

Antimicrobial peptide symposium



AMP 2014

June 4-6, 2014, Lorient, France

Proceedings
of the
**4th International
Symposium on
Antimicrobial
Peptides**

Lorient, France
June 4-6, 2014



Towards structure elucidation of albicidin, a potent DNA gyrase inhibitor produced by the plant pathogen *Xanthomonas albilineans*

Stéphane Cociancich¹ (cociancich@cirad.fr), Alexander Pesic², Stefanie Uhlmann², Daniel Petras², Julian Kretz², Vivien Schubert², Laura Vieweg², Sandrine Duplan¹, Mélanie Marguerettaz¹, Julie Noëll¹, Isabelle Pieretti¹, Manuela Hügelland², Sebastian Kemper², Philippe Rott¹, Monique Royer¹, Roderich Süssmuth²

¹ CIRAD - Biologie et génétique des interactions plante-parasite (BGPI) - Centre de coopération internationale en recherche agronomique pour le développement [CIRAD] : UMR54, Campus International de Baillarguet - TA A54/ K - 34398 Montpellier Cedex 05 - France

² Technische Universität Berlin (TUB) - Straße des 17. Juni 135 10623 Berlin - Germany

Keywords: Albicidin; antibacterial peptide; HPLC; mass spectrometry; nuclear magnetic resonance

Albicidin is a small molecule produced by the sugarcane pathogen *Xanthomonas albilineans*. Initially discovered as being involved in the occurrence of disease symptoms on sugarcane leaves, it was subsequently shown to possess a potent antibacterial activity. Albicidin exhibits antibacterial activity at the nanomolar range against *Escherichia coli* and, to a lower extent, against a wide range of Gram-negative and Gram-positive human pathogenic bacteria. It is a potent inhibitor of the supercoiling activity of the bacterial DNA gyrase by a mechanism that is different from those of other known DNA gyrase inhibitors (coumarins and quinolones, for instance). Although albicidin is a promising antibiotic for medical use because of its unique and potent antibacterial activity, the lack of structural knowledge has impeded its consideration as a new lead compound by the pharmaceutical industry. Three decades of intense work have therefore been dedicated to both the study of the biosynthesis and the structure elucidation of albicidin, which is synthesized by a hybrid polyketide synthase/nonribosomal peptide synthetase (PKS/NRPS) system, and which is produced only in minute amounts by *X. albilineans*. *In silico* analyses of the complete albicidin biosynthesis gene cluster, in addition to analytical data, resulted in only partial structural data of the molecule. In this work, we report the development of a structure elucidation strategy using a combination of HPLC purification with HPLC-ESI-orbitrap mass spectrometry and nuclear magnetic resonance (NMR) spectroscopy techniques along with studies of the biosynthesis pathway. Use of this protocol resulted in significant progress towards the structure elucidation of albicidin with the likely involvement of chorismate biosynthesis. The current status of albicidin structure elucidation and its potential for use as an antibiotic will be discussed.