NuGen: Database of rare and common genetic variations of genes related to nutrition

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CERTIFICATE

This is to certify that **Ms. NEHA KUMARI**, **(2K16/BIO/02)** M. Tech. student in the Department of Biotechnology Engineering, has submitted dissertation entitled **"NuGen: Database of rare and common genetic variations of genes related to nutrition"** in partial fulfilment of the requirement for the reward of the degree of Master of Technology in Bioinformatics Engineering, during the academic year 2016-18. It is an authentic record of the candidate's own work carried out by him/her under my guidance. The information and data enclosed in this thesis is original and has not been submitted elsewhere for honouring of any other degree.

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DECLARATION OF ORIGINALITY

I, NEHA KUMARI (2K16/BIO/02) declare that this M.Tech dissertation entitled **"NuGen: Database of rare and common genetic variations of genes related to nutrition"** submitted in partial fulfilment of the requirement for the award of the degree of Master of Technology, Delhi Technological University is an authentic record of my own work carried out under the guidance of Dr. Yasha Hasija. I undertake that this report neither infringes upon anyone's copyright nor violates any proprietary rights to the best of my knowledge. Any ideas, techniques, quotations, or any other material form of work of other people included in this report, published or otherwise, are fully acknowledged in accordance with the standard referring practices.

I declare that this is the true copy of my report, including all revisions, as approved by my advisor and supervisor, and that this report has not been submitted for any other degree to any other University or Institution.

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ABSTRACT

On

"NuGen: Database of rare and common genetic variations of genes related to nutrition"

by

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Food is one of the basic requirement for human being. However, it does not mean that whatever human intake is good for it individually. Every human being have different genetic makeup, hence it react differently with different nutrients and this reaction may or may not increase the risk of a disease. The relationship between the human genome and nutritional factors has led to the development of new field called nutrigenomics. In addition, this work is the extension to the field. For the diagnoses and better treatment decisions of various disease, it is necessary to gather information about it. As the data about the diseases caused by various food factors and genes related to nutritional diseases is scattered across a large number of electronic publications, several specialized databases and other repositories. Moreover, nutrigenomics is a new field hence the data is quite difficult to find.

Thus, my objective was to create an efficient, effective and accurate system to enable the extraction of the detailed information related to polymorphism, phenotype, function and relationship between various population and allele frequencies of genes causing nutritional disorder by contributing resources from various databases. It helps to maintain the research and biomedical community by providing a comprehensive repository of information related to genes causing diseases found through text mining.

KEYWORDS: - Nutrigenomics, Nutritional diseases, Database, Allele frequency, Polymorphism

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NEHA KUMARI

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ABBREVATIONS

HTML	Hypertext Markup Language
CSS	Cascading Style Sheets
ACB	African Caribbean's in Barbados
ASW	American of African Ancestry in SW USA
BEB	Bengali from Bangladesh
CDX	Chines Dai in Xishuangbanna, China
CEU	Utah Residents (CEPH) with North and Western European Ancestry
CHB	Han Chinese in Beijing, China
CHS	Sothern Han Chinese
CLM	Colombians from Medellin, Colombia
ESN	Esan in Nigeria
FIN	Finnish in Finland
GBR	British in England and Scotland
GIH	Gujarati Indian from Houston, Texas
GWD	Gambian in Western Division in the Gambia
IBS	Iberian Population in Spain
ITU	Indian Telugu from the UK
JPT	Japanese in Tokyo
KHV	Kinh in Ho Chi Minh City, Vietnam
LWK	Luhya in Webuye, Kenya
MSL	Mende in Sierra Leone

MXL	Mexican Ancestry from Los Angeles , USA
PEL	Peruvians from Lima, Peru
PJL	Punjabi from Lahore, Pakistan
PUR	Puerto Ricans from Puerto Rico
STU	Sri Lankan Tamil from the UK
TSI	Toscani in Italia
YRI	Yoruba in Ibadan, Nigeria

CHAPTER 1

INTRODUCTION

CHAPTER 1

INTRODUCTION

Nutrition is the intake of food required by organisms in order to maintain growth, reproduction, health of an organism. It is also known as the science of consuming and utilizing food for a healthy organism. Unfortunately, once in our lifetime, nearly everyone (infant, children, and adults) has some type of nutritional diseases such as anaemia, obesity, diabetes and osteoporosis. One of the main reason for chronic diseases that affect our community is Nutrition. Some nutrition related disease are minor and others can be life threatening. Assessing nutrient pattern rather than intake of individual nutrient gives better understanding into connections amongst nutrition and diseases.

Nutrigenomics provide us the data about how genes and nutrient associate with each other. It also focuses on the impacts of their interaction on our health and gene activity for e.g. like according to the DNA what proteins do they produce. It inspect certain range of nutrition, uses molecular tools to understand and examine the various reactions acquired by systematic method applied on individuals and different population sets [1]. So generally it covers the impact of dietary components, the proteome (the sum total of all proteins), and the metabolome (the sum of all metabolites) of the genome.

Nutrigenomics mostly focus on mutations, DNA sequence variations that includes 90% of all the human genetic variation. SNPs, which help in the maintenance of the cell also, disturb the function of "housekeeping genes" assumed to change the possibility of causing a disease. Dietary factors also change the effect of certain SNPs to increase or decrease the level of the disease risk. As example gene activity or gene structure of the human genome can be, alter by common dietary chemicals. Genes that are regulate by diets likely are involved in the starting and progression of chronic diseases.

As the data about the nutrigenomics, the genes ,there allele frequency, functions , mutations is scattered across a large number of electronic publications, several specialized databases

and other repositories, because of which searching for these information manually is very hectic and difficult task. Thus, the objective of my study was to create an efficient, effective and accurate system to enable the extraction of the detailed information. Like genes affected by nutrition, mutations because of which the gene is altered and cause disease due it, their allele frequencies in different population all over the world and interaction of genes, by contributing resources from various databases.

The purpose of NuGen Database is to provide a freely accessible interactive database of the information on nutrigenomics (genes, RS ID, mutation, function, allele frequency) and genes responsible for both nutritional and skin diseases. My database hopes to facilitate to help in understanding, and analysis of the relationships between specific populations and the frequency of the gene responsible for a specific nutritional disease in that population. Further evaluation of the data can give some interesting facts related to different populations eating habit sometimes end in causing a disease.

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CHAPTER 2

REVIEW OF LITERATURE

CHAPTER 2

REVIEW OF LITERATURE

2.1 Nutrigenomics

Nutrigenomics is one of the developing sciences that looks into the area of nutrition and study genes related to it by using molecular tools [1]. It focus on understanding the molecular mechanism of gene -diet interaction and tries to prevent nutrient related diseases. Some experiments report that many genetic variations can alter protein structural function. Nutrigenomics is one part of the nutritional genomic era, which investigate the interaction between components of the diet and the genome. It also study changes in proteins occurring due to regulation and other metabolism. The second field is the Nutrigenetics that analyse the response happening because of dietary components with regard to genetic differences [2].

There are many studies based on humans, which have denoted the proof of interaction between metabolic response to a diet and SNPs in several genes. However, analysis of the SNPs gives a molecular tool, which is potential for investigating the importance of nutrition in human health, causing diseases and identification of optimal diets for better health[3]. Epidemiological studies show that there is a deep association between the chronic diseases severity and the intake of food [4][5]. Many of the nutrition related diseases (metabolic syndromes, type 2 diabetes, obesity, and some types of cancers) are polygenic and multifactorial. In addition, the onset and progression of these diseases is dependent on their variant, multiple genes and especially the diet[6]. Now there are certain benefits from nutrigenomics, which gives us more clear sight of nutrigenomics involvement in human healthcare.

1. By the help of nutrigenomics individuals can get a clearer understanding on how their body works on the foods they consume. After analysing information on one specific individual persons genes and their variants, diet, lifestyle and environment. A nutritional plan or chart made specifically for that individual which will eventually

improve body's health and will give information on what type of diseases is that individual most vulnerable to.

2.2 Nutritional Diseases

Nutrition is one of the most important and utmost need of the body, it gives strength and power to do anything to body. However, once in their lifetime, nearly everybody have one or other type of nutritional disease ranging from the age of infants, children, teenagers, adults and the elderly. Lack of nutrition may cause deficiency, anaemia, and many more but a certain type of nutrition can cause serious disease in an individual based on his genetic makeup. Just as some bodies react differently than the normal to certain foods. The range for the diseases varies broadly based on the type of symptoms and severity; it can be classify by, as by duration i.e. temporary or permanent duration, painless/painful or causes can be situational/genetic.

2.3 Nutritional Diseases and their associated Gene

As the data about the Nutrigenomics is scattered across a large number of electronic publications, several specialized databases, and other repositories, thus, by contributing various online as well as offline resources from various databases the list of the nutritional disorder was extracted and comprehensive repository found through text mining.

2.3.1 1000 Genome Browser

The aim of the **1000 Genomes Project (http://www.internationalgenome.org/1000-genomes-browsers/)** is to provide a resource, which can leads to understanding of the genetic contribution to disease. The database gives information about different population having individuals, which carry different profiles of rare and common variants and that substantial geographic differentiation can be shown by low frequency variants. In addition, the action of purifying selection can increase the geographical differentiation. The aim of

the project was to identify over 95% of SNPs at 1% frequency in a wide range of different populations[7] .

2.3.2 HumSavar

The URL for **HumSavar** is ***http://www.uniprot.org/support/docs/humsavar.html,*** in which the variations of the sequences are noted for human proteins and are recorded in humsavar.txt, which grants the sequence amino acid substitution and its position, it also mentions the variation type into two categories either polymorphism or disease mutation [8]. It provide information related to Gene, Entrez ID, dbSNP, Swiss-Prot-AC, AA-change, KEGG Link and dbSNP Link to the database.

2.4 Common Phrases

There are twelve different types of attributes used in this database, which can be explained as following:-

1. Minor allele
2. Major allele
3. Mutation
4. Function
5. Phenotype
6. RS ID
7. Population Origin
8. ODD Ratio
9. P-value
10. Allele Frequency
11. Gene Id
12. PubMed Id

An Allele is a variant form of a given gene [9]. **Allelomorph** is the full name of the word allele[10]. There are two types of allele: - Major and Minor allele. Minor allele frequency is

the frequency at which the allele occurs at second most common frequency in a given population [10].

Mutation is the permanent change in gene sequences, which may or may not results in the alteration of structure and function of specific genes. Mutation usually occurs in two different types: - Transitions and Transversions. Transitions mutation states that Purine nucleotide can replace to Pyrimidine nucleotide (Adenine and Guanine) (Cytosine and Thymine) [11]. Transversions mutation refers to substitution of purine ring for pyrimidine ring or vice versa [12].

Phenotypes are the characteristics that are shown by the offspring from the previous generation. These phenotypes can be colour of the eyes, shape of the nose, or any function of the gene performed by the cells [13].

RS ID is a specific accession code given to represent a specific SNP. It is represented by the symbol “rs”. This accession code is unique in itself and degenerate.

ODD Ratio (OR) is a measure of association between an exposure and an outcome. OR is a statistical operation used to quantify how strongly the presence or absence of property A is associated with the presence or absence of property B in a given population [14][15].
If the OR is greater than 1, then having "A" is considered to be "associated" with having "B" in the sense that the having of "B" raises (relative to not-having "B") the odds of having "A". Note that this does not establish that B is a contributing cause of "A": it could be that the association is due to a third property, "C", which is a contributing cause of both "A" and "B" (confounding). The odds ratio compares the occurrence of the outcome in the presence of a particular exposure, with the occurrence of the outcome in the absence of a particular exposure.

p-Value also known as probability value, it’s the probability for a given statistical model that, when the null hypothesis is true, the statistical summary would be the same as or of greater magnitude than the actual observed results. In other, it is used in context of null hypothesis testing in order to quantify the idea of statistical significance of evidence [16].

Diseases having p value less than 0.05 are considered fatal, of high risk and diseases having more than 0.05 value are not considered for evaluation and not stated as fatal.

Gene ID is a unique identifier that is assigned to a gene recorded in entrez. It is an integer and is species specific. It is same as the Locus ID.

PubMed ID (PubMed identifier) is a unique integer value starting at one, which is assigned to each and every record of the PubMed database. A PMID is different from PMCID, which is an identifier for all the works publish in the free to access PubMed Central[17].

CHAPTER 3

MATERIAL AND METHODS

CHAPTER 3

MATERIALS AND METHODS

The NuGen (database for genes associated with nutritional disorders): is a computational framework for the analysis of genes associated with nutrition disorders would be a database. The data for various genes associated to Nutrition Related Disease, extracted across a large number of published literature, several specialized databases and other repositories that gives an insight data regarding nutrigenomics.

The NuGen database will contain around 38 column namely Gene name, Major and Minor allele, Mutation, Phenotype, PubMed ID, Molecular Function, RS ID, Population, Origin, ODD Ratio, P-value and allele frequency of 26 population around the world. The 26 population are ACB, CLM, ASW, BEB, CDX, CHB, CEU, FIN, GBR, GIH, GWD, PJL, PUR, STU IBS, ITU, JPT, KHV, LWK, MSL, MXL, PEL, TSI, CHS, YRI, and ESN.

The web service implemented used the HTML, CSS, JavaScript, MySQL and PHP format. In addition, the graphical user interface (GUI) shown using a local host, developed by AMPPS. AMPPS used in developing PHP, MySQL applications. The web service will be having the functionality for searching various aspects like allele frequency, p value, and ODD ratio search by Gene name, RS ID, and PubMed ID. Clicking on PubMed ID will open the page of respective research paper.

METHODOLOGY

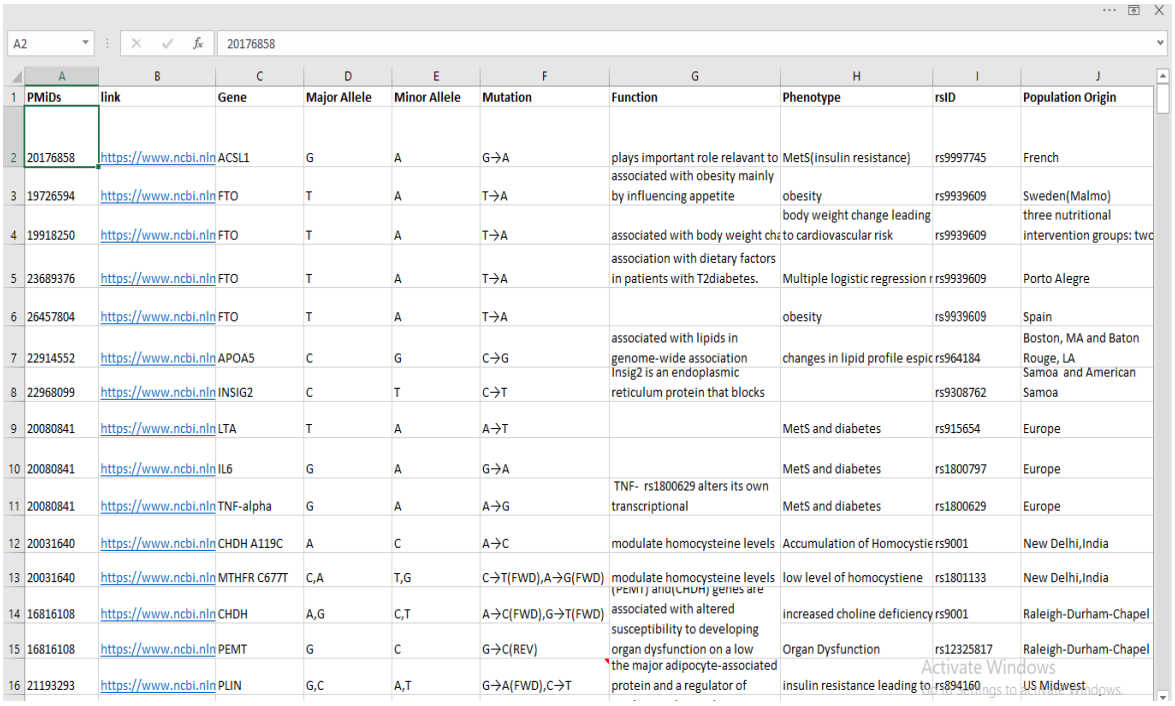
3.1. Data Collection and Data Curation for NuGen database creation

There are mainly five types of data included in the database: (i) Diseased Gene (ii) Population Genetics data (Allele Frequency) (iii) Mutation data, (iv) Gene/Disease Ontology (Gene Phenotype, Molecular Function) and (v) Statistical data (p-value, ODD Ratio). In order to study the diseases causing gene, the gene-disease data integrated from annotated bibliography containing many review papers available on PubMed.

The SNiP (Single Nucleotide Polymorphism) and mutations data are mainly from **HumSavar**, which provide information related to Gene Name, dbSNP, AA-change. The population genetics data is mainly from **1000 Genome Browser,** which comprises of allele frequencies of respective RS ID's in 26 population around the world.

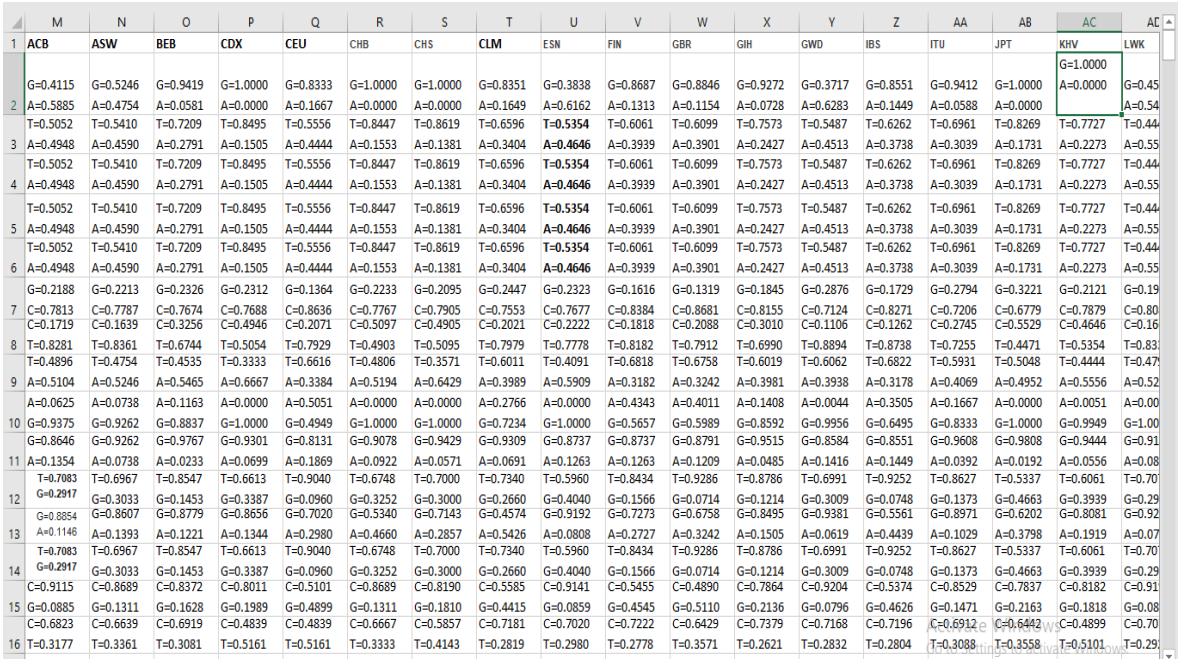
3.2 Data Integrity (Uniqueness)

As the data from various resources are heterogeneous, first, we need to create a uniform format to describe the broad data and then integration of the data is done by mapping the corresponding data with respect to the gene related to Nutritional Diseases. Hence the excel sheet formed after the entire step shown below:-



	A	B	C	D	E	F	G	H	I	J
1	PMIDs	link	Gene	Major Allele	Minor Allele	Mutation	Function	Phenotype	rsID	Population Origin
2	20176858	https://www.ncbi.nln	ACSL1	G	A	G→A	plays important role relavant to	MetS(insulin resistance)	rs9997745	French
3	19726594	https://www.ncbi.nln	FTO	T	A	T→A	associated with obesity mainly by influencing appetite	obesity	rs9939609	Sweden(Malmo)
4	19918250	https://www.ncbi.nln	FTO	T	A	T→A	associated with body weight cha	body weight change leading to cardiovascular risk	rs9939609	three nutritional intervention groups: two
5	23689376	https://www.ncbi.nln	FTO	T	A	T→A	association with dietary factors in patients with T2diabetes.	Multiple logistic regression r	rs9939609	Porto Alegre
6	26457804	https://www.ncbi.nln	FTO	T	A	T→A		obesity	rs9939609	Spain
7	22914552	https://www.ncbi.nln	APOA5	C	G	C→G	associated with lipids in genome-wide association	changes in lipid profile espic	rs964184	Boston, MA and Baton Rouge, LA
8	22968099	https://www.ncbi.nln	INSIG2	C	T	C→T	Insig2 is an endoplasmic reticulum protein that blocks		rs9308762	Samoa and American Samoa
9	20080841	https://www.ncbi.nln	LTA	T	A	A→T		MetS and diabetes	rs915654	Europe
10	20080841	https://www.ncbi.nln	IL6	G	A	G→A		MetS and diabetes	rs1800797	Europe
11	20080841	https://www.ncbi.nln	TNF-alpha	G	A	A→G	TNF- rs1800629 alters its own transcriptional	MetS and diabetes	rs1800629	Europe
12	20031640	https://www.ncbi.nln	CHDH A119C	A	C	A→C	modulate homocysteine levels	Accumulation of Homocystie	rs9001	New Delhi,India
13	20031640	https://www.ncbi.nln	MTHFR C677T	C,A	T,G	C→T(FWD),A→G(FWD)	modulate homocysteine levels	low level of homocystiene	rs1801133	New Delhi,India
14	16816108	https://www.ncbi.nln	CHDH	A,G	C,T	A→C(FWD),G→T(FWD)	(PEMT) and(CHDH) genes are associated with altered	increased choline deficiency	rs9001	Raleigh-Durham-Chapel
15	16816108	https://www.ncbi.nln	PEMT	G	C	G→C(REV)	susceptibility to developing organ dysfunction on a low	Organ Dysfunction	rs12325817	Raleigh-Durham-Chapel
16	21193293	https://www.ncbi.nln	PLIN	G,C	A,T	G→A(FWD),C→T	the major adipocyte-associated protein and a regulator of	insulin resistance leading to	rs894160	US Midwest

Figure 1 – Excel sheet showing distribution of information in different section



	M	N	O	P	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD
1	ACB	ASW	BEB	CDX	CEU	CHB	CHS	CLM	ESN	FIN	GBR	GIH	GWD	IBS	ITU	JPT	KHV	LWK
	G=0.4115	G=0.5246	G=0.9419	G=1.0000	G=0.8333	G=1.0000	G=1.0000	G=0.8351	G=0.3838	G=0.8687	G=0.8846	G=0.9272	G=0.3717	G=0.8551	G=0.9412	G=1.0000	G=1.0000 A=0.0000	G=0.45
2	A=0.5885	A=0.4754	A=0.0581	A=0.0000	A=0.1667	A=0.0000	A=0.0000	A=0.1649	A=0.6162	A=0.1313	A=0.1154	A=0.0728	A=0.6283	A=0.1449	A=0.0588	A=0.0000		A=0.54
	T=0.5052	T=0.5410	T=0.7209	T=0.8495	T=0.5556	T=0.8447	T=0.8619	T=0.6596	**T=0.5354**	T=0.6061	T=0.6099	T=0.7573	T=0.5487	T=0.6262	T=0.6961	T=0.8269	T=0.7727	T=0.44
3	A=0.4948	A=0.4590	A=0.2791	A=0.1505	A=0.4444	A=0.1553	A=0.1381	A=0.3404	**A=0.4646**	A=0.3939	A=0.3901	A=0.2427	A=0.4513	A=0.3738	A=0.3039	A=0.1731	A=0.2273	A=0.55
	T=0.5052	T=0.5410	T=0.7209	T=0.8495	T=0.5556	T=0.8447	T=0.8619	T=0.6596	**T=0.5354**	T=0.6061	T=0.6099	T=0.7573	T=0.5487	T=0.6262	T=0.6961	T=0.8269	T=0.7727	T=0.44
4	A=0.4948	A=0.4590	A=0.2791	A=0.1505	A=0.4444	A=0.1553	A=0.1381	A=0.3404	**A=0.4646**	A=0.3939	A=0.3901	A=0.2427	A=0.4513	A=0.3738	A=0.3039	A=0.1731	A=0.2273	A=0.55
	T=0.5052	T=0.5410	T=0.7209	T=0.8495	T=0.5556	T=0.8447	T=0.8619	T=0.6596	**T=0.5354**	T=0.6061	T=0.6099	T=0.7573	T=0.5487	T=0.6262	T=0.6961	T=0.8269	T=0.7727	T=0.44
5	A=0.4948	A=0.4590	A=0.2791	A=0.1505	A=0.4444	A=0.1553	A=0.1381	A=0.3404	**A=0.4646**	A=0.3939	A=0.3901	A=0.2427	A=0.4513	A=0.3738	A=0.3039	A=0.1731	A=0.2273	A=0.55
	T=0.5052	T=0.5410	T=0.7209	T=0.8495	T=0.5556	T=0.8447	T=0.8619	T=0.6596	**T=0.5354**	T=0.6061	T=0.6099	T=0.7573	T=0.5487	T=0.6262	T=0.6961	T=0.8269	T=0.7727	T=0.44
6	A=0.4948	A=0.4590	A=0.2791	A=0.1505	A=0.4444	A=0.1553	A=0.1381	A=0.3404	**A=0.4646**	A=0.3939	A=0.3901	A=0.2427	A=0.4513	A=0.3738	A=0.3039	A=0.1731	A=0.2273	A=0.55
	G=0.2188	G=0.2213	G=0.2326	G=0.2312	G=0.1364	G=0.2233	G=0.2095	G=0.2447	G=0.2323	G=0.1616	G=0.1319	G=0.1845	G=0.2876	G=0.1729	G=0.2794	G=0.3221	G=0.2121	G=0.19
7	C=0.7813	C=0.7787	C=0.7674	C=0.7688	C=0.8636	C=0.7767	C=0.7905	C=0.7553	C=0.7677	C=0.8384	C=0.8681	C=0.8155	C=0.7124	C=0.8271	C=0.7206	C=0.6779	C=0.7879	C=0.80
	C=0.1719	C=0.1639	C=0.3256	C=0.4946	C=0.2071	C=0.5097	C=0.4905	C=0.2021	C=0.2222	C=0.1818	C=0.2088	C=0.3010	C=0.1106	C=0.1262	C=0.2745	C=0.5529	C=0.4646	C=0.16
8	T=0.8281	T=0.8361	T=0.6744	T=0.5054	T=0.7929	T=0.4903	T=0.5095	T=0.7979	T=0.7778	T=0.8182	T=0.7912	T=0.6990	T=0.8894	T=0.8738	T=0.7255	T=0.4471	T=0.5354	T=0.83
	T=0.4896	T=0.4754	T=0.4535	T=0.3333	T=0.6616	T=0.4806	T=0.3571	T=0.6011	T=0.4091	T=0.6818	T=0.6758	T=0.6019	T=0.6062	T=0.6822	T=0.5931	T=0.5048	T=0.4444	T=0.47
9	A=0.5104	A=0.5246	A=0.5465	A=0.6667	A=0.3384	A=0.5194	A=0.6429	A=0.3989	A=0.5909	A=0.3182	A=0.3242	A=0.3981	A=0.3938	A=0.3178	A=0.4069	A=0.4952	A=0.5556	A=0.52
	A=0.0625	A=0.0738	A=0.1163	A=0.0000	A=0.5051	A=0.0000	A=0.0000	A=0.2766	A=0.0000	A=0.4343	A=0.4011	A=0.1408	A=0.0044	A=0.3505	A=0.1667	A=0.0000	A=0.0051	A=0.00
10	G=0.9375	G=0.9262	G=0.8837	G=1.0000	G=0.4949	G=1.0000	G=1.0000	G=0.7234	G=1.0000	G=0.5657	G=0.5989	G=0.8592	G=0.9956	G=0.6495	G=0.8333	G=1.0000	G=0.9949	G=1.00
	G=0.8646	G=0.9262	G=0.9767	G=0.9301	G=0.8131	G=0.9078	G=0.9429	G=0.9309	G=0.8737	G=0.8737	G=0.8791	G=0.9515	G=0.8584	G=0.8551	G=0.9608	G=0.9808	G=0.9444	G=0.91
11	A=0.1354	A=0.0738	A=0.0233	A=0.0699	A=0.1869	A=0.0922	A=0.0571	A=0.0691	A=0.1263	A=0.1263	A=0.1209	A=0.0485	A=0.1416	A=0.1449	A=0.0392	A=0.0192	A=0.0556	A=0.08
12	T=0.7083 G=0.2917	T=0.6967 G=0.3033	T=0.8547 G=0.1453	T=0.6613 G=0.3387	T=0.9040 G=0.0960	T=0.6748 G=0.3252	T=0.7000 G=0.3000	T=0.7340 G=0.2660	T=0.5960 G=0.4040	T=0.8434 G=0.1566	T=0.9286 G=0.0714	T=0.8786 G=0.1214	T=0.6991 G=0.3009	T=0.9252 G=0.0748	T=0.8627 G=0.1373	T=0.5337 G=0.4663	T=0.6061 G=0.3939	T=0.70 G=0.29
13	G=0.8854 A=0.1146	G=0.8607 A=0.1393	G=0.8779 A=0.1221	G=0.8656 A=0.1344	G=0.7020 A=0.2980	G=0.5340 A=0.4660	G=0.7143 A=0.2857	G=0.4574 A=0.5426	G=0.9192 A=0.0808	G=0.7273 A=0.2727	G=0.6758 A=0.3242	G=0.8495 A=0.1505	G=0.9381 A=0.0619	G=0.5561 A=0.4439	G=0.8971 A=0.1029	G=0.6202 A=0.3798	G=0.8081 A=0.1919	G=0.92 A=0.07
14	T=0.7083 G=0.2917	T=0.6967 G=0.3033	T=0.8547 G=0.1453	T=0.6613 G=0.3387	T=0.9040 G=0.0960	T=0.6748 G=0.3252	T=0.7000 G=0.3000	T=0.7340 G=0.2660	T=0.5960 G=0.4040	T=0.8434 G=0.1566	T=0.9286 G=0.0714	T=0.8786 G=0.1214	T=0.6991 G=0.3009	T=0.9252 G=0.0748	T=0.8627 G=0.1373	T=0.5337 G=0.4663	T=0.6061 G=0.3939	T=0.70 G=0.29
15	C=0.9115 G=0.0885	C=0.8689 G=0.1311	C=0.8372 G=0.1628	C=0.8011 G=0.1989	C=0.5101 G=0.4899	C=0.8689 G=0.1311	C=0.8190 G=0.1810	C=0.5585 G=0.4415	C=0.9141 G=0.0859	C=0.5455 G=0.4545	C=0.4890 G=0.5110	C=0.7864 G=0.2136	C=0.9204 G=0.0796	C=0.5374 G=0.4626	C=0.8529 G=0.1471	C=0.7837 G=0.2163	C=0.8182 G=0.1818	C=0.91 G=0.08
16	C=0.6823 T=0.3177	C=0.6639 T=0.3361	C=0.6919 T=0.3081	C=0.4839 T=0.5161	C=0.4839 T=0.5161	C=0.6667 T=0.3333	C=0.5857 T=0.4143	C=0.7181 T=0.2819	C=0.7020 T=0.2980	C=0.7222 T=0.2778	C=0.6429 T=0.3571	C=0.7379 T=0.2621	C=0.7168 T=0.2832	C=0.7196 T=0.2804	C=0.6912 T=0.3088	C=0.6442 T=0.3558	C=0.4899 T=0.5101	C=0.70 T=0.29

Figure 2 – Other portion of excel sheet containing allele frequencies of different populations around the world.

3.3 Graphical User Interface for Database

The construction of the user interface done by using the PHP format, JavaScript, CSS, MySQL and HTML. In total seven (.php) pages are made, namely index.php, Search.php, Contact.php, Network.php, SerachResult.php, GeneSearch.php, and PmIDSearch.php. Index.php page contains the welcome page-containing introduction to NuGen Database. GeneSearch.php takes command to search by the gene name similarly SearchResult.php and PmIDSearch.php asks for RS ID and PMID to show results respectively.

The user interface constructed have seven pages, which work like: **GeneSearch.php** page contains a dropdown for selecting single gene name, after which RS ID's related to that gene pops up containing other additional information. A gene may have many RS ID so it is possible to get multiple answers for one gene query. **SearchResult.php** page contains search box for various rs ID. Unlikely to GeneSearch.php it show information related to the specific query rs ID. PmIDSearch.php contains the dropdown for selecting single PM ID of research paper on nutrigenomics, whose information is included in this database. The code used for the whole database is as follows:-

CHAPTER 4

RESULTS

NuGen Database catalogues information about genes, RS ID, allele frequency, function, phenotype and mutation associated with nutritional related diseases. It Query in the database is entered individually with the gene name, RS ID and PubMed id. NuGen currently has information on more than 500 genes associated with different type of nutritional disorder. The result page mainly contains three different sections; the first section is regarding the **RS ID** that provides details regarding Gene Name, Disease Name, major allele, minor allele, p-value, ODD Ratio, PubMed ID, allele frequency, and type of mutation responsible for disease. The next section is **GENE search** that gives information similar to RS ID, and the gene name column highlighted in a different colour. The third section is **PubMed search** that also show the same page of result as the other and clicking on any PubMed Id in the PubMed Id column, leads to the site of research paper or source of paper.

4.1 ANALYSIS OF THE DATA

After the data collection for the database, simple analysis were done on the data to find out which RS ID have the smallest p-value. It seemed that **RS ID rs780094** had the smallest **p-value 0.000063** leading to being the most lethal and responsible reason for causing the diseases. The RS ID rs780094 belong to gene **GCKR** that exert an additive effect on plasma fasting and postprandial triacylglycerol concentration. Although the allele frequency of the RS ID is of the population of Puerto Rican, European, Greek, Valencia region of Spain, Singapore only. The mutation occurring in the gene, which causes it to become lethal, is C/T (REV). GCKR is actually the symbol for glucokinase regulatory protein [18]. The other top 10 genes having lowest p-value are shown below in the table:

Out of the top 10 genes responsible for nutritional diseases, one gene is responsible for Skin Related Diseases also i.e. – **STAT 3** (Signal transducer and activator of transcription 3). It causes psoriasis having disease id as MESH: D011565.

GENE ID	RS ID	P-VALUE
GCKR	rs780094	0.000063
FADS	rs5082, rs174575	0.0001
LRP1	rs4759277	0.0003
CDKN2B-AS1	rs2383206	0.0004
STAT3	rs8069645	0.0005
AGER	rs184003	0.0006
TCF7L2, ABCG4	rs290481, rs3802885	0.0007
IRS1	rs7578326, rs2943641	0.0008
AGT M253T, PEMT	rs699, rs7946	0.001

Table 1:- Top 10 Genes having lowest p-value with their RS ID.

4.2 **GRAPHICAL USER INTERFACE**

NuGe gives us a user-friendly interface to query broad information on each gene associated to nutritional diseases. Users can query the database for either retrieving Population genetics data, Mutation data, Statistical data (p- value, ODD Ratio), General Gene Information data or for Gene Ontology data through either by Genes name or RS ID or PubMed Id. In total seven (.php) pages namely index.Php, search.Php, contact.Php, network.Php, searchpage.php, genesearch.php, and Pmidsearch.php was constructed. The screenshots of the graphical user interface of every page are shown below-

Figure 3 – index.php page contains the Welcome page-containing introduction to NuGen Database and Data source

Figure 4 - A user can search by either RS ID, Gene name, or PubMed Id.

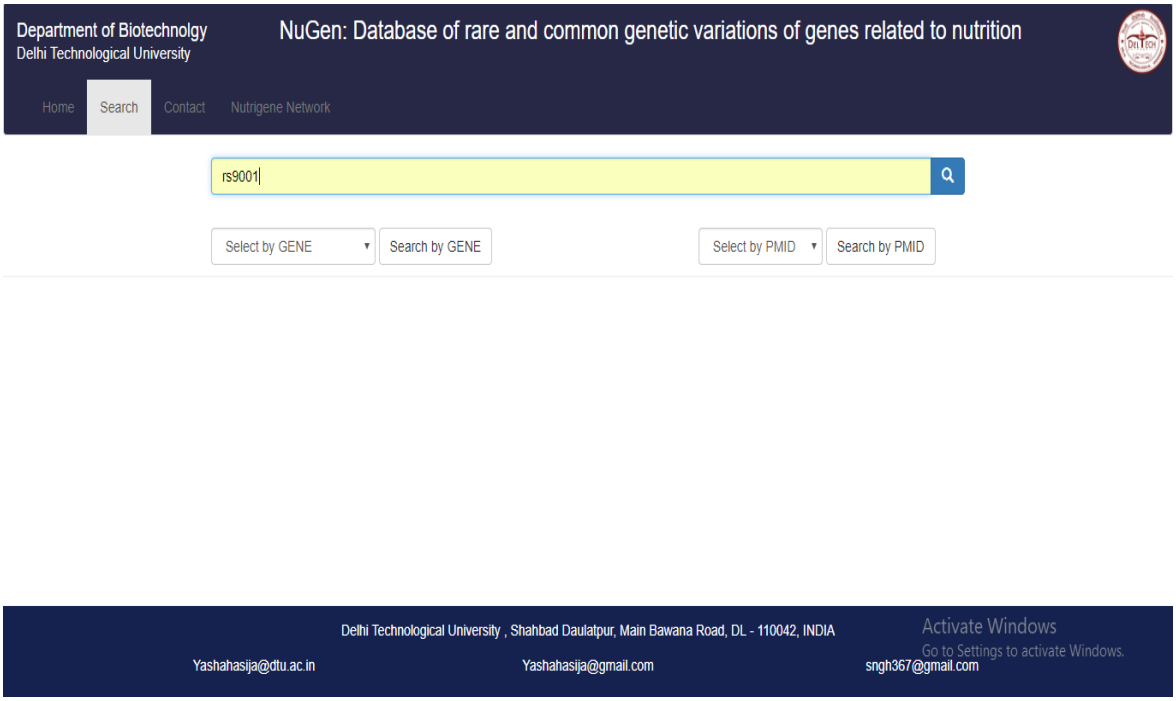


Figure 5 – Search.php showing different boxes for different search attributes. The highlighted one is for RS ID.

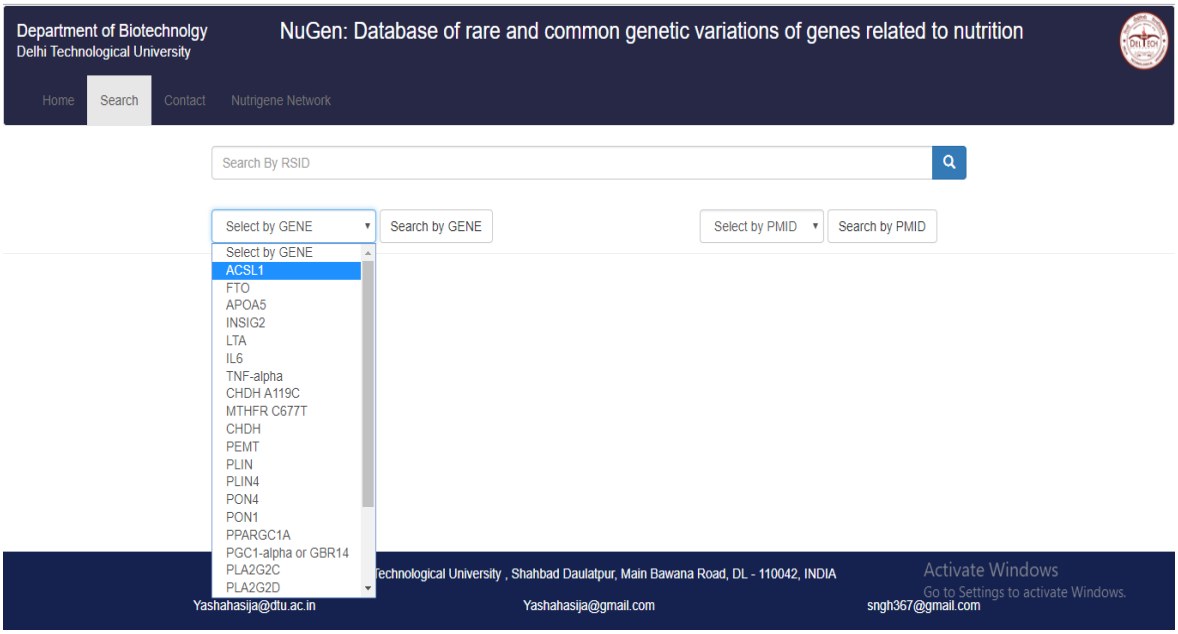


Figure 6- Search. Php page for giving query by selecting gene name.

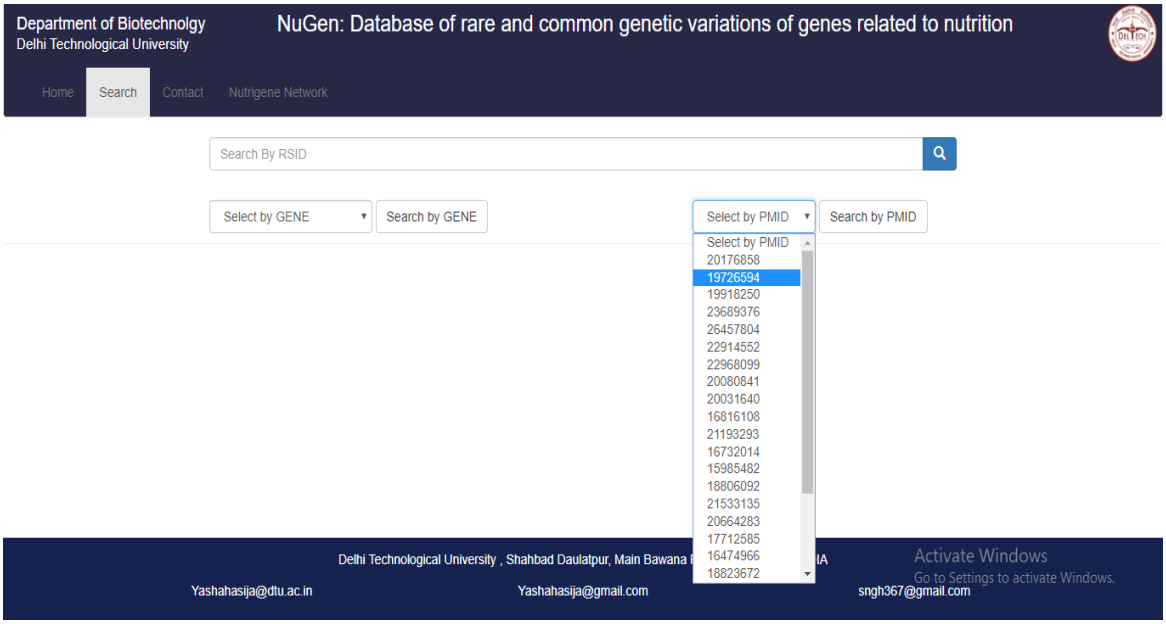


Figure 7 - Search. Php page for giving query by selecting PubMed Id.

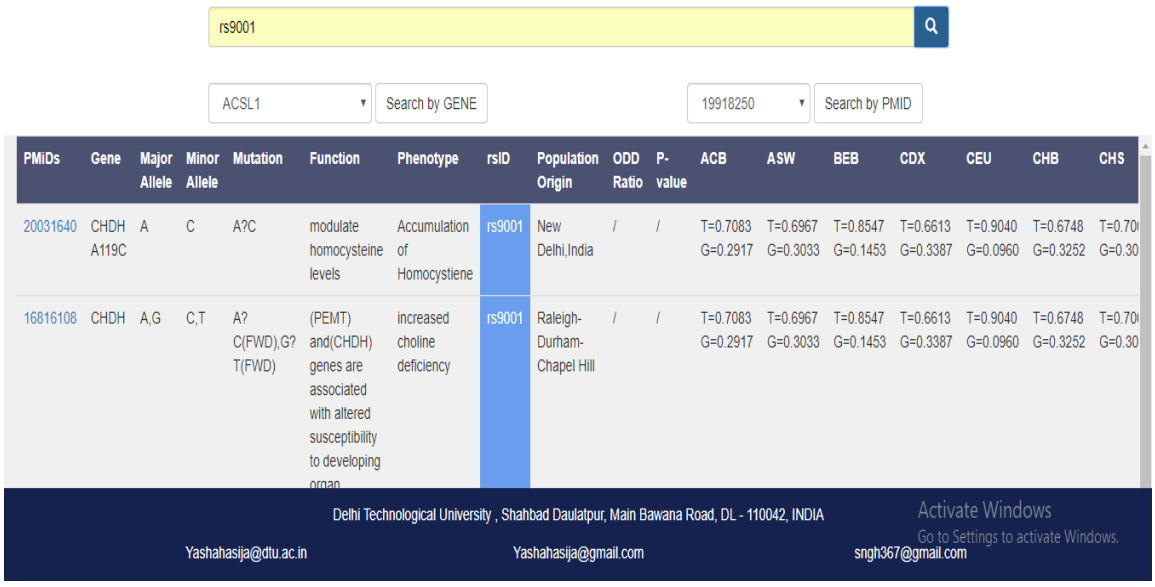


Figure 8 – Searchresult.php page showing results for query of RS Id.

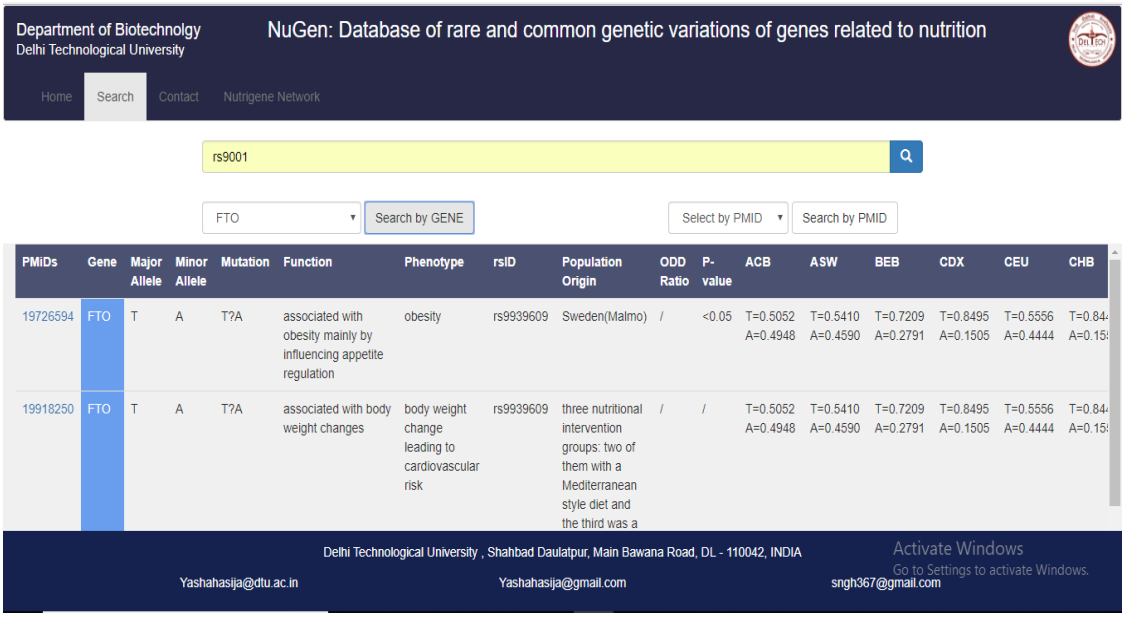


Figure 9 - Searchresult. Php page for showing result of query by selecting gene name.

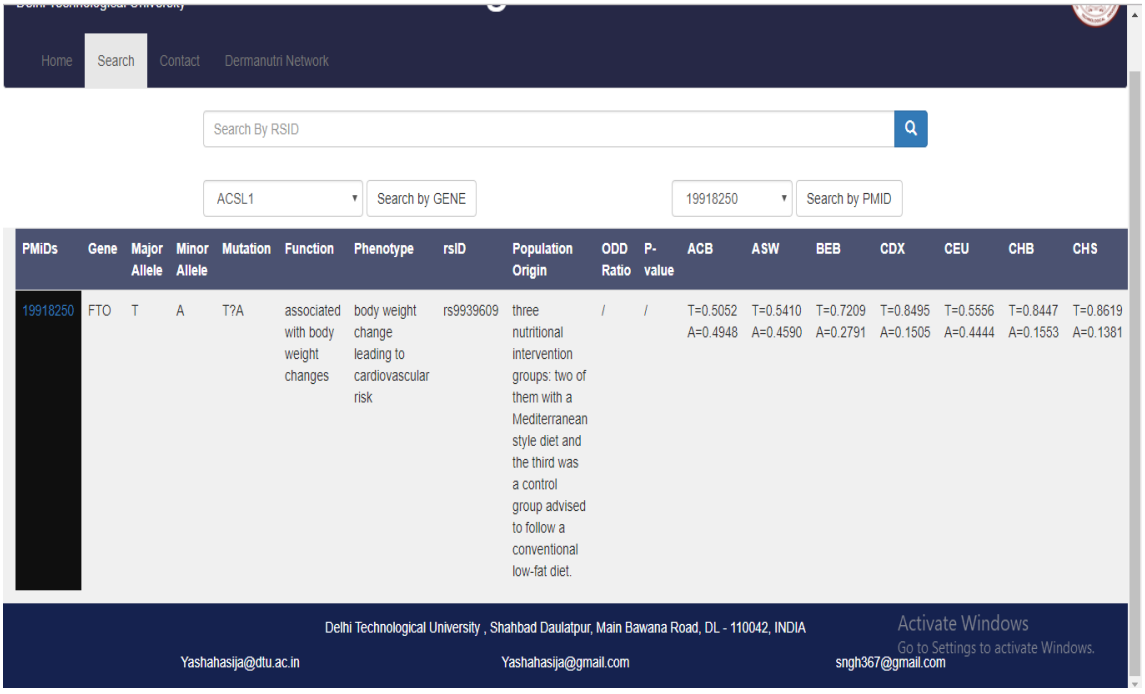


Figure 10 - Result page for search by PubMed ID

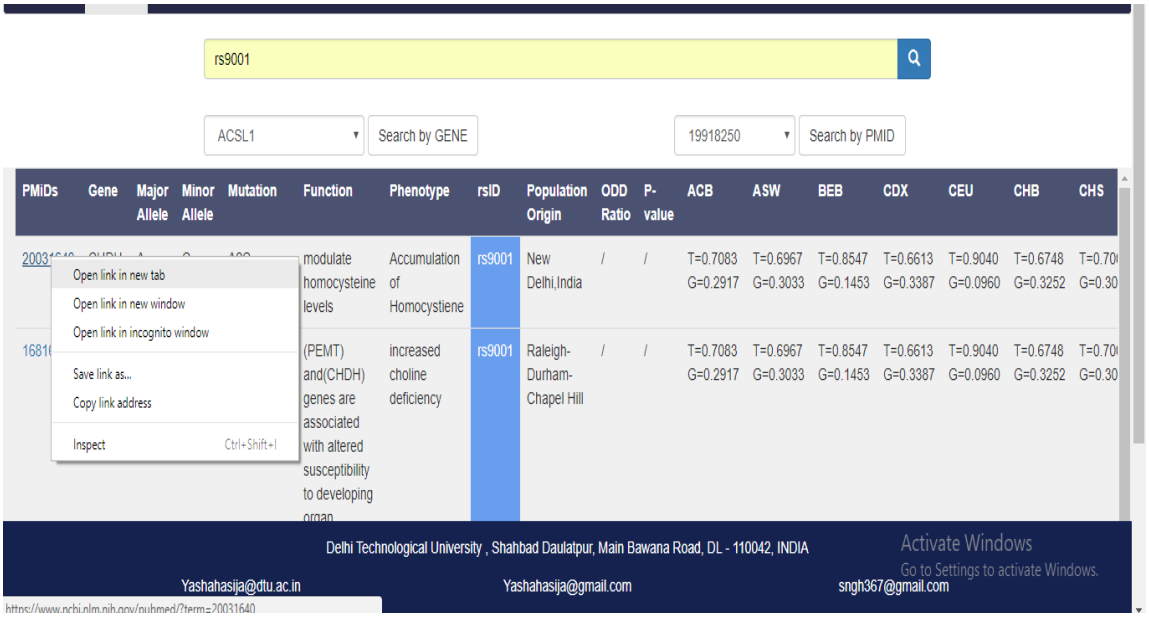


Figure 11– Clicking on specific PMID open that specific research paper in the other tab.

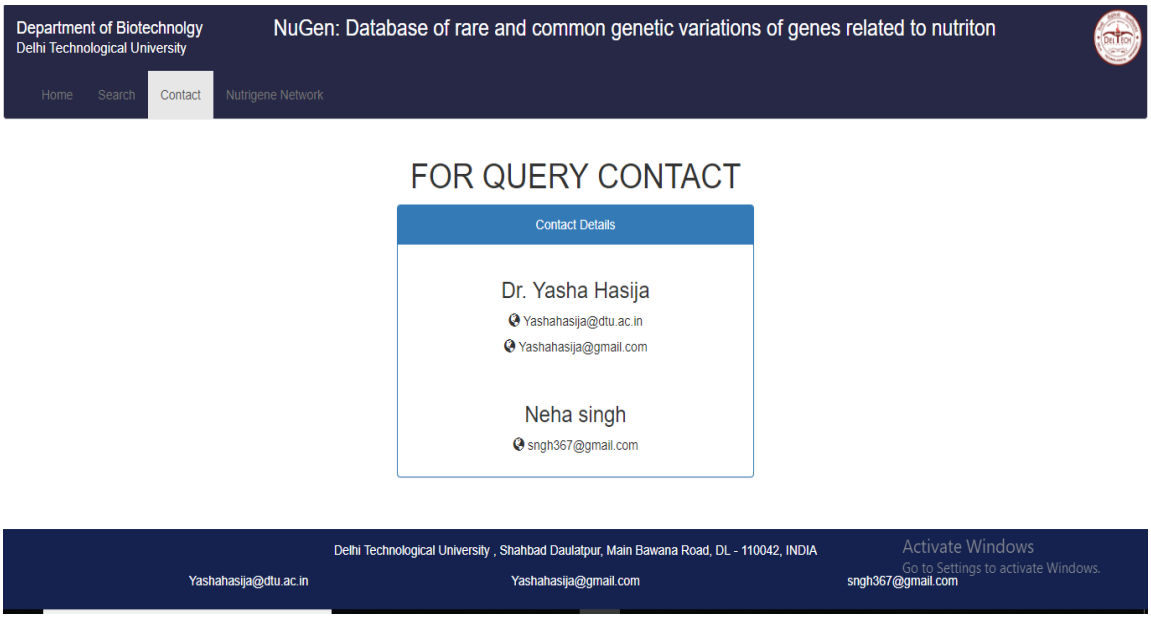


Figure 12 – contact.php page showing email address to contact to admin.

4.3 Validation of the data

For the efficacy of the NuGen to be up to the mark, we took experimentally validated nutritional diseases associated with NuGen by reviewing previous literature. To accomplish the purpose of testing the association of NuGen with the nutritional diseases we used several online available tools like NCBI, NutriGene Databse, KEGG and thoroughly checked the query for published literature by providing RS ID's and PubMed Id's. We found various nutritional disease like Obesity, Lower HDL-C, MetS, Type 2 Diabetes, Insulin resistance, Crohn's disease etc. that were caused due to mutation in protein's amino acid sequence

Crohn's Diseases have an inflamed intestinal tract. A meta-analysis of the Disease implicated 32 susceptibility loci but only accounted for 20% of the genetic contribution to disease risk, suggesting that more loci await discovery[19]. Two additional loci, encompassing CARD9 and IL18RAP, had previously been reported as associated with Crohn's disease in a candidate gene study[20]. Another five loci were identified at genome-wide significance in GWAS: the FUT2 locus, was found in a recent adult Crohn's disease GWAS6 and other four (in ZMIZ1 at 10q22, in IL27 at 16p11, 19q13 and 22q12) were identified in a paediatric IBD population[21].

Type 2 diabetes is characterised by hyperglycaemia that can occur through mechanisms such as impaired insulin secretion, insulin resistance in peripheral tissues and increased glucose output by the liver[22].There is evidence of genetic components to the risk of type 2 diabetes[23]. To date, genes implicated in type 2 diabetes have conferred modest risk[24].There are reports on linkage of type 2 diabetes to chromosome 5q in the Icelandic population[25] There is also evidence of linkage in 10q and 12q. The 10q linkage region has also been observed in Mexican Americans[26]. All the Above cases are properly described in our database and show result of this.

DISCUSSION AND CONCLUSION

Our aim is to provide a well-organised, easy to use web interface that allow users to understand the interaction between genetic variations, allele frequency and the function of the gene responsible for the disease. Based on many studies on nutrients it was observed that they effect on the gene expression and alter the transcription, translation, and metabolic profile of the individual thereby leading to diseases. Hence, to study the effects and causes of nutritional diseases the database created. The current database consists of more than 500 genes that are associated with nutritional diseases. These nutritional related genes leads to various diseases such as Obesity, T2 Diabetes, Organ dysfunction, High Cholesterol, breast cancer and many others. NuGen is a first of its type, user-interactive repository of the information on mutation, allele frequency, function and genes associated with nutritional diseases that was developed. This database enables the user to retrieve intricate information of genes linked with nutritional diseases at genome-widespread level. Data mining of the NuGen for biologically meaningful data is likely to reveal the indefinite facts of the underlying reasons of nutritional diseases. As we understand the importance of the integrative analysis of data, we hereby will collect new data from new sources regularly to enhance or to increase the analytical depths and importance of the database.

Our database will always extend by including more and more data sets available and will introduce tools that will use in the development of the identification of nutritional disease-related new RS ID for specified genes using other updated tools. The primary data in the NuGen represents association of genes and their RS ID with different population frequencies related to Nutritional Disorders. All the known and complex genetic disorders that are believe to be prevalent in nutrition were used for the purpose of this work. The deep information on genes was obtain from the articles published in high-quality journals and various online medical forums discussing nutritional and associated diseases. The data from the existing databases assessed carefully and corrected with reference to the original articles.

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ANNEXURE I

Home page Code ;- starting from the first page (Welcome page) the code in python goes as

```
<!DOCTYPE html>

<html lang="en">

  <head>

    <meta charset="utf-8">

    <meta http-equiv="X-UA-Compatible" content="IE=edge">

    <meta name="viewport" content="width=device-width, initial-scale=1">
<title></title>
    <link

rel="stylesheet"

href="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/css/bootstrap.min.css">

    <link rel="stylesheet" href="https://maxcdn.bootstrapcdn.com/font-
awesome/4.4.0/css/fontawesome.min.css">
    <link rel="stylesheet" href="./user.css">

    <!--[if lt IE 9]>

      <script src="https://oss.maxcdn.com/libs/html5shiv/3.7.2/html5shiv.js"></script>

      <script src="https://oss.maxcdn.com/libs/respond.js/1.4.2/respond.min.js"></script>

    <![endif]-->

  </head>

  <body>

    <nav class="navbar navbar-default" style="background-color:#262846">

  <div class="container-fluid">

    <!-- Brand and toggle get grouped for better mobile display -->

    <div class="navbar-header" style="width: 100%;">

      <button

type="button"

class="navbar-toggle

collapsed"
```

```
data-toggle="collapse"

datatarget="#bs-example-navbar-collapse-1" aria-expanded="false">
      <span class="sr-only">Toggle navigation</span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

    </button>

    <div id="headerNav" class="navbar-brand" href="#" style="width: 20%;margin-bottom:

15px;">Department of Biotechnolgy

      <small>Delhi Technological University</small>

    </div>

    <a id="headerNav" class="navbar-brand" href="#" style="margin-left:3%;font-size:

23%px;">Nugen: Database for rare and common genetic variants of genes related to nutrition </a>

    <img class="navbar-right" src="dtu-logo.png" style="max-width:75px;padding: 5px;">
</div>


   <!-- Collect the nav links, forms, and other content for toggling -->

   <div class="collapse navbar-collapse" id="bs-example-navbar-collapse-1">

     <ul class="nav navbar-nav">

       <li

class="active"><a

href="./index.php">Home

<span

class="sronly">(current)</span></a></li>
      <li><a href="./search.php">Search</a></li>

      <li><a href="./contact.php">Contact</a></li>

      <li><a href="./network.php">Nutrigene Network</a></li>

    </ul>
```

```
    </div><!-- /.navbar-collapse -->
  </div><!-- /.container-fluid -->
</nav>
<div class="container-fluid backImg">
  <div class="row">
    <div class="col-lg-6">
      <div class="panel panel-primary">
        <div class="panel-heading">
          <h3 class="panel-title text-center"> database</h3>
        </div>
        <div class="panel-body">
          <p>NuGen database comprises of the various gene and other information's of nutritional genes. you can search with respective rs id's, Pm ID's and gene name. The result will include major minor mutation, phenotype, function, p- value, ODD ratio and allele frequency of the respective rs id of a gene in 26 population around the world, derived from 1000 genome project.  </p>        </div>
      </div>
    </div>
    <div class="col-lg-6">
      <div id="carousel-generic" class="carousel slide" data-ride="carousel">
        <!-- Indicators -->
        <ol class="carousel-indicators">
          <li data-target="#carousel-generic" data-slide-to="0" class="active"></li>
          <li data-target="#carousel-generic" data-slide-to="1"></li>
          <li data-target="#carousel-generic" data-slide-to="2"></li>        </ol>
        <!-- Wrapper for slides -->
        <div class="carousel-inner">
          <div class="item active">
            <img class="col-lg-12" src="image1.jpg" alt="">
            <div class="carousel-caption">
            </div>
          </div>
```

```
<div class="item">
  <img class="col-lg-12" src="image2.jpg" alt="">
  <div class="carousel-caption">
  </div>
</div>
<div class="item">
  <img class="col-lg-12" src="image3.jpg" alt="">
  <div class="carousel-caption">
  </div>
</div>
<div class="item">
  <img class="col-lg-12" src="image4.png" alt="">
  <div class="carousel-caption">
  </div>
</div>
<div class="item">
  <img class="col-lg-12" src="image5.jpg" alt="">
  <div class="carousel-caption">
  </div>
</div>
<div class="item">
  <img class="col-lg-12" src="image6.jpg" alt="">
  <div class="carousel-caption">
  </div>
</div>
<div class="item">
  <img class="col-lg-12" src="image7.jpg" alt="">
  <div class="carousel-caption">
  </div>
```

```
        </div>
        <div class="item">
          <img class="col-lg-12" src="image8.jpg" alt="">
          <div class="carousel-caption">
          </div>
        </div>
        <div class="item">
          <img class="col-lg-12" src="image9.jpg" alt="">
          <div class="carousel-caption">
          </div>
        </div>
      </div>
      <!-- Controls -->
      <a class="left carousel-control" href="#carousel-generic" data-slide="prev">
        <span class="glyphicon glyphicon-chevron-left"></span>
      </a>
      <a class="right carousel-control" href="#carousel-generic" data-slide="next">
        <span class="glyphicon glyphicon-chevron-right"></span>
      </a>
    </div>
  </div>
 </div>
</div>
<div class="footer-bottom">
        <div class="container">
                <div class="row">
                        <div class="col-xs-12 col-sm-6 col-md-6 col-lg-12 text-center">
                                <div class="copyright">
                                        Delhi Technological University , Shahbad Daulatpur,
```

```
Main Bawana Road, DL - 110042, INDIA
                                    </div>
                                </div>
                                <div class="col-lg-4 text-center" style="color:white;">
        <P>Yashahasija@dtu.ac.in</p>
                                    </div>
            <div class="col-lg-4 text-center" style="color:white;">
<P>Yashahasija@gmail.com</p>
                                    </div>
                                <div class="col-lg-4 text-center" style="color:white;">
        <P>sngh367@gmail.com</p>
                                    </div>
                                </div>
                        </div>
                    </div>
</div>
    <script src="https://ajax.googleapis.com/ajax/libs/jquery/1.11.3/jquery.min.js"></script>
    <script
src="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/js/bootstrap.min.js"></script>
  </body>
</html>
```

ANNEXURE II

Search page Code:- the code for query request is as follows:-

```
<!DOCTYPE html>
<html lang="en">
  <head>
    <meta charset="utf-8">
    <meta http-equiv="X-UA-Compatible" content="IE=edge">
    <meta name="viewport" content="width=device-width, initial-scale=1">
    <title></title>
    <link
rel="stylesheet"
href="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/css/bootstrap.min.css">
    <link rel="stylesheet" href="https://maxcdn.bootstrapcdn.com/font-awesome/4.4.0/css/fontawesome.min.css">
    <link rel="stylesheet" href="./user.css">
    <!--[if lt IE 9]>
      <script src="https://oss.maxcdn.com/libs/html5shiv/3.7.2/html5shiv.js"></script>
      <script src="https://oss.maxcdn.com/libs/respond.js/1.4.2/respond.min.js"></script>
    <![endif]-->
  </head>
  <body>
    <nav class="navbar navbar-default" style="background-color:#262846">
  <div class="container-fluid">
    <!-- Brand and toggle get grouped for better mobile display -->
    <div class="navbar-header" style="width: 100%;">
      <button
type="button"
class="navbar-toggle
collapsed"
```

```
data-toggle="collapse"

datatarget="#bs-example-navbar-collapse-1" aria-expanded="false">
      <span class="sr-only">Toggle navigation</span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

    </button>

    <div  id="headerNav"  class="navbar-brand" href="#" style="width: 20%;margin-bottom:

15px;">Department of Biotechnolgy

      <small>Delhi Technological University</small>

    </div>

    <a  id="headerNav"  class="navbar-brand" href="#" style="margin-left:3%;font-size:

23%px;">NuGen:  Databas for rare and common genetic variations of genes related to nutrition</a>

    <img  class="navbar-right"  src="dtu-logo.png"  style="max-width:75px;padding:  5px;">
</div>
  <!-- Collect the nav links, forms, and other content for toggling -->

  <div class="collapse navbar-collapse" id="bs-example-navbar-collapse-1">

    <ul class="nav navbar-nav">

      <li><a href="./index.php">Home <span class="sr-only">(current)</span></a></li>

      <li class="active"><a href="./search.php">Search</a></li>

      <li><a href="./contact.php">Contact</a></li>

      <li><a href="./network.php">Nutrigene Network</a></li>

    </ul>

  </div><!-- /.navbar-collapse -->

 </div><!-- /.container-fluid -->

</nav>

<div class="container-fluid">

<div class="row">

 <form id="myForm" action="./searchResult.php" method="post">
```

```
    <div class="col-lg-offset-2 col-lg-8 col-xs-6 col-md-4">
     <div class="input-group">
      <input name="searchKey" type="text" class="form-control" placeholder="Search By
RSID" id="txtSearch"/>
      <div class="input-group-btn">
       <button class="btn btn-primary" type="submit">
        <span class="glyphicon glyphicon-search"></span>
       </button>
      </div>
     </div>
    </div>
  </form>
  </div>
  <br/>
  <div class="row">
   <form id="myFormGene" class="form-inline" action="./GeneSearch.php" method="post">
    <div class=" form-group col-lg-4 col-lg-offset-2 ">
     <select class="form-control" name="GeneSelect">
      <option value="">Select by GENE</option>
      <option value="ACSL1">ACSL1</option>
      <option value="FTO">FTO</option>
      <option value="APOA5">APOA5</option>
      <option value="INSIG2">INSIG2</option>
      <option value="LTA">LTA</option>
      <option value="IL6">IL6</option>
      <option value="TNF-alpha">TNF-alpha</option>
      <option value="CHDH A119C">CHDH A119C</option>
      <option value="MTHFR C677T">MTHFR C677T</option>
      <option value="CHDH">CHDH</option>
```

```
        <option value="PEMT">PEMT</option>
        <option value="PLIN">PLIN</option>
        <option value="PLIN4">PLIN4</option>
        <option value="PON4">PON4</option>
        <option value="PON1">PON1</option>
        <option value="PPARGC1A">PPARGC1A</option>
        <option value="PGC1-alpha or GBR14">PGC1-alpha or GBR14</option>
        <option value="PLA2G2C">PLA2G2C</option>
        <option value="PLA2G2D">PLA2G2D</option>
        <option value="PLA2G2F">PLA2G2F</option>
        <option value="PLA2G4A">PLA2G4A</option>
        <option value="PLA2G6">PLA2G6</option>
        <option value="PLA2G7">PLA2G7</option>
        <option value="LEPR">LEPR</option>
        <option value="STAT3">STAT3</option>
      </select>
      <button class="btn btn-default btn-group-vertical" type="submit" name="button">Search
by GENE</button>
    </div>
  </form>
  <form id="myFormPmid" class="form-inline" action="./PmidSearch.php" method="post">
    <div class="form-group col-lg-4 col-lg-offset-1">
      <select class="form-control" name="PmidSelect">
        <option value = ""> Select by PMID </option>
        <option value = "20176858"> 20176858 </option>
        <option value = "19726594"> 19726594 </option>
        <option value = "19918250"> 19918250 </option>
        <option value = "23689376"> 23689376 </option>
        <option value = "26457804"> 26457804 </option>
        <option value = "22914552"> 22914552 </option>
        <option value = "22968099"> 22968099 </option>
```

```
        <option value = "20080841"> 20080841 </option>
        <option value = "20031640"> 20031640 </option>
        <option value = "16816108"> 16816108 </option>
        <option value = "21193293"> 21193293 </option>
        <option value = "16732014"> 16732014 </option>
        <option value = "15985482"> 15985482 </option>
        <option value = "18806092"> 18806092 </option>
        <option value = "21533135"> 21533135 </option>
        <option value = "20664283"> 20664283 </option>
        <option value = "17712585"> 17712585 </option>
        <option value = "16474966"> 16474966 </option>
        <option value = "18823672"> 18823672 </option>
        <option value = "25889305"> 25889305 </option>
        <option value = "16971225"> 16971225 </option>
        <option value = "19776189"> 19776189 </option>
        <option value = "23118204"> 23118204 </option>
        <option value = "19543202"> 19543202 </option>
        <option value = "17823441"> 17823441 </option>
      </select>
      <button class="btn btn-default btn-group-vertical" type=submit" name="button">Search by PMID</button>
    </div>
  </form>
 </div>
</div>
<div class="container-fluid" style="margin-bottom: 49px;">
 <div class="row">
  <div id="output1" class="col-lg-12 contentOver" style="max-height: 500px;backgroundcolor:#f0f0f0;">
  </div>
 </div>
```

```
</div>
<div class="footer-bottom">
        <div class="container">
                <div class="row">
                        <div class="col-xs-12 col-sm-6 col-md-6 col-lg-12 text-center">
                                <div class="copyright">
                                        Delhi Technological University , Shahbad Daulatpur,
Main Bawana Road, DL - 110042, INDIA
                                </div>
                        </div>
                        <div class="col-lg-4 text-center" style="color:white;">
      <P>Yashahasija@dtu.ac.in</p>
                                </div>
                        <div class="col-lg-4 text-center" style="color:white;">
      <P>Yashahasija@gmail.com</p>
                                </div>
                        <div class="col-lg-4 text-center" style="color:white;">
      <P>sngh367@gmail.com</p>
                                </div>
                        </div>
                </div>
          </div>
   <script src="https://ajax.googleapis.com/ajax/libs/jquery/1.11.3/jquery.min.js"></script>
   <script
src="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/js/bootstrap.min.js"></script>
   <script src="http://malsup.github.com/jquery.form.js"></script>
   <script src="./user.js"></script>
  </body>
</html>
```

ANNEXURE III

Contact page Code:- Page containing contact information for any personal query:-

```
<!DOCTYPE html>
<html lang="en">
  <head>
    <meta charset="utf-8">
    <meta http-equiv="X-UA-Compatible" content="IE=edge">
    <meta name="viewport" content="width=device-width, initial-scale=1">     <title></title>
    <link
rel="stylesheet"
href="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/css/bootstrap.min.css">
    <link rel="stylesheet" href="https://maxcdn.bootstrapcdn.com/font-awesome/4.4.0/css/fontawesome.min.css">
    <link rel="stylesheet" href="./user.css">
    <!--[if lt IE 9]>
      <script src="https://oss.maxcdn.com/libs/html5shiv/3.7.2/html5shiv.js"></script>
      <script src="https://oss.maxcdn.com/libs/respond.js/1.4.2/respond.min.js"></script>
    <![endif]-->
  </head>
  <body>
    <nav class="navbar navbar-default" style="background-color:#262846">
  <div class="container-fluid">
    <!-- Brand and toggle get grouped for better mobile display -->
    <div class="navbar-header" style="width: 100%;">
      <button
type="button"
class="navbar-toggle
collapsed"
```

```
data-toggle="collapse"

datatarget="#bs-example-navbar-collapse-1" aria-expanded="false">
      <span class="sr-only">Toggle navigation</span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

      <span class="icon-bar"></span>

    </button>

    <div  id="headerNav"  class="navbar-brand" href="#" style="width: 20%;margin-bottom:

15px;">Department of Biotechnolgy

      <small>Delhi Technological University</small>

    </div>

    <a  id="headerNav"  class="navbar-brand" href="#" style="margin-left:3%;font-size:

23px;">NuGen: Database for rare and common genetic variations of genes related to
nutrition</a>

    <img class="navbar-right" src="dtu-logo.png" style="max-width:75px;padding: 5px;">
</div>


   <!-- Collect the nav links, forms, and other content for toggling -->

   <div class="collapse navbar-collapse" id="bs-example-navbar-collapse-1">

     <ul class="nav navbar-nav">

       <li><a href="./index.php">Home <span class="sr-only">(current)</span></a></li>

       <li><a href="./search.php">Search</a></li>

       <li class="active"><a href="./contact.php">Contact</a></li>

       <li><a href="./network.php">Nutrigene Network</a></li>

     </ul>

   </div><!-- /.navbar-collapse -->

  </div><!-- /.container-fluid -->

</nav>

<div class="container-fluid">

  <div class="row">

    <div class="col-lg-12 text-center">
```

```
  <h1>FOR QUERY CONTACT</h1>
 </div>
 <div class="col-lg-4 col-lg-offset-4">
    <div class="panel panel-primary text-center">
  <div class="panel-heading">Contact Details</div>
  <div class="panel-body">
    <h3>Dr. Yasha Hasija</h3>
    <h5><span class="glyphicon glyphicon-globe"></span>  Yashahasija@dtu.ac.in</h5>
    <h5><span class="glyphicon glyphicon-globe"></span>  Yashahasija@gmail.com</h5>
    <br>
    <h3>Neha singh</h3>
    <h5><span class="glyphicon glyphicon-globe"></span>  sngh367@gmail.com</h5>
  </div>
 </div>
 </div>
  </div>
</div>
<div class="footer-bottom">
          <div class="container">
                  <div class="row">
                          <div class="col-xs-12 col-sm-6 col-md-6 col-lg-12 text-center">
                                  <div class="copyright">

Delhi Technological University , Shahbad Daulatpur, Main
Bawana Road, DL - 110042, INDIA
                                  </div>
                          </div>
                          <div class="col-lg-4 text-center" style="color:white;">
        <P>Yashahasija@dtu.ac.in</p>
                                  </div>
```

```
                    <div class="col-lg-4 text-center" style="color:white;">
        <P>Yashahasija@gmail.com</p>
                    </div>
                    <div class="col-lg-4 text-center" style="color:white;">
        <P>sngh367@gmail.com</p>
                    </div>
                </div>
            </div>
    <script src="https://ajax.googleapis.com/ajax/libs/jquery/1.11.3/jquery.min.js"></script>
    <script
src="https://maxcdn.bootstrapcdn.com/bootstrap/3.3.5/js/bootstrap.min.js"></script>
  </body>
</html>
```

ANNEXURE IV

Search Result Page Code:- This page takes query for rs id :-

```
<?php setlocale(LC_ALL, "en_US.UTF8"); $searchKey = $_POST['searchKey']; define('DB_SERVER', 'localhost'); define('DB_USERNAME', 'root'); define('DB_PASSWORD', 'mysql'); define('DB_DATABASE', 'nehaGenome');
$db = mysqli_connect(DB_SERVER,DB_USERNAME,DB_PASSWORD,DB_DATABASE);
if(mysqli_connect_errno())
{ echo "Failed to connect to MySQL: " . mysqli_connect_error(); exit(); // **this is missing**
}

$result = mysqli_query($db,"select * from lakshay_nutri_PMIDs Where rsID = '$searchKey'"); $row = "";
$tableHead =  "<table class=\"table col-lg-12\">

<tr class=\"TableRow\">

<th>PMiDs</th>

<th>Gene</th>

<th>Major Allele</th>

<th>Minor Allele</th>

<th>Mutation</th>

<th>Function</th>

<th>Phenotype</th>

<th>rsID</th>

<th>Population Origin</th>

<th>ODD Ratio</th>

<th>P-value</th>

<th>ACB</th>

<th>ASW</th>

<th>BEB</th>

<th>CDX</th>

<th>CEU</th>

<th>CHB</th>

<th>CHS</th>
```

```
<th>CLM</th>
<th>ESN</th>
<th>FIN</th>
<th>GBR</th>
<th>GIH</th>
<th>GWD</th>
<th>IBS</th>
<th>ITU</th>
<th>JPT</th>
<th>KHV</th>
<th>LWK</th>
<th>MSL</th>
<th>MXL</th>
<th>PEL</th>
<th>PJL</th>
<th>PUR</th>
<th>STU</th>
<th>TSI</th>
<th>YRI</th>
</tr>";
$tableFoot = "</table>";
while($row = mysqli_fetch_array($result))
{
$tableRowStart = "<tr>";
$col1 =  "<td><a href=\"".$row['link']."\" target=\"_blank\">".$row['PMiDs']."</a></td>";
$col2 =  "<td>".$row['Gene']."</td>";
$col3 =  "<td>".$row['Major Allele']."</td>";
$col4 =  "<td>".$row['Minor Allele']."</td>";
$col5 =  "<td>".$row['Mutation']."</td>";
```

```
$col6 =  "<td>".$row['Function']."</td>";
$col7 =  "<td>".$row['Phenotype']."</td>";
$col8 =  "<td class=\"colorBlue\">".$row['rsID']."</td>";
$col9 =  "<td>".$row['Population Origin']."</td>";
$col10 =  "<td>".$row['ODD Ratio']."</td>";
$col11 =  "<td>".$row['P-value']."</td>";
$col12 =  "<td>".$row['ACB']."</td>";
$col13 =  "<td>".$row['ASW']."</td>";
$col14 =  "<td>".$row['BEB']."</td>";
$col15 =  "<td>".$row['CDX']."</td>";
$col16 =  "<td>".$row['CEU']."</td>";
$col17 =  "<td>".$row['CHB']."</td>";
$col18 =  "<td>".$row['CHS']."</td>";
$col19 =  "<td>".$row['CLM']."</td>";
$col20 =  "<td>".$row['ESN']."</td>";
$col21 =  "<td>".$row['FIN']."</td>";
$col22 =  "<td>".$row['GBR']."</td>";
$col23 =  "<td>".$row['GIH']."</td>";
$col24 =  "<td>".$row['GWD']."</td>";
$col25 =  "<td>".$row['IBS']."</td>";
$col26 =  "<td>".$row['ITU']."</td>";
$col27 =  "<td>".$row['JPT']."</td>";
$col28 =  "<td>".$row['KHV']."</td>";
$col29 =  "<td>".$row['LWK']."</td>";
$col30 =  "<td>".$row['MSL']."</td>";
$col31 =  "<td>".$row['MXL']."</td>";
$col32 =  "<td>".$row['PEL']."</td>";
$col33 =  "<td>".$row['PJL']."</td>";
$col34 =  "<td>".$row['PUR']."</td>";
```

```
$col35 =  "<td>".$row['STU']."</td>";

$col36 =  "<td>".$row['TSI']."</td>";

$col37 =  "<td>".$row['YRI']."</td>";

$tableRowEnd = "</tr>";

$allRows
                                                    =

$allRows.$tableRowStart.$col1.$col2.$col3.$col4.$col5.$col6.$col7.$col8.$col9.$col10.$col
11.$
col12.$col13.$col14.$col15.$col16.$col17.$col18.$col19.$col20.$col21.$col22.$col23.$col2
4.$c
ol25.$col26.$col27.$col28.$col29.$col30.$col31.$col32.$col33.$col34.$col35.$col36.$col37
; }


$Finalresult = $tableHead.$allRows.$tableFoot; echo $Finalresult; ?>
```

ANNEXURE V

Gene Search Page Code:- This code is to build gene search query page.

```
<?php

setlocale(LC_ALL, "en_US.UTF8"); $searchKey = $_POST['GeneSelect']; define('DB_SERVER', 'localhost'); define('DB_USERNAME', 'root'); define('DB_PASSWORD', 'mysql'); define('DB_DATABASE', 'nehaGenome');
$db = mysqli_connect(DB_SERVER,DB_USERNAME,DB_PASSWORD,DB_DATABASE);
if(mysqli_connect_errno())

{ echo "Failed to connect to MySQL: " . mysqli_connect_error(); exit(); // **this is missing**
}

$result = mysqli_query($db,"select * from lakshay_nutri_PMIDs Where Gene = '$searchKey'"); $row = "";
$tableHead =  "<table class=\"table col-lg-12\">

<tr class=\"TableRow\">

<th>PMiDs</th>

<th>Gene</th>

<th>Major Allele</th>

<th>Minor Allele</th>

<th>Mutation</th>

<th>Function</th>

<th>Phenotype</th>

<th>rsID</th>

<th>Population Origin</th>

<th>ODD Ratio</th>

<th>P-value</th>

<th>ACB</th>

<th>ASW</th>

<th>BEB</th>

<th>CDX</th>

<th>CEU</th>

<th>CHB</th>
```

```
<th>CHS</th>
<th>CLM</th>
<th>ESN</th>
<th>FIN</th>
<th>GBR</th>
<th>GIH</th>
<th>GWD</th>
<th>IBS</th>
<th>ITU</th>
<th>JPT</th>
<th>KHV</th>
<th>LWK</th>
<th>MSL</th>
<th>MXL</th>
<th>PEL</th>
<th>PJL</th>
<th>PUR</th>
<th>STU</th>
<th>TSI</th>
<th>YRI</th>
</tr>";
$tableFoot = "</table>";
while($row = mysqli_fetch_array($result))
{
$tableRowStart = "<tr>";
$col1 =  "<td><a href=\"".$row['link']."\" target=\"_blank\">".$row['PMiDs']."</a></td>";
$col2 =  "<td class=\"colorBlue\">".$row['Gene']."</td>";
$col3 =  "<td>".$row['Major Allele']."</td>";
$col4 =  "<td>".$row['Minor Allele']."</td>";
```

```
$col5 =  "<td>".$row['Mutation']."</td>";
$col6 =  "<td>".$row['Function']."</td>";
$col7 =  "<td>".$row['Phenotype']."</td>";
$col8 =  "<td>".$row['rsID']."</td>";
$col9 =  "<td>".$row['Population Origin']."</td>";
$col10 =  "<td>".$row['ODD Ratio']."</td>";
$col11 =  "<td>".$row['P-value']."</td>";
$col12 =  "<td>".$row['ACB']."</td>";
$col13 =  "<td>".$row['ASW']."</td>";
$col14 =  "<td>".$row['BEB']."</td>";
$col15 =  "<td>".$row['CDX']."</td>";
$col16 =  "<td>".$row['CEU']."</td>";
$col17 =  "<td>".$row['CHB']."</td>";
$col18 =  "<td>".$row['CHS']."</td>";
$col19 =  "<td>".$row['CLM']."</td>";
$col20 =  "<td>".$row['ESN']."</td>";
$col21 =  "<td>".$row['FIN']."</td>";
$col22 =  "<td>".$row['GBR']."</td>";
$col23 =  "<td>".$row['GIH']."</td>";
$col24 =  "<td>".$row['GWD']."</td>";
$col25 =  "<td>".$row['IBS']."</td>";
$col26 =  "<td>".$row['ITU']."</td>";
$col27 =  "<td>".$row['JPT']."</td>";
$col28 =  "<td>".$row['KHV']."</td>";
$col29 =  "<td>".$row['LWK']."</td>";
$col30 =  "<td>".$row['MSL']."</td>";
$col31 =  "<td>".$row['MXL']."</td>";
$col32 =  "<td>".$row['PEL']."</td>";
$col33 =  "<td>".$row['PJL']."</td>";
```

```
$col34 =  "<td>".$row['PUR']."</td>";

$col35 =  "<td>".$row['STU']."</td>";

$col36 =  "<td>".$row['TSI']."</td>";

$col37 =  "<td>".$row['YRI']."</td>";

$tableRowEnd = "</tr>";

$allRows

=

$allRows.$tableRowStart.$col1.$col2.$col3.$col4.$col5.$col6.$col7.$col8.$col9.$col10.$col
11.$
col12.$col13.$col14.$col15.$col16.$col17.$col18.$col19.$col20.$col21.$col22.$col23.$col2
4.$c
ol25.$col26.$col27.$col28.$col29.$col30.$col31.$col32.$col33.$col34.$col35.$col36.$col37
; }


$Finalresult = $tableHead.$allRows.$tableFoot; echo $Finalresult; ?>
```

ANNEXURE VI

PM ID Search Page Code:- This page codes for taking query in the form of PM ID's :-

```
<?php setlocale(LC_ALL, "en_US.UTF8"); $searchKey = $_POST['PmidSelect']; define('DB_SERVER', 'localhost'); define('DB_USERNAME', 'root'); define('DB_PASSWORD', 'mysql'); define('DB_DATABASE', 'nehaGenome');
$db = mysqli_connect(DB_SERVER,DB_USERNAME,DB_PASSWORD,DB_DATABASE);
if(mysqli_connect_errno())
{ echo "Failed to connect to MySQL: " . mysqli_connect_error(); exit(); // **this is missing**

}

$result = mysqli_query($db,"select * from lakshay_nutri_PMIDs Where PMiDs = '$searchKey'"); $row = "";
$tableHead = "<table class=\"table col-lg-12\">

<tr class=\"TableRow\">

<th>PMiDs</th>

<th>Gene</th>

<th>Major Allele</th>

<th>Minor Allele</th>

<th>Mutation</th>

<th>Function</th>

<th>Phenotype</th>

<th>rsID</th>

<th>Population Origin</th>

<th>ODD Ratio</th>

<th>P-value</th>

<th>ACB</th>

<th>ASW</th>

<th>BEB</th>

<th>CDX</th>

<th>CEU</th>

<th>CHB</th>

<th>CHS</th>
```

```
<th>CLM</th>
<th>ESN</th>
<th>FIN</th>
<th>GBR</th>
<th>GIH</th>
<th>GWD</th>
<th>IBS</th>
<th>ITU</th>
<th>JPT</th>
<th>KHV</th>
<th>LWK</th>
<th>MSL</th>
<th>MXL</th>
<th>PEL</th>
<th>PJL</th>
<th>PUR</th>
<th>STU</th>
<th>TSI</th>
<th>YRI</th>
</tr>";
$tableFoot = "</table>";

while($row = mysqli_fetch_array($result))
{
$tableRowStart = "<tr>";
$col1
=
"<td
class=\"colorBlue
```

```
colorBlack\"><a

href=\"".$row['link']."\"  target=\"_blank\">".$row['PMiDs']."</a></td>";  $col2  =
"<td>".$row['Gene']."</td>";
$col3 =  "<td>".$row['Major Allele']."</td>";

$col4 =  "<td>".$row['Minor Allele']."</td>";

$col5 =  "<td>".$row['Mutation']."</td>";

$col6 =  "<td>".$row['Function']."</td>";

$col7 =  "<td>".$row['Phenotype']."</td>";

$col8 =  "<td>".$row['rsID']."</td>";

$col9 =  "<td>".$row['Population Origin']."</td>";

$col10 =  "<td>".$row['ODD Ratio']."</td>";

$col11 =  "<td>".$row['P-value']."</td>";

$col12 =  "<td>".$row['ACB']."</td>";

$col13 =  "<td>".$row['ASW']."</td>";

$col14 =  "<td>".$row['BEB']."</td>";

$col15 =  "<td>".$row['CDX']."</td>";

$col16 =  "<td>".$row['CEU']."</td>";

$col17 =  "<td>".$row['CHB']."</td>";

$col18 =  "<td>".$row['CHS']."</td>";

$col19 =  "<td>".$row['CLM']."</td>";

$col20 =  "<td>".$row['ESN']."</td>";

$col21 =  "<td>".$row['FIN']."</td>";

$col22 =  "<td>".$row['GBR']."</td>";

$col23 =  "<td>".$row['GIH']."</td>";

$col24 =  "<td>".$row['GWD']."</td>";

$col25 =  "<td>".$row['IBS']."</td>";

$col26 =  "<td>".$row['ITU']."</td>";

$col27 =  "<td>".$row['JPT']."</td>";

$col28 =  "<td>".$row['KHV']."</td>";
```

```
$col29 =  "<td>".$row['LWK']."</td>";

$col30 =  "<td>".$row['MSL']."</td>";

$col31 =  "<td>".$row['MXL']."</td>";

$col32 =  "<td>".$row['PEL']."</td>";

$col33 =  "<td>".$row['PJL']."</td>";

$col34 =  "<td>".$row['PUR']."</td>";

$col35 =  "<td>".$row['STU']."</td>";

$col36 =  "<td>".$row['TSI']."</td>";

$col37 =  "<td>".$row['YRI']."</td>";

$tableRowEnd = "</tr>";

$allRows

=

$allRows.$tableRowStart.$col1.$col2.$col3.$col4.$col5.$col6.$col7.$col8.$col9.$col10.$col
11.$
col12.$col13.$col14.$col15.$col16.$col17.$col18.$col19.$col20.$col21.$col22.$col23.$col2
4.$c
ol25.$col26.$col27.$col28.$col29.$col30.$col31.$col32.$col33.$col34.$col35.$col36.$col37
; }


$Finalresult = $tableHead.$allRows.$tableFoot; echo $Finalresult;
?>
```