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Identification of small RNA pathway and human disease loci genes from eukaryotic genomes

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Different eukaryotes have developed extraordinary traits such as genetic resistance to cancer and hypoxia, increased life span, ability to hibernate, regeneration of lost tissue, and adaptation to sever environments. Comparing the genomes of these and other species can reveal the genetic - phenotype - environmental crosstalk and tackle fundamental bio-medical challenges. In the recent years we have been analyzing hundreds eukaryotes genomes, evaluating simultaneously the evolution of each protein across the tree of life. By mapping all human genes into about 1000 clusters of genes, with distinct patterns of conservation across eukaryotic phylogeny,we demonstrated that sets of genes associated with different cancers, metabolic diseases and hundreds of diseases phenotypes in addition to most gene networks have similar phylogenetic profile. Furthermore,by integrating the evolutionary map with comprehensive omic data we identified novel connection between the microphthalmia-associated transcription factor (MITF), a key factor in melanoma, and the Notch signaling pathway. Using this method to study miRNA and RNAi pathways, we identified sets of 88 proteins that show similar phylogenetic profiles with known small RNA cofactors and are essential to the RNAi machinery function. Our analysis thus establishes connectivity between different diseases and pathways, linking diseases phenotypes and functional gene groups.

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Easy as pie: Solution for controlling diabetes mellitus: *In-silico* targeted inhibition of secreted frizzled-related protein 4

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Diabetes mellitus is the second most dangerous non-communicable disease after cancer. Scientists around the globe try to hunt a cost effective and permanent treatment of this deadly malady. The recent trend is to control the disease by targeting the enzymes/proteins with inhibitors. Secreted frizzled-related protein 4 (SFRP4) is found to arouse five folds more risk of diabetes in patients when its expression is up-regulated. This study was designed to find out potential inhibitors of SFRP4. SFRP4 was analyzed by bioinformatics tools (sequence tool, structure tool and docking tools). The assessment of SFRP4 was done by PROCHECK, ERRAT, Ramachandran and VERIFY-3D to add confidence in its analysis. Three inhibitors namely cyclothiazide, clopamide and perindopril were found to have strong affinity for catalytic site residues (Pro120, Gln60, Tyr61, and Tyr81) of SFRP4 which results in down regulation of SFRP4 expression. These inhibitors showed significant interactions with SFRP4 as compared to other inhibitors as well as with control (acetohexamide) that have binding affinity with Gln60, Tyr61, Tyr81 residues. The findings suggest the possible hope for the treatment of diabetes mellitus type 2 by inhibiting the SFRP4.

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