Protonation State Analysis of Epoxide Hydrolase B in *Mycobacterium tuberculosis*

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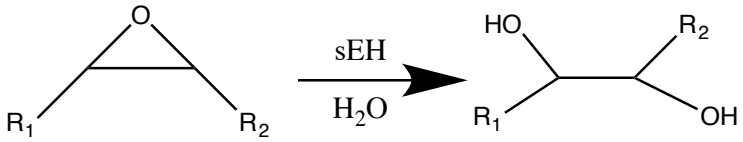
Epoxide hydrolase is an enzyme that catalyzes epoxide conversion to vicinal diols.



EPOXIDE DIOL

It is ubiquitous to almost all organisms including humans, with roles in detoxification, metabolism and regulation of signaling molecules. The genome of the causative agent of tuberculosis, *Mycobacterium tuberculosis,* encodes for six separate epoxide hydrolases and there is evidence that these may play a role in establishing an infection.

The structure of the active site in the human soluble Epoxide Hydrolase (sEH) is similar to that of the Epoxide hydrolase B in the tuberculosis bacteria as shown in Figure 1. The focus of this study is to establish the protonation state of two active-site histidine residues, His103 and His333. The methods used to evaluate these protonation states include: visual inspection, PropKa, explicit solvent molecular dynamics simulations and constant pH implicit solvent molecular dynamics simulations. In this work, we present the preliminary results of these studies.

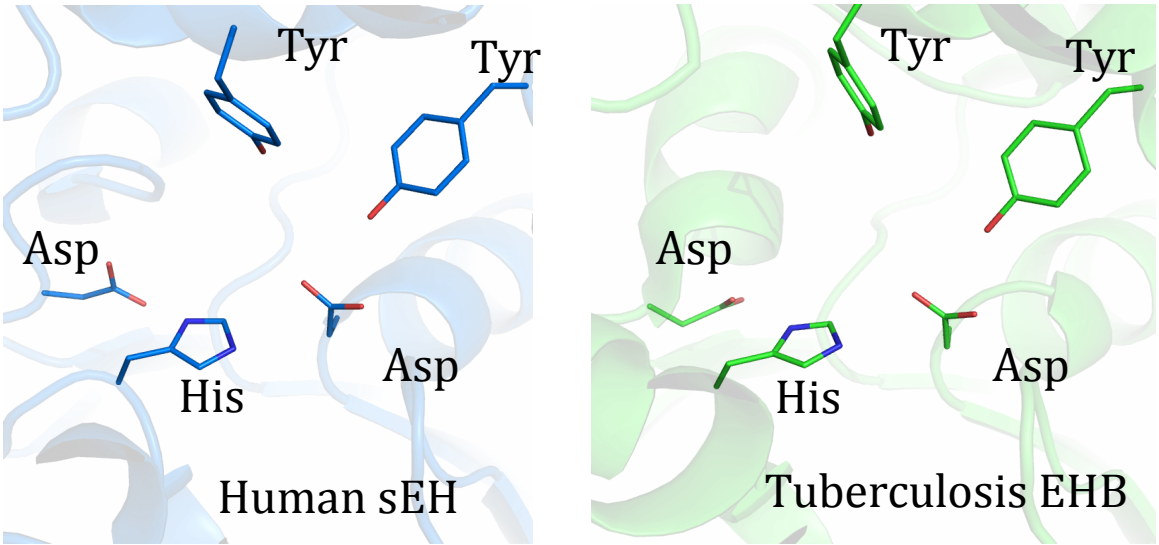


Figure 1. Active site comparison of human soluble Epoxide Hydrolase and tuberculosis Epoxide Hydrolase B