



Inserm

Institut national
de la santé et de la recherche médicale



Paris, 4 March 2009

Press information

Discovery of a new antibiotic resistance strategy

Thanks to their high capacity for adaptation, bacteria progressively learn how to resist antibiotic treatments. French scientists from Inserm, Paris Descartes University, INRA, Pasteur Institute, and the CNRS have recently shown that one of their strategies consists in the diversion of fatty acids present in human blood for their own growth.

These studies are published in the review Nature on 5 March 2009.

In order to survive, bacteria are able to rapidly adapt to new environments, in particular in the presence of antibiotics. Their genetic material evolves and diversifies, resistant microorganisms are selected and treatments then become ineffective. During recent years, most bacteria pathogenic for man have become resistant to antibiotic treatments.

French scientists from Inserm, Paris Descartes University, INRA, the Pasteur Institute and CNRS showed that the most important gram-positive bacteria pathogenic for man (streptococci, enterococci and staphylococci) are able to use the fatty acids abundantly present in human blood to form their membrane. They thereby escape the activity of antibiotics supposed to prevent them from manufacturing their own fatty-acids.

Fatty acids are the major components of the bacterial membrane and their biosynthesis is regarded as essential for the integrity of the bacterial cell. Because of this action, enzymes involved in fatty acid biosynthesis are proposed as potential targets for the development of antibiotics and some of these have already been validated by pharmaceutical laboratories as they inhibit the growth of bacteria *in vitro*.

"We started from findings made on group B streptococci, the main cause of infection in the new-born infants" explains Claire Poyart. In this work, streptococci devoid of genes encoding enzymes involved in the biosynthesis of fatty acids are unable to grow in conventional culture media.

However, these mutant streptococci do not present any growth defect in media supplemented with human serum which provides the bacterial membrane with essential fatty acids. In addition, their virulence is normal in animal models. These results show a form of "parasitism" in which bacteria use ingredients in human blood to escape the activity of antibiotics which target the fatty acid biosynthesis pathway.

This work underlines the importance of testing the activity of antibiotics using tests that are close to the real conditions of infection and treatment.

To learn more:

Type II fatty acid synthesis is not a suitable antibiotic target for Gram-positive pathogens

Sophie Brinster^{1,2}, Gilles Lamberet³, Bart Staels⁴, Patrick Trieu-Cuot⁵, Alexandra Gruss³ & Claire Poyart^{1,2,5,6}

¹Institut Cochin, Université Paris Descartes, CNRS (UMR 8104), Paris, France.

²INSERM, U567, Paris, France.

³INRA, UR888, Unité Bactéries Lactiques et Pathogènes Opportunistes, F-78350, Jouy en Josas, France.

⁴Institut Pasteur de Lille, INSERMUMR545, Université Lille 2, Lille, France.

⁵Institut Pasteur, Unité de Biologie des Bactéries Pathogènes à Gram Positif, URA CNRS 2172, Paris, France.

⁶Assistance Publique Hôpitaux de Paris, Centre National de Référence des Streptocoques, Hôpital Cochin, Paris, France.

Nature <http://dx.doi.org/10.1038/nature07772>

Scientists contact details

Claire Poyart

Institut Cochin Unité Inserm 567, Université Paris Descartes

Tel : 01 58 41 15 60

Email: claire.poyart@cch.aphp.fr

Alexandra Gruss

Unité INRA U888

Tel: 01 34 65 21 68

Email: Alexandra.gruss@jouy.inra.fr

Patrick Trieu-Cuot

Unité de Biologie des Bactéries à Gram-positif

Institut Pasteur

Tel.: 01 44 38 95 92

Email : patrick.trieu-cuot@pasteur.fr