SCIENCE HALL SEMINARS

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Understanding two enzymes as potential drug targets in the treatment of filariasis & tuberculosis

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Abstract: Targeting Wuchereria bancrofti dihydrofolate reductase. This part focuses on dihydrofolate reductase from the parasite Wuchereria bancrofti, which causes lymphatic filariasis. We used computer-based screening to identify antifolate compounds that may bind to this enzyme. Promising compounds were then tested in inhibition assays and their interactions with the active site were studied using X-ray crystallography. These experiments showed how small molecules interact with the active site and helped identify features that improve binding and inhibition. We also tested several helical peptide mimetics as allosteric inhibitors.

Probing Mycobacterium tuberculosis indole-3-glycerol phosphate synthase. This part examines indole-3-glycerol phosphate synthase from Mycobacterium tuberculosis, an enzyme that catalyzes the fourth step in tryptophan biosynthesis. We mutated key amino acids in the active site and measured how these changes affect enzyme activity and the rate limiting step. The results identified residues that are essential for catalysis. An inverse kinetic solvent viscosity effect was observed for several mutants and suggested a rate-limiting conformational change. These mechanistic insights help guide future efforts to design inhibitors.

Wednesday, January 21st | 2:00pm-3:15pm | Science Hall 126 & Zoom

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