BIOINFORMATICS AND COMPUTATIONAL BIOSCIENCES

Our research area is Bioinformatics, which is the application of computational approaches to understand how biological systems function. Bioinformatics addresses key problems in biomolecular, biomedical and chemical sciences, using computational approaches. Our group focusses on comparative genome sequence analysis, computational structural biology and biodiversity analysis.

ALTERNATIVE SPLICING AND HUMAN DISEASES

Alternative pre-mRNA splicing is an important mechanism for controlling gene expression in higher eukaryotes. A single gene produces several functionally diverse proteins by alternative usage of exons or introns within pre-mRNA transcripts. These gene products can be specific to tissue, developmental stage, and disease state. We have pioneered the use of graph theory for genome-wide analysis of alternative splicing in the fruitfly, chicken compared to mouse and human (1) and more recently, the cow.

The major alternative splicing events involved in human diseases are shown below, in the splicing graph formalism:

1. exon skipping (cassette exon) and 2. intron retention.

Why are some exons skipped and some introns ignored? A detailed genome-wide analysis of the information content of the regions surrounding the splice sites for all “normal” exons and “disease-related” alternatively spliced exons could provide the answer.

SECRETOME DATABASE OF HELMINTH PARASITES

Excretory-secretory (ES) proteins are an important class of proteins in many organisms, spanning from bacteria to human beings, and are potential drug targets for several diseases. ES proteins constitute the secretome of any organism and are particularly relevant for parasitic organisms. Helminth parasites are responsible for a range of neglected tropical diseases, such as ancylostomatosis, necatoriasis, lymphatic filariasis, onchocerciasis, ascariasis and strongyloidiasis in humans and others can cause massive production or economic losses to farmers as well as to animal and plant industries.

Recent transcriptomic and proteomic analysis (2) has shown that parasites adopt non-classical pathways to generate ES products. To identify novel genes for parasite intervention, the secretome of helminth parasites needs to be compiled. This project is aimed at developing a searchable helminth parasite secretome database with experimentally identified ES proteins.
MAPPING DISEASE GENE MUTATIONS TO PROTEIN STRUCTURE FOR GENOME-PHENOME CORRELATIONS

Mapping disease mutations to the structure of the protein can help in understanding the functional consequences of these mutations and thus indirectly, the finer aspects of the pathology and clinical manifestations of the disease, including phenotypic severity as a function of the genotype. Recently, we studied mutations in the gene (MAN2B1), encoding lysosomal α-D-mannosidase, causing improper coding and resulting in dysfunctional or non-functional protein and resulting in the disease α-mannosidosis.

We would like to extend this approach to other human diseases, using data from OMIM, OMIA and PDB databases, to predict regions prone to disease-causing mutations, known as mutational hotspots.

CORRELATING AUSTRALIAN ABORIGINAL PLANT HABITATS WITH THE STRUCTURE AND PROPERTIES OF THEIR BIOACTIVE COMPOUNDS

Australia covers a diverse range of habitats, from alpine heaths to tropical rainforests, and is recognised as a megadiverse country. Due to the great age and consequent low levels of fertility of the continent and its extremely variable weather patterns and long-term geographic isolation, much of Australia’s biota is unique and diverse. It is known that the beneficial medicinal effects of plant materials typically result from the combinations of bioactives present in the plant. We have integrated Australian Aboriginal customary medicinal plant knowledge into a database, CMKb (4). The database stores information related to taxonomy, phytochemistry, biogeography, biological activities of customary medicinal plant species as well as images of individual species.

This project aims to organise Australian aboriginal medicinal plants based on their habitats and then correlate the location attributes to the bioactives identified.

Selected Publications

2. E. Chacko, S. Ranganathan “Comprehensive splicing graph analysis of alternative splicing patterns in chicken, compared to human and mouse” BMC Genomics, 2009, 10, Suppl 1, S5.