Chemists reveal novel biocatalysts for bioactive alkaloid synthesis

February 21 2017

Alkaloids are natural nitrogen-containing compounds produced by plants and microbes. These molecules, such as morphine and quinine, are important human medicines. Alkaloids are typically polycyclic in nature. While the polycyclic characteristics are important for their bioactivities, these features impede their chemical syntheses in the laboratory and their applications as pharmaceuticals.

Hapalindole-type alkaloids are renowned for potent antimicrobial and antitumor activities. These alkaloids are typically tricyclic and tetracyclic in nature and synthetically challenging to access in the laboratory for drug discoveries.

In an article published online Feb. 20 in *Chemical Communications* titled "Molecular and genetic basis for early stage structural diversifications in hapalindole-type alkaloid biogenesis," the group led by Xinyu Liu, an assistant professor of chemistry within Pitt's Kenneth P. Dietrich School of Arts and Sciences, disclosed a novel family of enzymes (protein catalysts) that can direct the biogenetic assembly of the polycyclic scaffolds in the hapalindole-type alkaloids.

Liu and postdoctoral associate Qin Zhu utilized bacterial E. coli as a heterologous host and demonstrated that the proteins encoded by previously uncharacterized U-family genes in several hapalindole pathways are novel cyclization biocatalysts that can morph simple acyclic precursors into three distinct hapalindole scaffolds. Bioinformatic analysis further revealed each hapalindole producer often

encodes one or several copies of U genes to direct the divergent assembly of several hapalindoles in the same producers.

Their work provides conclusive evidence on the biochemical basis for the origin of early structural diversity in hapalindole-type natural products. "With the U-family proteins characterized as a novel family of cyclization enzymes, we now have the complete biocatalyst tool sets in hand to synthesize these molecules in our laboratory. After six years of efforts and several groundbreaking works generated from my lab on the biosynthesis of hapalindole-type alkaloids, we finally have a chemoenzymatic platform to advance these remarkable molecules for drug discoveries. It is a great feeling and exciting time for us," said Liu.

Provided by University of Pittsburgh

Citation: Chemists reveal novel biocatalysts for bioactive alkaloid synthesis (2017, February 21) retrieved 9 April 2024 from https://phys.org/news/2017-02-chemists-reveal-biocatalysts-bioactive-alkaloid.html