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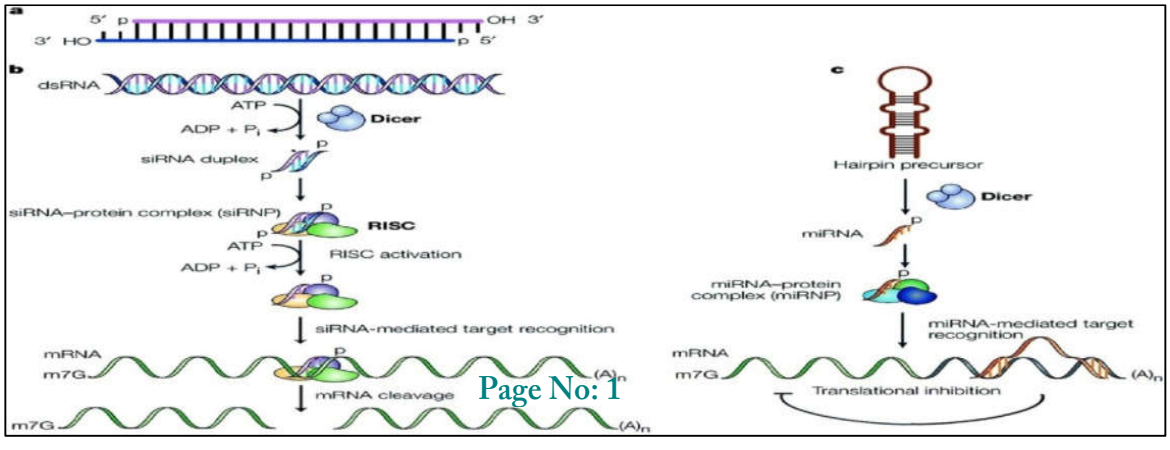
Simulation for SNP study of Human FTO gene

Deepak Kapoor and Gurmeet Singh

University Institute of Biotechnology (UIBT), Chandigarh University, Mohali, India.

RNA interference (RNAi) may be a phenomenon utilized by cells to show off or silence unwanted or harmful genes. The initial discovery of the development was in 1991, by scientists making an attempt to deepen the color of petunias, astonishingly by the introducing a factor for color, they found that they'd turned off the factor. Many years once the flower experiments, the mechanism of RNA interference was revealed: it's triggered by ethical code RNA not usely in healthy cells, however required to show factor of, if the cell vulnerable or broken by incursive viruses. In natural RNA interference, double stranded RNA (dsRNA) within the cell's living substance is cut by associate degree accelerator referred to as mechanical device into ethical code small interfering RNA (siRNA) molecules that are 20-25 nucleotides long. This siRNA binds 2 ends RNA Induced silencing complex (RISC) that separated the 2 strands into the sense and antisense strand. The sense strand is degraded whereas the reduced instruction set computer takes the antisense strand to a particular mRNA site, cleaving it in order that unwanted target protein molecule can't be created.

Much excitement encompassing siRNA mediated therapeutics arises from the very fact that this approach overcomes several of the shortcomings antecedently knowledgeable about with approaches like antibodies, antisense oligonucleotides and pharmacologic inhibitors. Administration of siRNA molecule has effectively been achieved for the treatment of cancer, infectious disease and infective agent infections (Ichim et al, 2004).



a) Structure of siRNA; (b) siRNA pathway; (c) miRNA pathway (Dykxhoorn *et al*, 2003).

In the most common choronic disease including diabetes, cardiovascular disease (CVD) and cancer; the major risk factors are obesity & overweight (Haslam and James, 2005). Once they were thought of a tangle of developed countries, however now-a-days, overweight and obesity are currently significantly increasing within the developing countries. Over the past few years, many genes are known from genome wide association studies (GWAS) with common variants related to variations in avoirdupois. Over fifty genes play a major role in obesity formation. Fat mass and obesity associated (FTO) factor encodes iron (II) and 2-OG dependent dioxygenase, conjointly called fat mass and obesity associated (FTO) protein molecule. A deficiency of FTO gene results in postnatal growth retardation and conjointly inform to some of the basic role. Gene FTO is located in 16th Chromosome and is having 9 exons having the length of over 400 Kb nucleotide sequence. The expression of FTO gene is found to be in fetal and adult tissue of human, mice with highest expression found within the brain (Vaisse et al, 1998 and Frayling et al, 2003). From the Genome-wide association studies (GWAS) the most important candidate gene responsible for the obesity is found to be FTO gene. In 2005, study carried out by Veugelers and Fitzgerald shown that the development of childhood obesity and overweight is majorly developed due to unhealthy food intake and socio-demographic characteristics. Over consumption of fried/fatty food, chocolates, junk food could resul in prime cause of type 2 diabetes (T2D) and cardiovascular disease (CVD) (Veugelers and Fitzgerald, 2005).

The survey carried out by National Family Health Survey (NFHS), revealed the significant increase in the value of weight and obesity in married women of 15-49 years of age from 11% in 1998-99 (NFHS-2) to 15% in 2005-06 (NFHS-3). As per the survey (NFHS-3) among the south Indian women, the highest percentage of obesity and overweight were found in Kerala (34%) . the percentage values for Tamilnadu, Andhra Pradesh and Karnataka are 24.4 %, 22.7% and 17.3% respectively and is related to breast cancer, high blood pressure and diabetes. Among the school going children of 10-16 years of age of Bhuvaneswar area of India, the occurrence of obesity & overweight was seen to be as high as of 27.8% (16.4% Overweight and 11.4% obesity) (Patnaik et al, 2015).

Various online biological programs are available that can be used to predict neutral or harmful SNPs. Two such bioinformatics algorithms used in study were PolyPhen-2 and PANTHER.

***(i)* Extraction of data sets**

The SNP data for FTO gene was taken from NCBI dbSNP available at the web link http://www.ncbi.nlm.nih.gov/snp/.

(ii) Simulation for functional change in coding nsSNP by PolyPhen

the tool PolyPhen developed and offered by Harvard School of Medicine and is available at web link http://genetics.bwh.harvard.edu/pph predicts the attainable impact of substitution of amino acids on the structure and function of human proteins. This prediction is based on information of phylogenetic, structural and sequence annotationswhich may characterize the mutation and its position within the protein molecule. It works by putting the sequence of the protein or its accession number along with sequence position with amino acid variant (Ramensky, 2002). The program searches for 3-D structure of protein and does the multiple alignments of homologues sequence in different protein databases. Then position specific Independent count (PSIC) score is calculated for the two varients. The score is directly proportional to the functional impact of the substitutions occurrence means if the PSIC score is high that means the functional impact of the amino acid substitution is going to happen. The PolyPhen score may be classified as in all probability of damaging (>2.00), possibly damaging (1.50-1.99), potentially damaging (1.25-1.49), and benign (0.00-0.99).

(iii) Simulation for functional change in coding nsSNP by PANTHER

PANTHER, a database of protein families and subfamilies, is freely available web server found at http://www.pantherdb.org/ and is maintained by Thomas Lab at the University of Southern California. It predicts the frequency of occurrence of particular amino acid at particular position among different species in a evolutionary related protein family (Mi et al, 2007). PANTHER uses Hidden Markov Model (HMM) and Multiple sequence alignment and perform the phylogenetic analysis if coding non-synonymous SNP.

(iv) STRING

Search tool for the retrieval of interacting genes/Proteins) STRING is a tool which is available freely on http://string-db.org/ and is a database having interactions of known and Predicted Protein molecules. The interactions embody direct (physical) and indirect (functional) associations. There are around 5.2 millions of proteins from 1133 organisms that STRING holds. It covers presently on top of five.2 millions proteins from 1133 organisms (Franceschini et al, 2013).

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