Postdoc position in cofactor/natural product biosynthesis
Duke University Medical Center, Department of Biochemistry
Yokoyama Lab

An opportunity for postdoctoral training in the Yokoyama lab is available for highly motivated new PhD scientists interested in studying mechanistic enzymology and chemical biology of natural products and cofactors. Our research is focused on functional and mechanistic characterizations of enzymes from pathways relevant to infectious disease and human inheritable disease. Our approaches are highly interdisciplinary spanning the chemistry, biology and biophysics fields, and our specific methodologies include synthetic organic chemistry, natural product analysis and isolation, bacterial and fungal/yeast genetics, proteomics, NMR, EPR and fluorescence microscopy. We are seeking for highly motivated postdocs in the following area of research:

Project 1. Mechanistic understanding in the biosynthesis of molybdenum cofactor (Moco) that plays key roles in chronic bacterial infection and human inheritable disease (human Moco deficiency). We recently discovered a previously undescribed biosynthetic intermediate 3',8-cH2GTP, which lead to the revision in the functions of two biosynthetic enzymes, MoaA and MoaC (Hover et al., JACS 2013; Hover et al., PNAS 2015). We are now characterizing the mechanisms of these enzymes. Specific aims of this project are (1) to prepare and characterize GTP analogs to capture reaction intermediates of MoaA and MoaC, and (2) to enzymologically and structurally characterize peptides that rescue the catalytic function of MoaA variants relevant to human Moco deficiency.

Project 2. Elucidation and engineering of biosynthetic pathway of naturally occurring antifungal antibiotics. Fungal infections have been emerging as a consequence of increasing number of immunocompromised patients in hospitals. Development of novel antifungal therapy has been hampered due to the difficulties in selective killing of eukaryotic fungal cells without adverse toxicity to humans. To change this situation, we are studying naturally occurring antifungals targeting cell-wall biosynthetic machinery. Fungal cell wall and its biosynthetic enzymes do not exist in human cells, and hence its pharmacological inhibition provides selective killing of fungi. Our current focus is to understand the biosynthesis and mode of action of such antifungal agents and use the knowledge to discover novel antifungals or to modify the existing ones. Specific aims of this project are (1) to identify and genetically manipulate antifungal producing bacteria, (2) functionally and mechanistically characterize the antibiotic biosynthetic enzymes, and (3) prepare and use antibiotic derivatives to understand their modes of action.

We are looking for highly motivated hard working candidates with strong background in molecular biology, protein biochemistry or (bio)organic chemistry. Duke University Medical School offers an outstanding training environment for postdoctoral scholars and a strong track-record of alumni achievement in academic and industrial careers. To apply, please send a cover letter explaining your career goals and research interests, a CV and names of three references to ken.yoko@duke.edu. Please also feel free to contact with any questions.