparation*.

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