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Active Site Binding Is Not Sufficient for Reductive Deiodination by Iodotyrosine Deiodinase

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Host: Dr Deepak Choudhury

Seminar Abstract

Iodotyrosine deiodinase is crucial for iodide homeostasis and generation of thyroid hormone in chordates. The minimal requirements for its substrate recognition and turnover were examined to learn basis of its catalytic specificity. 2-Iodophenol binds only very weakly to the human enzyme and is inefficiently dehalogenated (k_{cat}/K_m is $>10^4$ lower than that for iodotyrosine). This discrimination likely protects against a futile cycle of iodinating and deiodinating precursors of thyroid hormone biosynthesis.

Surprisingly, a very similar catalytic selectivity was expressed by a bacterial homologue although its physiological function in bacteria is unknown. Likewise, the bacterial enzyme is activated for single electron transfer as observed with the human enzyme. A cocrystal structure of bacterial deiodinase and 2-iodophenol indicates that this ligand stacks on the active site flavin mononucleotide (FMN) in an orientation analogous to that of bound iodotyrosine. However, 2-iodophenol association is not sufficient to activate the FMN chemistry required for catalysis.

About the Speaker

Nattha Ingavat received her Ph.D. in Chemistry (Biochemistry research-based) from Johns Hopkins University, Maryland, USA before pursuing her career path in start-up and mid-size pharmaceutical companies. Her downstream process development experiences started in 2020, where her focus was on purification process development/improvement for biosimilar monoclonal antibodies. She joins A*Star (BTI) in September 2022 under supervision of Dr. Zhang Wei to advance her knowledge in biologic purification and analysis for more challenging antibody formats, bispecific antibodies. Besides science, Nattha also loves to spend her leisure time traveling, working out, cooking, and doing food exploration.

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