Abstract

The project aims to characterize substrate specificity of two recently discovered human cytosolic 5′ nucleotidases, called cN-IIIA and cN-IIIB, and investigate their roles in mRNA metabolism. The modulation of the half-life of mRNA is a powerful and versatile mechanism to swiftly alter the expression of proteins in response to changes in physiological conditions. Nucleotides, which are mRNA degradation products, have to be utilized in cells to maintain the quantitative and qualitative balance of nucleotide pools in living cells. In particular accumulation of modified nucleotides such as m^7GMP in the cytosol is potentially harmful to cells as it may lead to inhibition of important cap-dependent processes, including mRNA translation, and to erroneous incorporation of m^7G nucleotides into nucleic acids. The substrate preference for m^7GMP designates cN-IIIB as one of enzymes that prevent this undesired accumulation and thereby regulate homeostasis of cap-dependent processes. However, this hypothesis still requires experimental confirmation. We envisaged that a properly designed inhibitors or chemical probes could aid in the elucidation of biological roles of cN-IIIB as well as cN-IIIA enzymes and verify their function in mRNA metabolism.