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# Exploration of tRNA and the synthetase family of enzymes as novel targets for future generations of drugs

Pal Papsai[a], Haris Bjelosevic[b], Johannes Ghatnekar[b], Jasmin Aldag[a], Tina Persson[b], Sofi K. C. Elmroth[a]

[a]Inorganic chemistry, LMC, Chemical Center, Lund University, Lund, Sweden
[b]Organic chemistry 1, LMC, Chemical Center, Lund University, Lund, Sweden

## Abstract

All living cells depend on protein production for survival. The process relies on information transfer in many steps, from the genetic code stored in the DNA to the final protein synthesis on the ribozome. To minimize the risk of mistakes during the process, the cell has provided itself with clever control systems. The synthetase family comprises one such system, controlling the reaction in which the aminoacids are attached to their corresponding tRNA. The unique nature of the individual synthetases, together with their variation among organisms, makes this group of enzymes interesting from a therapeutic point of view, since protein synthesis could potentially be manipulated in a highly specific manner. To our knowledge, no drug candidates operating on these systems have been developed so far.

We have recently started research in this area, initially aiming at manipulation of the enzymatic reaction catalyzed by alanyl tRNA synthetase. Synthetic work and functional model system studies are combined with the goal of rapid evaluation and redesign of potential drug candidates. Our portfolio of compounds contain drug candidates that are likely to interfere with both reaction steps outlined in Figure 1., e.g. nucleoside derivatives, modifications of know platinum-based anticancer agents and polyamine derivatives. We here present preliminary studies of structural and kinetic work which indicates that the structure of the enzyme-recognition sequence near the 5-end of the tRNA may be particularly prone towards interactions with some of our drug candidates.