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SHORT COMMUNICATION

The human gut microbiome – In-silico methods of Lysene and Purine roboswitches.

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The human gut microbiome represents colonization of microbes in the human alimentary canal playing a vital role in human physiology, metabolism and immune response. These microbes show commensalism with human cells and do not allow the pathogenic microbes to settle and disrupt the normal functioning of the human gut. Thus major changes in normal gut microbiome colonization might cause diseased condition. The riboswitches control gene expression of these microbes as well as the pathogenic microbes and may act as potent drug targets. The chemical analogues of the riboswitches' natural ligand may bind to them and alter their activity causing dysfunctioning of normal cellular functions hence disrupting the normal colonization of the human gut. Therefore, we aim to study the distribution of various riboswitches, the genes regulated by them and their potential as RNA drug target. In this study, we identified 545 candidate riboswitches in 59 bacterial and 4 archaeal genomes of adult human gut. This study also revealed that the most abundant riboswitch is the TPP riboswitch (25%) followed by Cobalmin (17%), FMN (11%) and Lysine riboswitch (8%). The lower abundance was shown by YkkC/yxkD leader (2%), Cyclic di-GMP II (1%) and ZMP/ZTP riboswitch (1%); the rare ones included M. Florum (0.4%), Nico (0.2%), AdoCbl variant (0.2%) and SAM-I/IV variant riboswitch (0.2%). Further, we found the genes regulated by these riboswitches and predicted seven riboswitches such as c-di-GMP I, c-di-GMP II, SAM, glmS, THF, YdaO/YuaA leader, and glycine riboswitches that might act as drug targets in the pathogenic bacteria of the human gut. These riboswitches play important role in vital synthetic/metabolic pathways and are sparsely present in other non-pathogenic major microflora of the gut.

This class of riboswitches include amino acid binding ribowitches. The distribution pattern of lysine riboswitches showed that they are present in the 26 genomes. The genes regulated by lysine riboswitches belong to DAP biochemical pathway for synthesis of lysine, for example lysP, lysC, dapA, and asd. Since the genes controlled by lysine riboswitch belong to the biosynthesis pathway the lysine riboswitch can act as potential drug target but not for human gut microbiome as this riboswitch is also widely distributed among other essential commensal non-pathogenic bacterial genomes (16 out of 40).

Purine riboswitches were diversely distributed in 18 genomes and regulate alternative pathways. The genes regulated by purine riboswitches are purC, guaB, permease related such as xanthine /uracil permease, purine permease, aminohydrolase family permease, acetyl transferases, synthases, deaminases, and reductases which play role in cysteine and methionine metabolism pathways. Due to the presence of alternate pathways they are less suitable as drug target.

In this study, we identified the distribution pattern of riboswitches in the archaeal and bacterial genomes of human gut microbiome. The study revealed 545 candidate riboswitches belong to 23 different types of riboswitches present in 63 microorganisms residing in the human gut and also the adjacent genes being regulated by the ribowstiches were identified and annotated. It was observed that the presence of riboswitches in a particular genome is independent of its genome size. It is found that high number of riboswitches present in the pathogenic bacteria. The GC% analysis showed that the GC% of the riboswitches is higher than their genomes GC%. We also identified c-di-GMP I, c-di-GMP II, glmS, SAM, THF, YdaO/YuaA leader, and glycine riboswitches as potent drug target in pathogenic bacteria of the adult human gut microbiome. This study can be extended in future by analyzing the expression level of these riboswitches in healthy and diseased human gut microbiome and also the finding of this work such as the distribution of riboswitches, the genes regulated by them and their functions can be archived into a database for future applications.