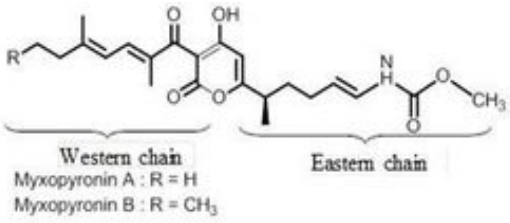
Technology Offer

Novel Myxopyronin Analogues and Myxopyronin Genecluster for Mutasynthesis

Reference Number 02-00303

Challenge

WHO estimates that tuberculosis (TB) infects one third of the world's population. Not all people infected with TB will necessarily become sick with the disease, because the TB bacilli can be "walled off" by a thick waxy coat and lie dormant for years, yet the chances of becoming sick are higher when the immune system is weakened. Despite a slow decline of the estimated number of people falling ill with TB each year, in 2011 still 8.7 million people were affected and an estimated 1.4 million people died from TB, including 430.000 HIV-positive patients. Although there are powerful anti-TB drugs like rifampicin and isoniazid available, after decades of use resistant pathogens have emerged. Particularly MDR-TB and even XDR-TB are insensitive not only to the first line but also to second line antibiotics. Therefore, the demand for innovative antibiotics, particularly those addressing new targets, remains high.



Technology

Myxopyronin belongs to the family of alpha-pyrone antibiotics known for their promising antibacterial activity. These molecules target the "switch region" of the RNA polymerase (RNAP) which is different from the interaction region of the first-line TB-antibiotic rifampicin, making emergence of a cross-resistance less likely and opening up opportunities for combined therapies. In addition, the recent in depth elucidation of the interaction between the RNAP and the alpha-pyrones allows targeted design of pharmacologically optimized myxopyronin derivatives. Even molecules with a broadened activity spectrum, e.g. against MRSA and alike, are thinkable. The provided technology comprises the myxopyronin biosynthesis genecluster for the targeted development of novel myxopyronin analogues using mutasynthetic approaches. Naturally, myxopyronin is synthesised in two halves (eastern and western chain) that are fused in a later step. This fact can be utilized by blocking the synthesis of one half while feeding synthetic precursors for incorporation, thereby generating novel myxopyronin analogues. First novel analogues are already available for evaluation.

Commercial Opportunity

The technology is offered for cooperative development of novel myxopyronin analogues by genetic engineering.

Patent Situation

Priority filed in 2013 at the EPO. International application filed in 2014 (WO2014181000A1). EP patent application pending.

Further Reading

Sucipto et al. 2013. Exploring Chemical Diversity of a-Pyrone Antibiotics: Molecular Basis of Myxopyronin Biosynthesis. ChemBioChem 2013, 14, 1581 – 1589.

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