# STRUCTURE AND FUNCTION OF UNUSUAL RIESKE-TYPE OXYGENASES FROM HUMAN MICROBIOTA INVOLVED IN CARNITINE METABOLISM

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L-carnitine is an abundant nutrient in red meat, and dietary intake of L-carnitine can promote cardiovascular diseases in humans through microbial production of trimethylamine (TMA) and its subsequent oxidation to trimethylamine N-oxide by liver hepatic flavin-containing monooxygenases. Targeting gut microbial production of TMA specifically and non-lethal microbial inhibitors in general may then serve as a potential therapeutic approach for the treatment of cardiometabolic diseases. A two-component oxygenase/reductase (CntA/B) from human microbiota bacterium *Acinetobacter baumannii*, as well as the alternative enzyme complex YeaW/X from *E. coli* DH10B strain, are two groups of previously reported unusual Rieske-type proteins that cleave carnitine to produce TMA, representing an important microbial pathway of TMA production. Despite YeaW/X having 71% and 50% sequence identity to CntA and CntB, YeaW/X was found to possess broader substrate usage and could produce TMA from either choline or carnitine as substrate. We are therefore pursuing structural investigation of these enzymes to elucidate the function-structure relationships of these Rieske-type enzymes and to decipher the structural basis for broader substrate specificity of YeaW. We have cloned, expressed, and purified the CntA/B and Yea W/X enzyme complexes in order to determine crystal structures of apo and carnitine-bound forms of both of these enzyme complexes. Such studies should aid in the design of more effective inhibitors for the treatment of atherosclerosis.