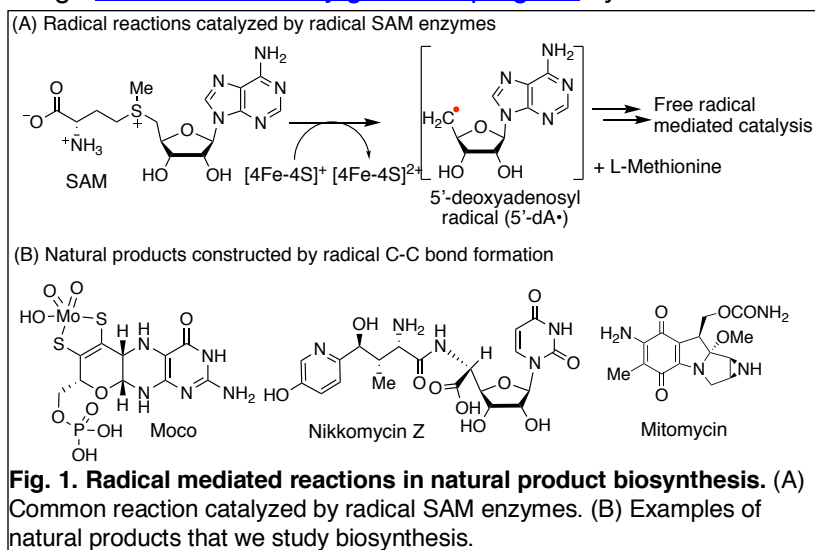


Postdoc and graduate positions in natural product biosynthesis

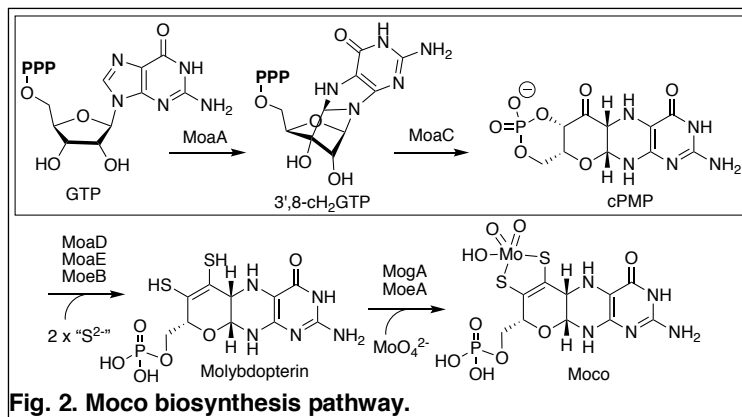
Duke University School of Medicine, Department of Biochemistry, Yokoyama Lab

NIH-funded postdoc and graduate positions are available in Kenichi Yokoyama's lab (<https://sites.duke.edu/yokoyamalab/>) for highly motivated young scientists interested in studying biosynthesis of natural products and cofactors. Our group studies the biosynthesis and mechanism of action of natural products and cofactors and apply the knowledge to discover novel therapeutics. We use a combination of approaches from organic chemistry, biochemistry, molecular biology and biophysics with particular focus on in vitro functional and mechanistic characterization of enzymes, small molecule characterization, bacterial and fungal/yeast genetics, synthetic organic chemistry, NMR, EPR and fluorescence microscopy. We are seeking for highly motivated postdocs and graduate students. Duke University School of Medicine offers an outstanding training environment for graduate and postdoctoral scholars and a strong track-record of alumni achievements in academic and industrial careers. To apply to the postdoc position, please send a cover letter explaining your career goals and research interests, a CV, and names of three references to ken.yoko@duke.edu by Oct 30. Applications after this date may be considered, but we will close the recruitment as we find appropriate candidate. Graduate applicants should submit applications through [Duke Biochemistry graduate program](#) by Dec 1. Please also feel free to contact with any questions.

Research focus: Understanding the mechanism of biosynthesis and action of natural products is important for their future development into novel therapeutics. Overall goal of our lab is to provide comprehensive understanding about the biosynthesis and mechanism of action of natural products and cofactors. Particularly, we focus on natural products whose biosynthesis requires free radical mediated reactions represented by radical SAM enzymes (Fig. 1). To this end, we combine (1) functional and mechanistic enzymology, (2) structural biology, (3) genome mining, and (4) gene knockout experiments.



For example, one of our foci is the molybdenum cofactor (Moco, Fig. 2) biosynthesis. Moco plays key roles in chronic bacterial infection and human inheritable disease (Moco deficiency). We recently discovered a novel and cryptic biosynthetic intermediate 3',8-cH₂GTP, and revealed the functions of two enzymes, MoaA and MoaC (Fig. 2; *JACS* **2013**, *135*, 7019-32; *PNAS* **2015**, *112*, 6347-52.). We are now characterizing the mechanisms of these enzymes with immediate focus on: (1) mechanistic enzymology using substrate analogs combined with biophysical spectroscopy, (2) enzymological and structural characterization of peptides that rescue the catalytic function of MoaA variants found in human Moco deficiency patients, (3) development of inhibitors against enzymes from bacterial pathogens. Recent example of our mechanistic studies can be found in *JACS* **2020**, *142*, 9314–9326. The project will be extended to humans and pathogenic bacteria.



Another example is antifungal nucleoside biosynthesis, in which we recently uncovered most of the steps required for nikkomycin Z biosynthesis (Fig. 1B, *Nature Chemical Biology* **2016**, *12*, 905-907; *Nature Chemical Biology* **2020**, *in press*). We are currently performing structural and mechanistic characterization of biosynthetic enzymes and genome mining discovery of novel antifungal nucleoside natural products. Thus, postdocs and students in our group will obtain comprehensive experience around the biochemistry of natural products.

Another example is antifungal nucleoside biosynthesis, in which we recently uncovered most of the steps required for nikkomycin Z biosynthesis (Fig. 1B, *Nature Chemical Biology* **2016**, *12*, 905-907; *Nature Chemical Biology* **2020**, *in press*). We are currently performing structural and mechanistic characterization of biosynthetic enzymes and genome mining discovery of novel antifungal nucleoside natural products. Thus, postdocs and students in our group will obtain comprehensive experience around the biochemistry of natural products.