Analysis of lincomycin biosynthetic genes usable for the preparation of hybrid compounds

Lincosamide antibiotics have relatively simple molecular structure compared with other types of antibiotics. However, these molecules contain so called "hot spots" whose modification leads to the development of more effective drugs. Combinatorial biosynthesis appears to be a promising way to design and preparation of lincosamides' derivatives. For this purpose a perfect knowledge of the natural biosynthetic pathway is needed.

The submitted doctoral thesis analyzed genes *lmbIH, K, N, Q, T, U* and *V* with unknown function from the lincomycin biosynthetic gene cluster. Mutation analysis of *lmbN* has proven its bifunctional character, 5 'end of the gene is coding for a potential N-demethyllincomycin synthetase subunit, while the rest of the gene encodes an enzyme for synthesis of sugar precursor methylthiolincosamide (MTL). Gene *lmbT* was also assigned to the biosynthesis of the sugar precursor. In the case of other genes the determination of function was not so clear. It is assumed that their roles in the biosynthetic pathway are more regulatory or supporting.

The mutasynthetic approach was used for the preparation of lincomycin derivatives with longer alkyl residues. Activity of obtained lincomycin derivatives was tested on a set of staphylococci resistant strains.

In the next part of the work the characterization of producer strains from different natural locations on a presence of new genes with interesting activities was performed.

The results of this work have brought the new knowledge on the biosynthesis of lincosamide antibiotics and outline possible ways for the preparation of hybrid compounds on their basis.