

Distribution and Structure of Polyketide Synthases in *Aspergillus*

Shu-Hsi Lin¹, Miwa Yoshimoto³, Ping-Chiang Lyu¹, Chuan-Yi Tang², and Masanori Arita³

¹Institute of Bioinformatics and Structural Biology, National Tsing Hua University, Hsinchu (Taiwan)

²Department of Computer Science, National Tsing Hua University, Hsinchu (Taiwan)

³Department of Biophysics and Biochemistry, The University of Tokyo, Tokyo (Japan)

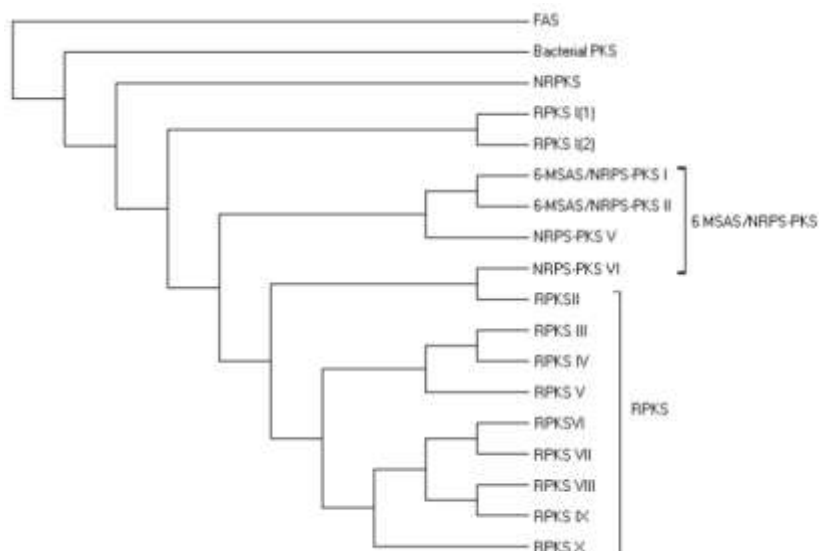
Polyketides, a rich source of medicinal compounds, are extensively studied in *Streptomyces*, *Penicillium*, and *Aspergillus*. While it has been difficult to genetically manipulate non-model organisms, recent advances in genome science are changing this situation. The key enzyme here is polyketide synthase (PKS), a giant multi-domain protein catalyzing a characteristic condensation of polyketones. Fungal PKSs are known to be iterative, ie, the same domains are multiply used in the course of condensation. However, the detailed mechanism is mostly unknown.

Aspergillus species is extremely important as the source of bioactive compound library and also as a bioprocess host. In Japan, Koji mold (*A. oryzae*) has been exploited to produce sake (rice wine), shochu (distilled sake), shoyu (soy source), miso (soy paste), and many other traditional food. The analysis of PKSs is therefore important for food safety and quality.

To compare and reveal evolutionary relationships among fungal PKSs, we classified the domain structures of over 400 iterative PKS genes, performed phylogenomic analyses focusing on eight *Aspergilli* (*A. clavatus*, *-flavus*, *-fumigatus*, *-nidulans*, *-niger*, *-oryzae*, *-terreus*, and *Neosartorya fischeri*), and created a web-based data repository so that users can easily check and reproduce the results of our analyses.

Our main findings include: 1) extensive gene duplication and diversification/shuffling even among very close species; and 2) correlation between non-ribosomal peptide synthases (NRPSs) and the ketoreductase- and dehydratase domains of PKSs. Specifically, PKS-NPRS genes share the domain ordering of KS-AT-DH-KR-ACP. We also created a wiki-based database and all data are accessible at <http://metabolomics.jp/wiki/Category:PK>.

Right: Phylogenetic tree of ketosynthase (KS) domains of 470 PKSs by the maximum parsimony method. PKSs are largely classified into non-reducing, hybrid- and reducing PKSs.



References

Lin, S.-H.; Yoshimoto, M.; Lyu, P.-C.; Tang, C.-Y.; Arita, M. *Evol. Bioinform* **2012**, *8*, 373-387.