**Poster Presentation**

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## *Structural Study of Thioesterase Domains in Complex with Covalent Inhibitors*

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Polyketide synthases (PKS) are large multifunctional enzymes that are responsible for the biosynthesis of a wide array of secondary metabolites that are of great interest for medical applications. PKS catalyze carbon-carbon bond formations by successive Claisen condensations of small thioesters. All PKS are organized in modules where each module is composed of catalytic domains that add a single ketide unit to the growing chain and optionally reduce the beta-keto function. The Thioesterase (TE) domain is responsible for the released of the final polyketide chain. Two ways are used by the TE domains: hydrolysis to form a linear chain or cyclization to form a macrolide. The molecular mechanism which controls the cyclization versus hydrolysis decision is not fully understood and a better understanding of this mechanism could be a great interest for generating new pharmaceutical compounds. To answer this question, we are studying the structure and function of PKS TE domains in collaboration with the group of Dr. Boddy (University of Ottawa). Recent results about the biochemical study in complex with inhibitors, crystallization and structures of one of these TE domains will be presented.

***[1]*** *A. Pinto, M. Wang, M. Horsman and C.N. Boddy, Organic Letters, 2012, 9, 2278-2281,* ***[2]*** *S-C. Tsai, L.J.W. Miercke, J. Krucinski, et al., Proceedings of the National Academy of Sciences, 2011, 26, 14808-14813*

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