Screening the activity of Thermostable Nucleoside Phosphorylases

The Biocatalysis group of the Department of Bioprocess engineering at TU Berlin is offering a bachelor or a master project for a highly motivated student who is interested in biocatalysis.

Background:

Nucleoside phosphorylase is a group of enzymes that catalyze the reversable phosphorolytic cleavage of nucleosides. These are interesting enzymes as they are important drug targets and are used for the enzymatic synthesis of nucleosides and their analogues which are important drug molecules. Nucleoside phosphorylases are present in almost all organisms and their substrate spectrum towards nucleoside analogues varies according to the origin of the enzyme. It has been proposed for long time that nucleoside phosphorylases derived from thermophilic organisms are able to utilize more substrates with various modifications compared to their counterpart of mesophilic origin. Thus, thermophilic nucleoside phosphorylases are valuable and interesting biocatalysts for nucleoside analogues synthesis.

Nucleosides comprise a class of small molecules that are naturally occurring and are considered as the building blocks for DNA and RNA. They are composed of two parts; a pentose moiety and a nitrogenous base linked together by an N-glycosidic bond. When these molecules are modified on either the base, the sugar or both moieties, they exert some clinical and biotechnological applications. One attractive group of nucleosides is the 7-deazapurine analogues. They are used for important biotechnological applications as sequencing. It has been reported previously that E. coli purine nucleoside phosphorylase doesn't utilize the 7-deazapurine analogues as substrates. However, the development of an efficient enzymatic synthesis process is of interest. With that in focus, the activity of different thermophilic purine nucleoside phosphorylases is to be tested towards 7-deazapurine nucleoside derivatives. Their activity is to be compared to purine nucleoside phosphorylase from *E. coli*.

Project aim:

Screening a library of thermophilic nucleoside phosphorylases for their activity towards an array of 7-deazapurine nucleoside analogues.

Approach:

Thermostable nucleoside phosphorylases are to be expressed and purified. Enzymatic reactions are to be conducted and the activity of the nucleoside phosphorylases towards the cleavage and the synthesis of 7-deazapurine nucleoside analogues is to be evaluated using HPLC.

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