Abstract:

Cytochrome P450 3A4 is integral membrane protein residing in endoplasmic reticular membrane. In human the highest concentration cytochrome P450 3A4 is expressed in liver, where it plays a major role in metabolism of many drugs and xenobiotics.

The main aim of the thesis was to evaluate the effect of gene optimization on heterologous expression of human cytochrome P450 3A4. At first expression constructs based on vectors pET22b were prepared. Then the efficiency of heterologous expression of optimized vs. natural gene sequence encoding truncated form of the human cytochrome P450 3A4 compared. The results show that the gen sequence optimized for *E. coli* strains K12 was expressed in significantly higher efficiency than the original human gene based on cDNA sequence.

Another aim was to evaluate the suitability of pET22b based expression vectors for recombinant production of native (complete) form of human cytochrome P450 3A4. The amount of native form of the protein found in bacterial membrane was however substantially lower then that of the truncated form.

Keywords: cytochrome P450 3A4, heterologous expression, pET22b, gene synthesis