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Striking features and complex regulation of polyketide antibiotic auricin from *Streptomyces lavendulae* subsp. *lavendulae* CCM 3239

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Bacteria of the genus *Streptomyces* are the main producers of bioactive natural products with a broad range of biological activities. A large number of these products belong to polyketides. These structurally diverse natural compounds are synthesized by a repeated decarboxylative condensation from acyl-CoA precursors by a polyketide synthase (PKS). Aromatic polyketides are synthesized by type II PKSs. Although a large repertoire of aromatic polyketides produced by type II PKSs was identified, they all belong to just a few common structural types that include pyranonaphthoquinones, tetracyclines, angucyclines, anthracyclines, tetracenomycines, aureolic acids. We identified the *aur1* gene cluster in *Streptomyces lavendulae* subsp. *lavendulae* CCM 3239 (formerly *Streptomyces* aureofaciens CCM 3239), which is responsible for the production of the angucycline-like antibiotic auricin. Interestingly, the *aur1* gene cluster is localized on the large (241 kb) linear plasmid pSA3239. Auricin was produced in low levels, which hampered its purification and structural elucidation for many years. Careful investigation revealed that auricin is transiently produced in a very narrow growth phase interval of several hours after entry into stationary phase and afterwards it was degraded to non-active metabolites because of its instability at the high pH reached after the production stage. This unusual pattern of auricin production arises from a strict, but complex regulatory mechanism, involving both feed-forward and feed-back control by auricin intermediates via several transcriptional regulators (gamma-butyrolactone system SagA/SagR, pathway-specific regulators Aur1P, Aur1O, Aur1R, Aur1PR3 and Aur1PR4. Auricin structural analysis revealed that it possesses intriguing structural features, distinguishing it from other known angucyclines. It is modified by D-forosamine and contains a unique aglycone similar to those of spiroketal pyranonaphthoquinones griseusins. In addition to its antibiotic activity, auricin also displayed modest cytotoxicity against several human tumor cell lines.

Biography

Jan Kormanec is the Head of Department of Genomics and Biotechnology at the Institute of Molecular Biology of Slovak Academy of Sciences (Bratislava, Slovakia), where he has been working since 1984. He graduated from the Comenius University (Bratislava, Slovakia) in 1984 and with a PhD from the Slovak Academy of Sciences in 1991. In 2001, he was awarded the highest scientific title (DrSc) by Comenius University. His main research interests include the role of sigma factors of RNA polymerase in stress-response, pathogenicity, and differentiation of bacteria, and investigation of antibiotics production and regulation in *Streptomyces*. He has published 116 papers in reputed journals and four chapters, which are cited by more than 1700 citations in Web of Science.

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