Journal Club No. 805

September 18, 2018
Sangkeun Son

Genomics-Driven Discovery of New Ribosomally and Non-Ribosomally Synthesized Peptides from an Actinobacterium

In this presentation, I would like to discuss new secondary metabolites produced by actinomycetes and methods applied for their detection and characterization. With the advances in sequencing technology and biosynthetic knowledge, the genome mining approach has become an important tool for discovering new bacterial natural products. It has been demonstrated that a combination of the genome mining approach with pleiotropic or pathway-specific methods for activating targeted cryptic gene clusters can rationally unearth new compounds. During chemical investigation of bacteria inhabiting diverse ecological niches in the Korean Peninsula through analysis of metabolic profiles, structurally novel non-ribosomal peptides named ulleungamides A and B were identified from an actinobacterium *Streptomyces* sp. KCB13F003. Following this discovery, the genome scanning program was then performed to further evaluate the biosynthetic potential of the strain, which indicated that it harbors two cryptic biosynthetic gene clusters encoding putatively new compounds. The encoded products were obtained by application of multiple culture conditions followed by LC-MS targeted isolation, and their structures were established by spectroscopic and chemical methods. The compounds were determined to be a new ribosomally synthesized class II lasso peptide and non-ribosomally synthesized hexapeptides. Bioassays in a preliminary biological screening revealed that the lasso peptide had cancer cell migration inhibitory activity, and hexapeptides showed antibacterial activity. These studies suggest that the genome-guided strategy could be rationally applied even for limited genomic information from in-house actinomycetes. In addition, several studies on discovery of new bioactive secondary metabolites that have been performed by the collaborative works of RIKEN and KRIBB will also be briefly introduced in this presentation.

References

• Son, S.; Hong, Y. S.; Jang, M.; Heo, K. T.; Lee, B.; Jang, J.-P.; Kim, J. W.; Ryoo, I.-J.; Kim, W.-G.; Ko, S.-K.; Kim, B. Y.; Jang, J.-H.; Ahn, J. S. "Genomics-Driven Discovery of Chlorinated Cyclic Hexapeptides Ulleungmycins A and B from a *Streptomyces* Species" ***J. Nat. Prod.*** 80(11):3025–3031. (2017)

• Son, S.; Ko, S.-K.; Kim, J. W.; Lee, J. K.; Jang, M.; Ryoo, I.-J.; Hwang, G. J.; Kwon, M. C.; Shin, K.-S.; Futamura, Y.; Hong, Y.-S.; Oh, H.; Kim, B. Y.; Ueki, M.; Takahashi, S.; Osada, H.; Jang, J.-H.; Ahn, J. S. "Structures and Biological Activities of Azaphilones Produced by *Penicillium* sp. KCB11A109 from a Ginseng Field" ***Phytochemistry*** 122:154–164. (2016)

• Son, S.; Ko, S.-K.; Jang, M.; Kim, J. W.; Kim, G. S.; Lee, J. K.; Jeon, E. S.; Futamura, Y.; Ryoo, I.-J.; Lee, J.-S.; Oh, H.; Hong, Y.-S.; Kim, B. Y.; Takahashi, S.; Osada, H.; Jang, J.-H.; Ahn, J. S. "New Cyclic Lipopeptides of the Iturin Class Produced by Saltern-Derived *Bacillus* sp. KCB14S006" ***Mar. Drugs*** 14(4):E72. (2016)

• Son, S.; Ko, S.-K.; Jang, M.; Lee, J. K.; Ryoo, I.-J.; Lee, J.-S.; Lee, K. H.; Soung, N.-K.; Oh, H.; Hong, Y.-S.; Kim, B. Y.; Jang, J.-H.; Ahn, J. S. "Ulleungamides A and B, Modified α,β-Dehydropipecolic Acid Containing Cyclic Depsipeptides from *Streptomyces* sp. KCB13F003" ***Org. Lett.*** 17(16):4046–4049. (2015)