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Alanine Racemase as a Template for Drug Design. Kurt Krause, Pierre Magueres, Hookang Im, Jim Briggs, Uli Strych, Jerry Ebalunode, Uli Strych, Mike Benedik, Harold Kohn, Biology and Biochemistry, Univ. of Houston, Houston Science Center, Houston, TX 77204.

We present progress from an academic structure-aided drug design program aimed at developing new agents for the treatment of tuberculosis. We have chosen to focus on the design of inhibitors of an essential prokaryotic enzyme, alanine racemase. Although we are specifically targeting *M. tuberculosis*, we are also studying this enzyme from several additional pathogens. Because of the broad importance of alanine racemase as a drug target, its inhibitors could prove useful in the development of antibiotics for most bacterial infections.

Our drug target development program is comprised of four components: microbial genetics, structural biology, computer aided drug design, and medicinal chemistry. One goal is to use the three-dimensional structure of alanine racemase from pathogens, like *M. tuberculosis* as a template for drug design.

We will present results from three racemase structure determinations and analyze them in terms of pharmacophore development. We will review the creation of pharmacophore models that incorporate the results of molecular dynamics simulations. These pharmacophore models have been used to survey, *in silico*, chemical databases for racemase inhibitors. From our most recent structure, the alanine racemase from *M. tuberculosis*, we present evidence for a conserved substrate entryway that may result in improved pharmacophore development.

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