DATABASE ON EPIGENETICS OF ALZHEIMER'S DISEASE

Enrollment no-171505

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Submitted in partial fulfillment of the requirement for the award of degree of

BACHELOR OF TECHNOLOGY

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JAYPEE UNIVERSITY OF INFORMATION TECHNOLOGY

WAKNAGHAT, SOLAN 173234, HIMACHAL PRADESH, INDIA

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I give my greatest acknowledgement to my Parents and Brother for all-round support during studies. The endless sacrifices from my parents have made me what I am today.

I also thank Ph.D Scholar Mr. Rohit Shukla for his encouragement and constant support.

DECLARATION BY THE STUDENT

I hereby declare that the report in the B.tech project report entitled “Database on Epigenetics of Alzheimer’s disease” was submitted at the Jaypee University of Information Technology, Waknaghat, Himachal Pradesh, India, is an authentic record of my work carried out under the supervision of Dr. Tiratha Raj Singh. I have not submitted this work elsewhere for any degree or diploma.

(Signature of Student)

Anjali Sharma(171505)

Department of Biotechnology and Bioinformatics,

Jaypee University of Information Technology,

Waknaghat, Himachal Pradesh, India

Date:16/05/2021

CERTIFICATE

This is to certify that the project entitled "Database on Epigenetics of Alzheimer's Disease", submitted by Anjali Sharma is in fulfillment for the award of the degree of Bachelors of Technology in Bioinformatics to the Jaypee University of Information Technology, Waknaghat, Solan(H.P.), India is an authentic record of candidate's own work carried out by her under my supervision.

This work has not been submitted partially of fully to any other university or institution in order to achieve any award or other degree.

Dr. Tiratha Raj Singh

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1. ABSTRACT

Alzheimer's Disease is an irreversible, progressive, neurodegenerative disorder. It is a cause of dementia.The word dementia means loss of conscious mental activities, ability to remember things, thinking abilities, and reasoning. It interferes with behavioral abilities to such a degree that it affects individuals everyday life. The main features of this disease include plaques and tangles in the brain. Other features include loss of communication due to the loss of connections between the neurons in the brain. Initially neuronal damage appears in the hippocampus, the part of the brain which is responsible for forming memories. As the neurons die in the hippocampus region of the brain, an additional part of the brain is affected. AD is a disease caused by simultaneous action of several genetic, epigenetic and environmental factors which lead to premature cell death.

Studies have shown that epigenetic processes, which determine how and when genes are expressed, without altering the genetic code lead to Alzheimer's Diseases. Epigenetics involves physical and cellular trait variations that are not caused by changes in the DNA sequence. It is the investigation of external or environmental factors that turns the gene off and on.The four main epigenetics factors that lead to Alzheimer's Disease are DNA Methylation, Histone Modifications, Chromatin Remodeling and Non-Coding RNA. DNA Methylation changes cytosine residues in cytosine/guanine-rich regions. Various posttranslational modifications such as histone acetylation, methylation, phosphorylation are seen in histones. Chromatin Remodelers are enzyme complexes that shift the nucleosome and alter the dynamics of chromatin structure. Non Coding RNAs located in the nucleus also play role in the epigenetic mechanism.

Our study focuses on finding out various genes and information related to those genes and environmental factors that led to the epigenetics of Alzheimer's Diseases. Our study includes the following components. Firstly, collecting various genes which are causing epigenetics of Alzheimer's, after that other information related to that gene is collected such as its gene id, protein id, the protein encoded by that gene, common names of that protein, aliases of that gene, length of that gene, length of the protein, SNPs involved and which gene is present in which epigenetic process and what information is present in

research papers about that gene. The process researches which have been done on that genes, information about that is also collected. The second component includes designing the database and graphical user interface through which we can make searches.

2. INTRODUCTION

Alzheimer's disease is a age-related, irreversible form of mental deterioration or senile dementia, which causes memory losses[2]. Dementia is a group of symptoms that come along with a diseases. Other conditions that cause dementia other than Alzheimer are chronic alcoholism, dehydration, side effects of some drugs, high fever, thyroid disorders, kidney disorders, liver disorders, brain tumors, blood clots etc[13]. Nerve cells progressively deteriorate in this disease[12]. Person suffering from this disease has trouble remembering new things, the person also faces problems while making the decision, it becomes difficult for a person to analyze things. Alzheimer is a chronic condition. Alzheimer and other dementia are major health concern. 400-500 lakh people worldwide are suffering from dementia. Comparining the gender ratios it is seen that it is more prevalant in females than in males. Many factors can lead to this disease development[1].

The main features characterized by this disease involve the accumulation of plaques in the brain. These plaques contain amyloid –β (Aβ) peptides and intracellular neurofibrillary tangles. Brain atrophy(loss of neurons and their connections) and death of nerve cells are hallmark features of Alzheimer. Other features of AD include inflammation at predromal stages. These inflammatory responses lead to the activation of astrocytes and microglia cells, which further switch on several signaling pathways leading to oxidative stress which further leads to neuronal loss or dysfunction[2]. Activated microglia led to many neurogdegenrative disorders, including Alzheimer's disease. Evidences suggests that microglial inflammatory activity in AD increases and microglial-mediated clearance activity is decreases[14].

In early stages of Alzheimer's dieases person faces language problems, mood swings low energy, changes in personality,problem in attention,problem in solving simple mathematical problems, person become slow in speech and understanding, difficulty in learning things, need assistance with complicated tasks. Patients in the intermediate stages may recall events from the distant past, but recent events are difficult for them to remember, they are unable to locate places and find time, and they do not recognize previously recognizable faces. At the final stage, Alzheimer's patients lose bodily control and need contant care, are not able to chew or swallow, become more insensitive, they become vulnerable to other illnesses like pneumonia[3].

For the diagnosis of the AD a patient has to go through several checks, including neurological checks, magnetic resonance imaging for neurons, lab trials as vitamin B12, family and medical history of the individual is also studied[15].The treatment of AD involves to mitigate the cognitive symptoms and to slow down the progression of disease[29].

Scientists still are not sure what causes Alzheimer's disease. But some risk factors led people to develop this incurable diseases. These factors are age, gender, family history, genes, head trauma, brain abnormalities ,head injuries, vascular diseases, smoking, obesity, high blood pressure, lack of physical and mental activity, unhealthy diet, epigenetics, environment[15]. As discussed earlier many factors led to Alzheimer's disease. Our current focus is on different epigenetic processes that led to this diseases.

Epigenetics is a major mechanism that accommodates gene-expression changes that occurs due to the interaction of genes and the environment[11]. Epigenetics is the heritable changes in gene expression. The epigenetic mechanisms have the ability to regulate DNA replication and repair,RNA transcription which influences transcriptional regulation and protein translation[16]. The various epigenetics mechanism that lead to gene alterations is DNA Methylation, Histone Modifications, Chromatin Remodeling, Non-Coding RNA. So in epigenetics gene expression gets modified. The four epigenetic mechanism studied here are as follows:

a)DNA Methylation

DNA Methylation is the only epigenetic process that directly effect /changes the DNA. The enzymes DNA methyltransferases transfers a methyl group to the fifth position of carbon of the cytosine ring of DNA. Methylation at this position in DNA turn down with age in all tissues and therefore researchers considered it as key factor for epigenetics[11].

In plants, cytosines are methylated in both asymmetrical or symmetrical settings. In mammals this occurs in any part of the genome. In somatic or vegetative cells more than 98% of DNA methylation occurs at sites called CpG islands, while in embryonic cells, up to one-fourth of all methylation occurs in a non-CpG surroundings. DNA methylation is normally removed during zygote formation and then established again in the embryo during implantation. When DNA methylation is imperfectly regulated, it can lead to diseases such as cancer[5].

DNA methylation has role in astrocyte differentiation and development[17].

Many genes act as a catalyst in the conversion of the methyl group from S-adenosylmethionine to DNA.The enzymes which are involved in this process include DNA methyltransferases(DNMT), of which DNMT1, DNMT3A, and DNMT3B are the most studied. The product of this reaction, S-adenosylhomocysteine, is converted back to S-adenosylmethionine via a cascade of reactions. An increase in plasma homocysteine levels is also important[5].

DNA methylation is traditionally linked to lower gene expression, but new evidence indicates That the effect of DNA methylation is based on its location in the genome. 5-methylcytosine is the most abundant altered base in mammals[5].

b)Histone Modifications

Hitones are proteins which help in packaging of DNA. The modifications that led to epigenetics of Alzheimer's related to histones are of following types,

Histone acetylation- Histone acetylases are enzymes that changes histone proteins by doing acetylation on lysine residues in the central histone tails. Acetylation of histones is often linked to transcriptional activation[6]. HATs are divided into two categories: Type A. and Type B. HATs of type A is found in the nucleus and function on the histones that are associated with chromatin. Type B HATs, on the other hand, are present in the cytoplasm and function on newly synthesized histones that have not yet been linked with chromatin[4].

HDACs, or histone deacetylases, are another form of enzyme that covalently modifies histone proteins. HATs acetylate lysine residues to neutralize histone tails, while HDACs deacetylate lysine residues to counteract their effects. They're linked to condensing chromatin and gene repression because they directly retrogress the histone tails to their charged state[5].

They are divided into four classes in mammals: classes I, II, III, and IV, based on a variety of factors including function and DNA sequence. These deacetylases can be present in the nucleus as well as in the cytoplasm of the cell, depending on the form of HDAC [4].

Other histone changes have also been linked to Alzheimer's disease. Phosphorylation is a modification in which a phosphate group is added to the nucleosome's histone tails[4]. Glycogen Synthase Kinase 3 beta is a major enzyme which have an effect on escalating the disease progression by the hyperphosphorylation of the tau protein[12].

H4 histone protein has notably higher levels of phosphorylation on Serine-47 in rats with high levels of APP in their neuroblastoma cells[19].
Examinations on tissue specimens from AD patients brains supported these findings, with high levels of phosphorylated H4 found[3].
The other processes which led to histone modifications are ubiquitination, sumoylation or ADP-ribosylation[18].

c)Chromatin Remodeling

Enzymes that form chromatin remodeling complexes are a distinct group of enzymes. By altering the interactions between DNA and histone proteins, these enzymes uses the ATP to change the position of the nucleosome and disturbs the chromatin structure. This is accomplished by a variety of processes, including nucleosome slipping, repositioning, and ejection[2].
The role of Vitamin D receptor to regulate chromatin structure in association with histone modifiers and chromatin remodelers is also studied[20].Studies have shown that histones are associated with memory function[21].
In eukaryotic cells, there are many groups of chromatin remodelers.SWI/SNF, ISW1, NuRD/Mi-2 CHD, INO80, and SWR1 are among these families. The ATPase domain of all of these chromatin remodelers is the same, but their unique remodeling functions are different[2]. CHD5, is a part of the CHD family, has been discovered to play a key role in Alzheimer's disease. The majority of remodeling ATPases are found in the human body, CHD5 is only found in the brain[8]. Furthermore, CHD5 depletion has an affects on SWI/SNF, another chromatin remodeler family. When CHD5 is depleted, it alters the expression levels of SWI/SNF subunits present in the brain.
CHD5 has also been related to genes linked to Alzheimer's disease. As studies shows that it controls them directly. As a result, a clear link between the function of CHD5 and Alzheimer's disease has been established[2].
Other chromatin remodelers have also been linked to Alzheimer's disease in other research. “SWI/SNF linked, matrix associated, actin-dependent regulator of chromatin subfamily, can also be found to be associated with Alzheimer's,” according to microarray research[2].

d) Non Coding RNA

Non Coding RNAs (ncRNA) are a large and diverse family that are not translated into proteins and regulate gene expression programes through a variety of mechanisms[10].

Non Coding RNAs are divided into two groups, one is housekeeping RNAs and the other one is regulatory RNAs.

Housekeeping ncRNAs are expressed ubiquitously and play role in the maintenance of the cell regularly. The RNAs that include in this group are micro RNAs, short interfering RNAs, piRNAs, long non-coding RNAs that plays role in AD pathogenesis[10].

In human genes, about 98.5 percent of sequences is classified as noncoding region. The noncoding sequences are transcribed into various forms of ncRNA including microRNAs (miRNAs)[9].

miRNAs controls the translational repression of messenger RNAs in a sequence-specific way. Most of the brain's miRNAs control the expression of target molecules that are important for neuronal and glial growth, differentiation, apoptosis , and metabolism[8].

PIWI-interacting RNAs are short ss non Coding RNAs (24-32 nucleotides). Uridine is present at the 5′ end and 2′-O-methylation at the 3′ end in them. They are manufactured by a Dicer-independent mechanism. By interacting with PIWI proteins, piRNAs regulate gene expression programs[10]. piRNAs is considered as a candidate biomarker for AD[23].

Long-chain ncRNA (lncRNA) are more than 200 nucleotides in length[22]. It regulates gene expression in a variety of ways, including epigenetic control and transcription control and has connections in the development of a variety of diseases, including Alzheimer's disease[10].

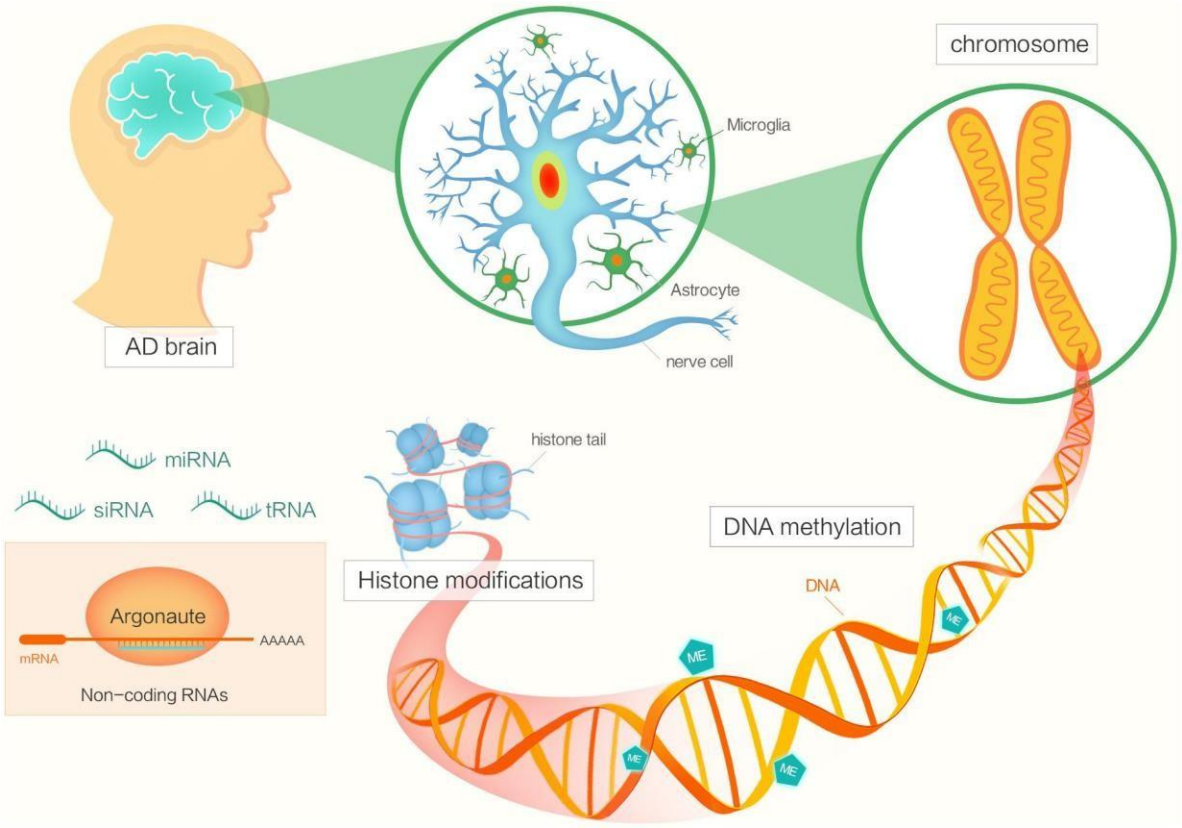


Figure1. Epigenetics of Alzheimer's Disease[6].

3.MATERIALS AND METHODS

The methodology used while constructing this database include:

3.1) Retrieval of information from the literature

A database is a collection of data that has been structured in a way that makes it easy to access and maintain.It is a systematic collection of data. The purpose of making a database is to keep information easily accessible and organized. It reduces the time you spend managing the data. Its features include minimum duplicity and redundancy, saves storage cost, anyone can work on it. To make a database on epigenetics of Alzheimer's disease, the literature review was done. Our main focus is on four epigenetic mechanisms i.e, DNA Methylation, Histone Modifications, Chromatin Remdeling, Non-Coding RNA.

Articles related to each epigenetic mechanism are studied separately by searching on PubMed.

PubMed is a search engine that accesses the MEDLINE database of life sciences and biomedical references and abstracts. The database is maintained by the National Library of Medicine. PubMed now contains more than 320 lakh citations[23].

An advance search on PubMed is done for each epigenetic process. For eg-The figure pasted below is the screenshot of the advance search done for the DNA methylation. This is done for each process.

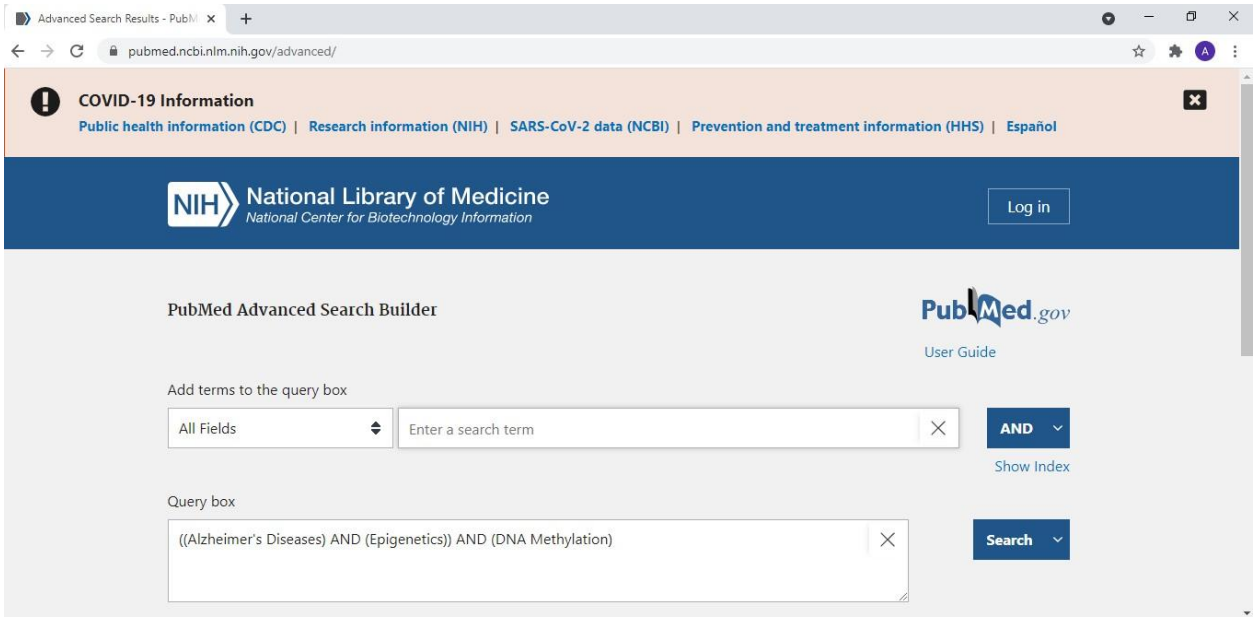


Figure 2. Advance PubMed Search performed.

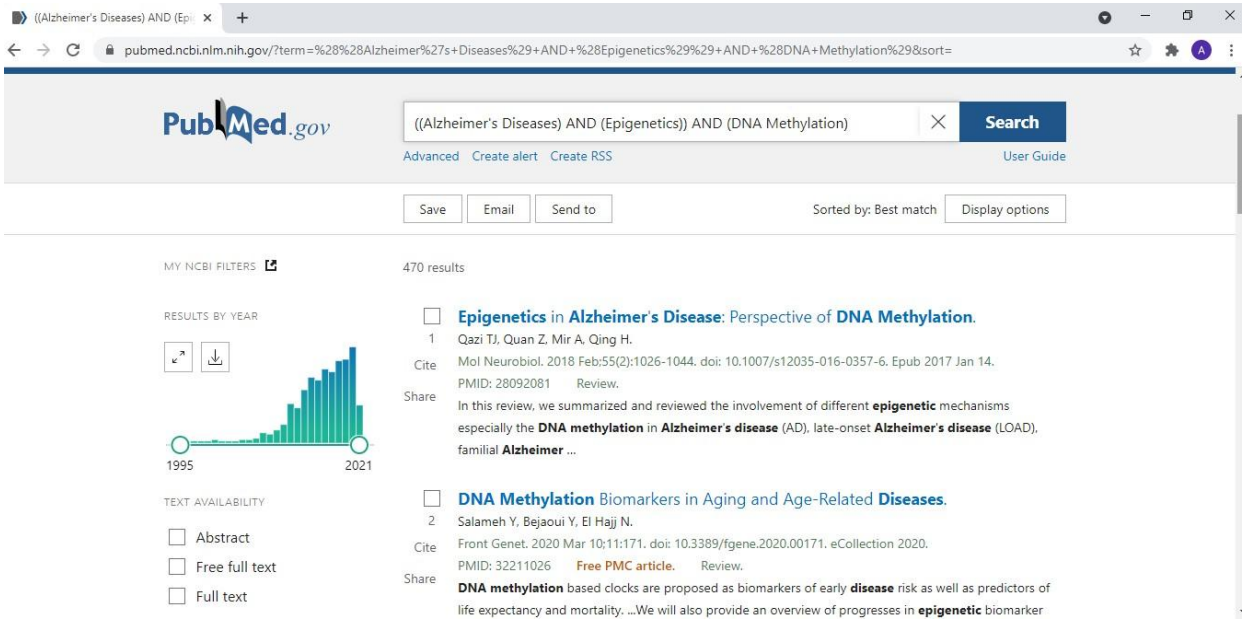


Figure3. Result page showing the PubMed search.

So the literature review is done and the genes and environmental factors which are involved in the 4 epigenetic processes i.e, DNA Methylation, Histone Modifications, Chromatin Remodeling, Non-Coding RNA were collected.

3.2) Retrieval of information from the Databases

After that information about the genes like Gene ID, Protein ID, Protein name, Gene length, Protein length, Aliases, SNPs were collected from databases like NCBI, Uniprot, GeneCards, SNPedia and stored in an Excel sheet.

NCBI-"National Center for Biotechnology Information".
NCBI is a leading source for public biomedical databases, applications for analyzing molecular and genomic data, and computational biology research[25].This database is very useful for researchers as it provides information like BioCollections, BioProjects, gene, nucleotide etc.

Uniprot- Its main aim is to provide a comprehensive, high-quality, and freely available database of protein sequence and functional knowledge to the scientific community[26].

GeneCards- GeneCards is a integrated database that contains detailed information on all human genes that have been annotated or predicted. GeneCards has gene-centric data from 150 different websites.It contains data including genomic, transcriptomic, proteomic, genetic, clinical, and functional data[27].

SNPedia- SNPedia is a bioinformatics website and it provides, description, links to scientific articles and microarray information about the SNP[28].

3.3) Redundancy removal

Redundancy means having duplicacy in data. While making entries of genes from the research papers there are chances of having redundant information. Or sometimes a gene is involved in more than two processes, so instead of making two entries for this, one entry is made and redundancy is removed.

3.4) Data Cleaning

Data cleaning is done to remove incorrect, inconsistent data, and to achieve uniformity in data.

3.5) ER diagram construction

ER Diagram means entity relationship diagram. This diagram shows the relationship between the entities in the databases. It helps to analyze the data to produce well-designed database.
Rectangles here represent an entity types.
Ellipses represent attributes.
The diamond represents a relationship.
Attributes that are underlined are the primary key.

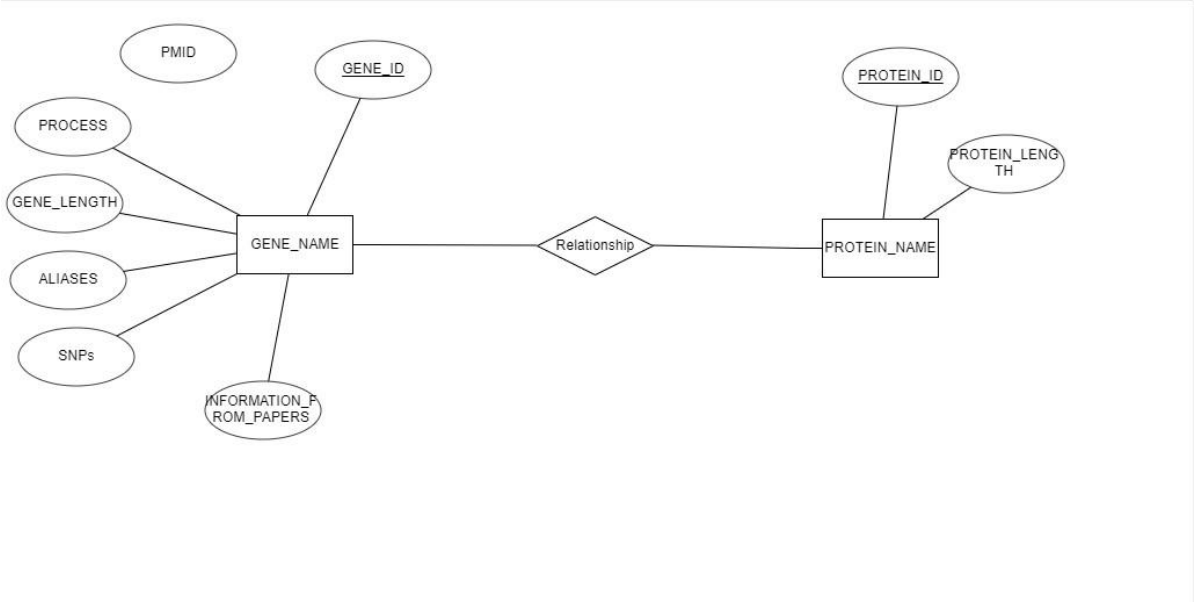


Figure 4. ER Diagram representing various fields and their respective relationships.

3.6) Database creation using XAMPP

The database is created using XAMPP version 3.2.4 software. The steps of creating a database in XAMPP version 3.2.4 are as follows:

- Go to the Drive where XAMPP is installed. Open the XAMPP.
- In the actions tab, start the apache and MySQL.
- After that open PHPMyAdmin on the localhost. It is done by entering 127.0.0.1 in the browser. 127.0.0.1 is the loopback Internet protocol address referred to as the localhost.
- A database named “dead” is created on XAMPP by clicking on create the database.

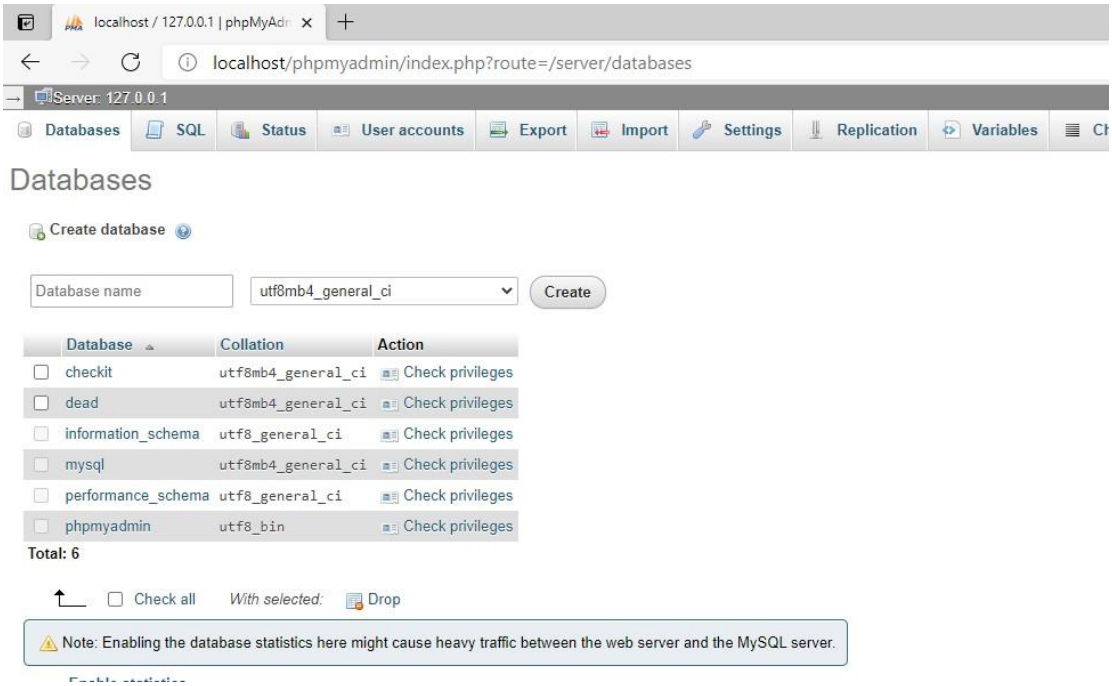
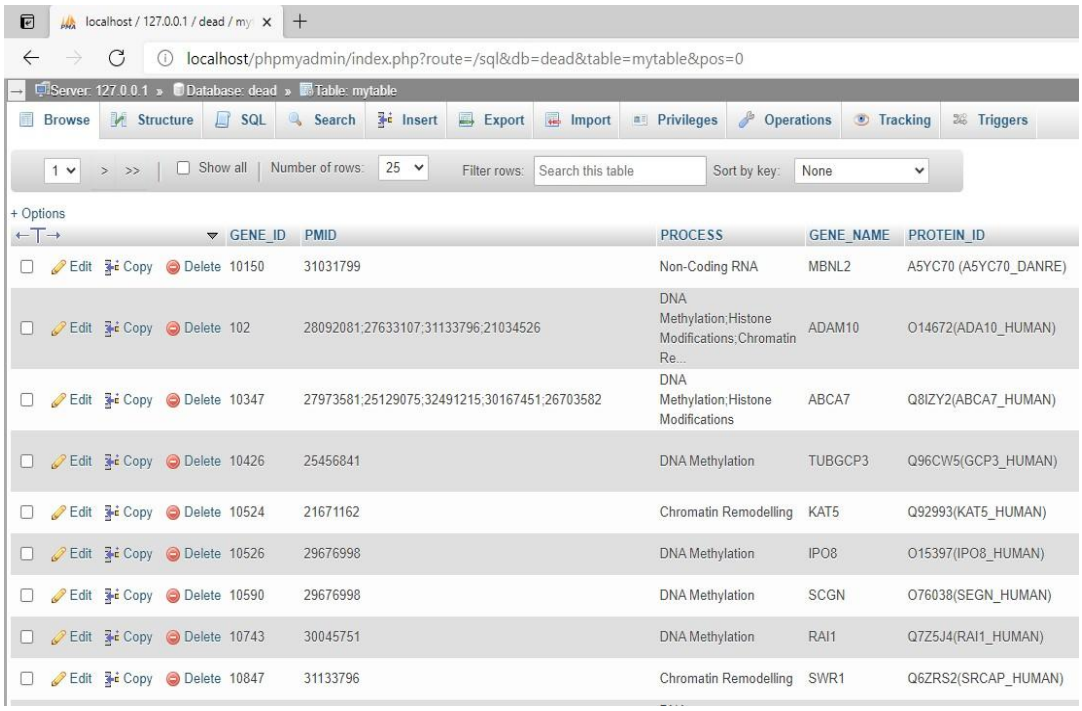


Figure 5. Database created(representing by name “dead” here).

- Now, to import the excel sheet into the XAMPP, the excel sheet is converted into a .sql file.
- After that .sql file is imported in the XAMPP by clicking on Import.
- Table “mytable” is created on XAMPP.



	GENE_ID	PMID	PROCESS	GENE_NAME	PROTEIN_ID
Edit Copy Delete	10150	31031799	Non-Coding RNA	MBNL2	A5YC70 (A5YC70_DANRE)
Edit Copy Delete	102	28092081;27633107;31133796;21034526	DNA Methylation;Histone Modifications;Chromatin Re...	ADAM10	O14672(ADA10_HUMAN)
Edit Copy Delete	10347	27973581;25129075;32491215;30167451;26703582	DNA Methylation;Histone Modifications	ABCA7	Q8IZY2(ABCA7_HUMAN)
Edit Copy Delete	10426	25456841	DNA Methylation	TUBGCP3	Q96CW5(GCP3_HUMAN)
Edit Copy Delete	10524	21671162	Chromatin Remodelling	KAT5	Q92993(KAT5_HUMAN)
Edit Copy Delete	10526	29676998	DNA Methylation	IPO8	O15397(IPO8_HUMAN)
Edit Copy Delete	10590	29676998	DNA Methylation	SCGN	O76038(SEGN_HUMAN)
Edit Copy Delete	10743	30045751	DNA Methylation	RAI1	Q7Z5J4(RAI1_HUMAN)
Edit Copy Delete	10847	31133796	Chromatin Remodelling	SWR1	Q6ZRS2(SRCAP_HUMAN)

Figure 6. Picture showing values stored in the database in the table named “mytable”.

PROTEIN_NAME	ALIASES	GENE_LENGTH	PROTEIN_LENGTH	SNP	INFORMATION_FROM_PAPERS
Muscleblind-like protein 2;Muscleblind-like protei...	MBLL;MBLL39;PRO2032	4730 bp	373 aa	rs9516855	1) A dMEP of exons in MBNL2; a gene implicated in...
Disintegrin and metalloproteinase domain-containin...	AD10; AD18; CD156c; CDw156; HsT18717; MADM; RAK; k...	3410 bp	748 aa	rs653765	1) The cleavage done by the ?-secretase (ADAM10 an...
Phospholipid-transporting ATPase ABCA7;ABCA-SSN;AT...	ABCA-SSN; ABCX; AD9	6815 bp	2146 aa	rs115550680	1) Candidate Gene Studies. The 34 studies showed t...
Gamma-tubulin complex component 3;GCP-3;hGCP3;Gamm...	104p; ALP6; GCP3; Grip104; SPBC98; Spc98; Spc98p	2479 bp	907 aa	rs75590369	1) The TUBGCP3 gene showed the strongest associati...
Histone acetyltransferase KAT5 ;60 kDa Tat-interac...	ESA1; HTATIP; HTATIP1; NEDFASB; PLIP; TIP; TIP60; ...	2215 bp	513 aa	NA	1)Abnormalities in histone and chromatin regulatio...
Importin-8;Imp8;Ran-binding protein 8;RanBP8	RANBP8	5208 bp	1037 aa	rs3214606	1) The five CpGs that are found in all three epige...
Secretagogin	CALBL; DJ501N12.8; SECRET; SEGN; setagin	1468 bp	276 aa	rs7752195	1) The five CpGs that are found in all three epige...
Retinoic acid-induced protein 1	SMCR; SMS	7677 bp	1906 aa	rs727504118	1) A set of new genes with clustered and prominent...
Helicase SRCAP ;Domino homolog 2;Snf2-related CBP ...	DOMO1;EAF1;FLHS;SWR1;SRCAP	11724 bp	3230 aa	rs34286592;rs3809627	1)Chromatin remodeling complexes are enzymes that ...
Clusterin;Aging-associated gene 4 protein;Apolipop...	AAG4; APO-J; APOJ; CLI; CLU1; CLU2; KUB1; NA1/NA2;...	402 bp	449 aa	rs4236673;rs4732728;rs485902;rs576748;rs73223431;r...	1) Prominent age-associated changes were observed ...
Ectodysplasin-A receptor-associated adapter protei	ECTD11A; ECTD11B; ED3; EDA3	3088 bp	215 aa	rs181126208	1) The five CpGs that are found in all three epige

Figure 7.Database on XAMPP, showing other set of values.

3.7) GUI Design

Now to fetch data from the database a website is created using HTML, CSS, PHP, Javascript. I have made four pages for the website which is Home page, About page, Search page and Contact page.

FLOWCHART OF THE DATABASE DESIGNING STRATEGY

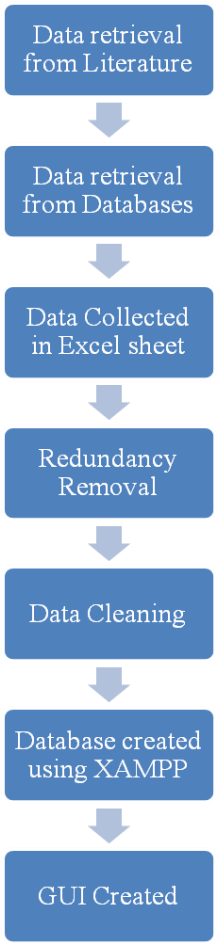


Figure 8. Flowchart of the Database designing strategy.

4.RESULTS

4.1) Genes and environmental factors were collected from the papers and an excel sheet is maintained. 103 genes and their information is collected.

11 columns were created named-
GENE_ID, PMID, PROCESS, PROTEIN_ID, PROTEIN_NAME, ALIASES, GENE_LENGTH, PROTEIN_LENGTH, SNPs, INFORMATION_FROM_PAPERS.
Information related to these fields for each gene was collected.

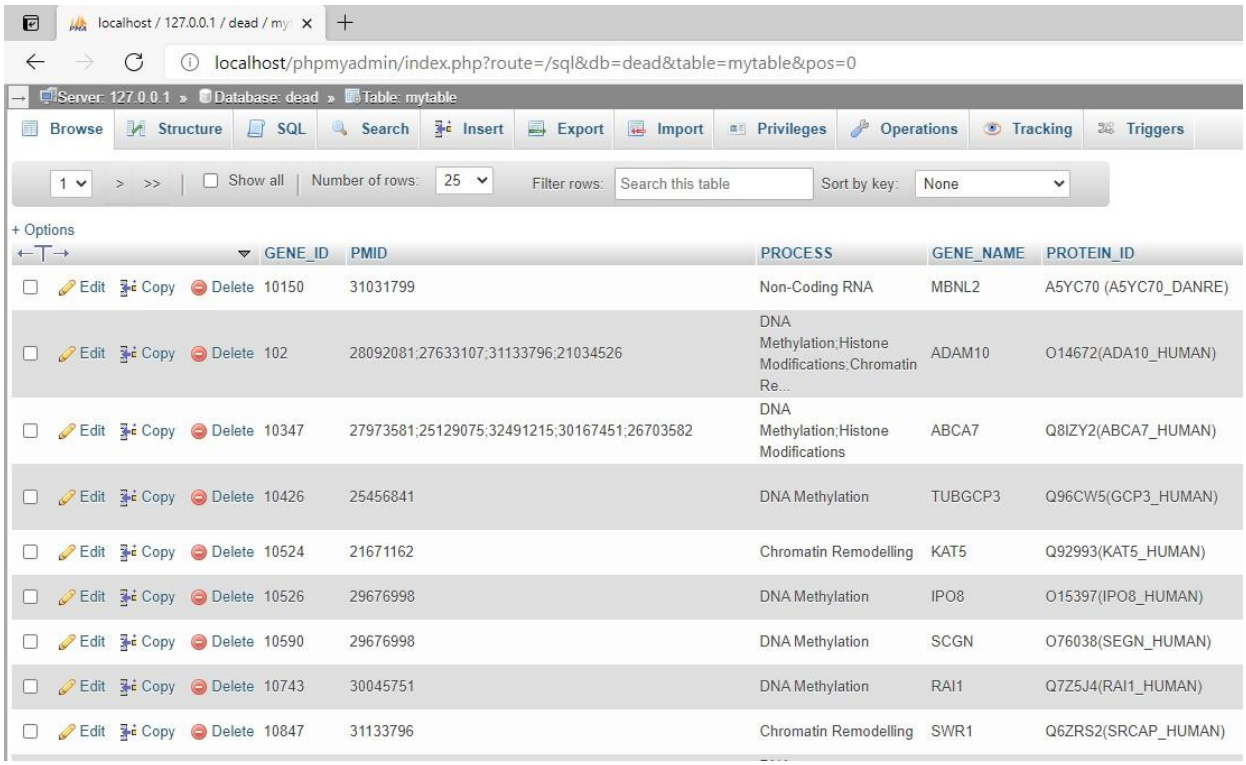
	A	B	C	D	E	F
1	**GENE_ID**	**PMID**	**PROCESS**	**GENE_NAME**	**PROTEIN_ID**	**PROTEIN_NAME**
2	5663	28092081;30045751;30898171;27973581;21671162	DNA Methylation;Histone Modifications	PSEN1	P49768 (PSN1_HUMAN)	Presenilin-1 ;PS-1;Protein S182
	5664	28092081;30045751;30898171;29885742	DNA Methylation	PSEN2	P49810 (PSN2_HUMAN)	Presenilin-2 ;PS-2;AD3LP;AD5;E5-1;STM-2

Figure 9. Screenshot of data collected in Excel sheet.

	G	H	I	J	K
1	**ALIASES**	**GENE_LENGTH**	**PROTEIN_LENGTH**	**SNP**	**INFORMATION_FROM_PAPERS**
2	ACNINV3; AD3; FAD; PS-1; PS1; S182	6905 bp	467 aa	rs63750592;rs63749824;rs63749967;rs63750599;rs63750815;rs63751141;rs63750831;rs63750601;rs63750852;rs63750321;rs63750450;rs63750730;rs63749805;rs63750550;rs63751272;rs63750800;rs63750353;rs63750522;rs63751106;rs63751037;rs63750322;rs63750004;r	1) Presenilin 1 and β-site AβPP cleaving enzyme (BACE1) plays essential roles in amyloid processing. 2)Folate functions in one-carbon metabolism where it acts as a methyl donor and also plays a role in DNA synthesis. Methyl donors provide methyl groups (CH3) for DNA methylation: an epigenetic mechanism that has the capacity to modulate gene expression and can be influenced by
	AD3L; AD4; CMD1V; PS2; STM2	2246 bp	448 aa	rs58973334; rs140501902; rs63749851; rs28936380; rs63750197; rs63750215; rs61761208; rs63750812; rs63749884; rs28936379	1) Mutations in these genes: APP; BACE; presenilin 1 (PSEN1; PS1); and presenilin 2 (PSEN2; PS2) causes FAD. 2) Minority of AD cases can be explained by mutations in the genes APP;PSEN1 and PSEN2. 3)Mendelian inheritance of mutations in the APP gene and the PSEN1 and PSEN2 genes; whichencode subunits of the γ-secretase enzyme; have been demonstrated in early-onset familial AD cases. 4) The increased levels of genes that promote Alzheimer's pathology (e.g.

Figure 10. Data collected in Excel sheet containing other fields(aliases, gene length, protein length, SNP, Information from papers).

4.2) Database is made on XAMPP.



	GENE_ID	PMID	PROCESS	GENE_NAME	PROTEIN_ID
Edit Copy Delete	10150	31031799	Non-Coding RNA	MBNL2	A5YC70 (A5YC70_DANRE)
Edit Copy Delete	102	28092081;27633107;31133796;21034526	DNA Methylation;Histone Modifications;Chromatin Re...	ADAM10	O14672(ADA10_HUMAN)
Edit Copy Delete	10347	27973581;25129075;32491215;30167451;26703582	DNA Methylation;Histone Modifications	ABCA7	Q8IZY2(ABCA7_HUMAN)
Edit Copy Delete	10426	25456841	DNA Methylation	TUBGCP3	Q96CW5(GCP3_HUMAN)
Edit Copy Delete	10524	21671162	Chromatin Remodelling	KAT5	Q92993(KAT5_HUMAN)
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Edit Copy Delete	10590	29676998	DNA Methylation	SCGN	O76038(SEGN_HUMAN)
Edit Copy Delete	10743	30045751	DNA Methylation	RAI1	Q7Z5J4(RAI1_HUMAN)
Edit Copy Delete	10847	31133796	Chromatin Remodelling	SWR1	Q6ZRS2(SRCAP_HUMAN)

Figure 11.Database made on XAMPP showing five attributes.

PROTEIN_NAME	ALIASES	GENE_LENGTH	PROTEIN_LENGTH	SNP	INFORMATION_FROM_PAPERS
Muscleblind-like protein 2;Muscleblind-like protei...	MBLL;MBLL39;PRO2032	4730 bp	373 aa	rs9516855	1) A dMEP of exons in MBNL2; a gene implicated in...
Disintegrin and metalloproteinase domain-containin...	AD10; AD18; CD156c; CDw156; HsT18717; MADM; RAK; k...	3410 bp	748 aa	rs653765	1) The cleavage done by the ?-secretase (ADAM10 an...
Phospholipid-transporting ATPase ABCA7;ABCA-SSN;AT...	ABCA-SSN; ABCX; AD9	6815 bp	2146 aa	rs115550680	1) Candidate Gene Studies. The 34 studies showed t...
Gamma-tubulin complex component 3;GCP-3;hGCP3;Gamm...	104p; ALP6; GCP3; Grip104; SPBC98; Spc98; Spc98p	2479 bp	907 aa	rs75590369	1) The TUBGCP3 gene showed the strongest associati...
Histone acetyltransferase KAT5 ;60 kDa Tat-interac...	ESA1; HTATIP; HTATIP1; NEDFASB; PLIP; TIP; TIP60; ...	2215 bp	513 aa	NA	1)Abnormalities in histone and chromatin regulatio...
Importin-8;Imp8;Ran-binding protein 8;RanBP8	RANBP8	5208 bp	1037 aa	rs3214606	1) The five CpGs that are found in all three epige...
Secretagogin	CALBL; DJ501N12.8; SECRET; SEGN; setagin	1468 bp	276 aa	rs7752195	1) The five CpGs that are found in all three epige...
Retinoic acid-induced protein 1	SMCR; SMS	7677 bp	1906 aa	rs727504118	1) A set of new genes with clustered and prominent...
Helicase SRCAP ;Domino homolog 2;Snf2-related CBP ...	DOMO1;EAF1;FLHS;SWR1;SRCAP	11724 bp	3230 aa	rs34286592;rs3809627	1)Chromatin remodeling complexes are enzymes that ...
Clusterin;Aging-associated gene 4 protein;Apolipop...	AAG4; APO-J; APOJ; CLI; CLU1; CLU2; KUB1; NA1/NA2;...	402 bp	449 aa	rs4236673;rs4732728;rs485902;rs576748;rs73223431;r...	1) Prominent age-associated changes were observed ...
Ectodysplasin-A receptor-associated adapter protei	ECTD11A; ECTD11B; ED3; EDA3	3088 bp	215 aa	rs181126208	1) The five CpGs that are found in all three epige

Figure 12. Database made on XAMPP showing six attributes.

4.3) Graphical User Interface(GUI)

HOME PAGE:-

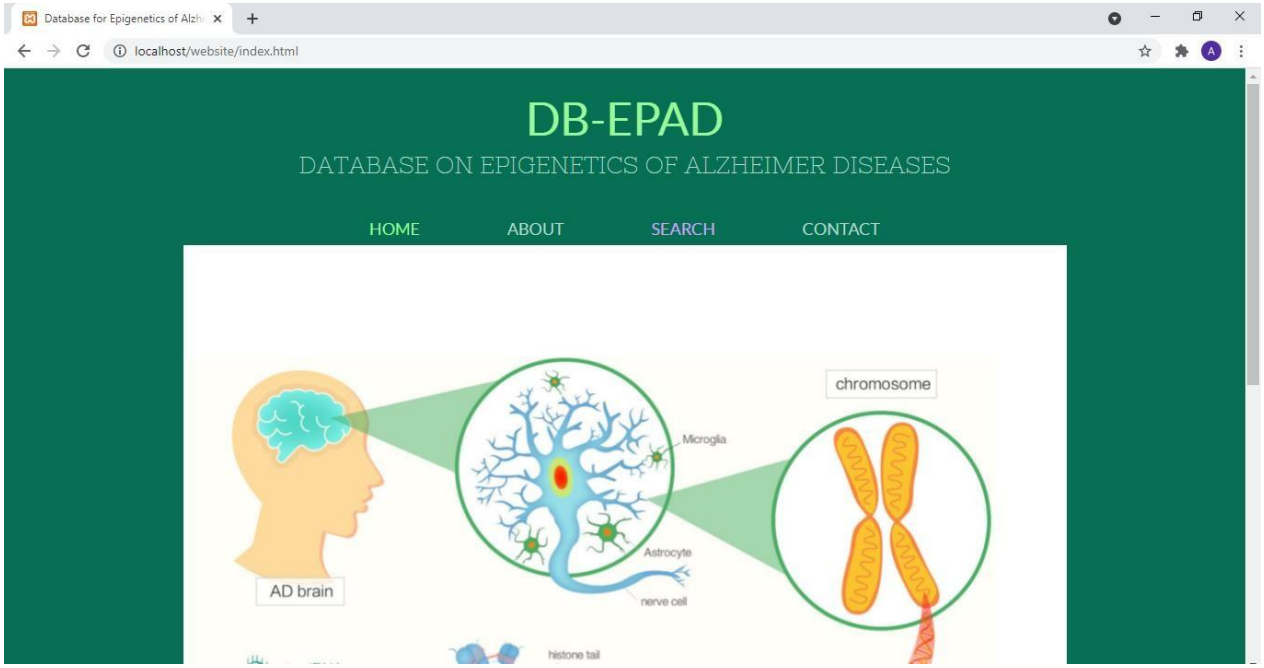

Figure 13: Home page of the website.

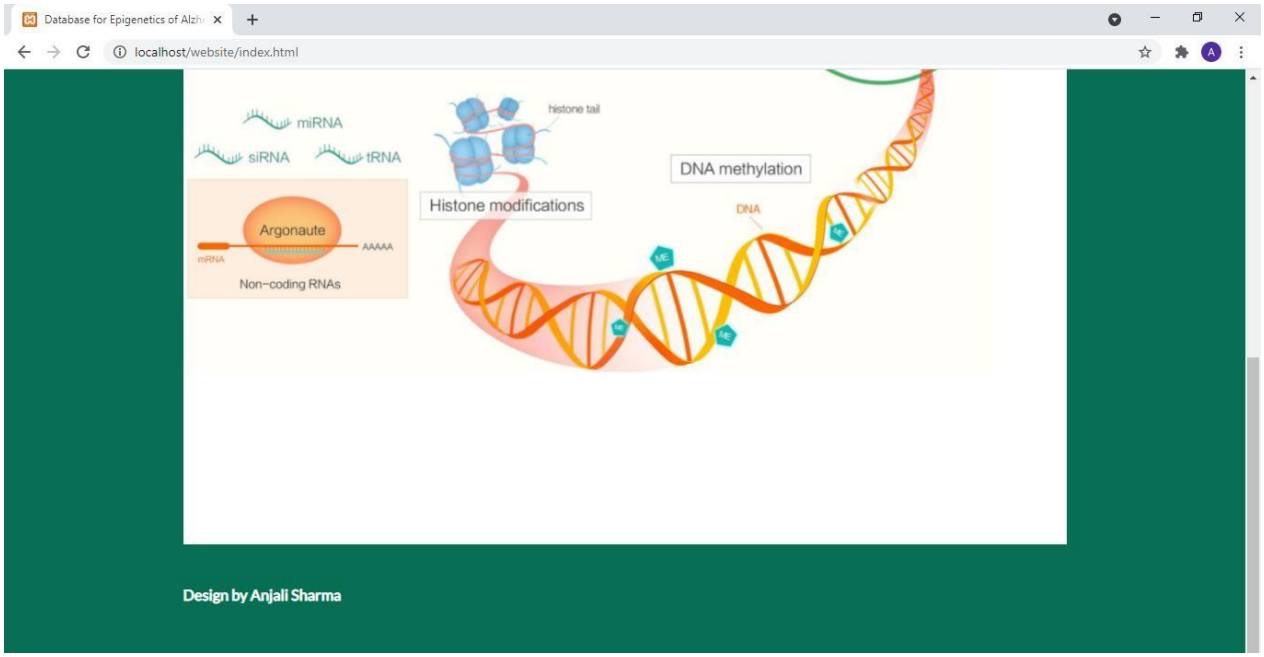

Figure 14. The bottom part of the Home page of the website.

ABOUT PAGE:-

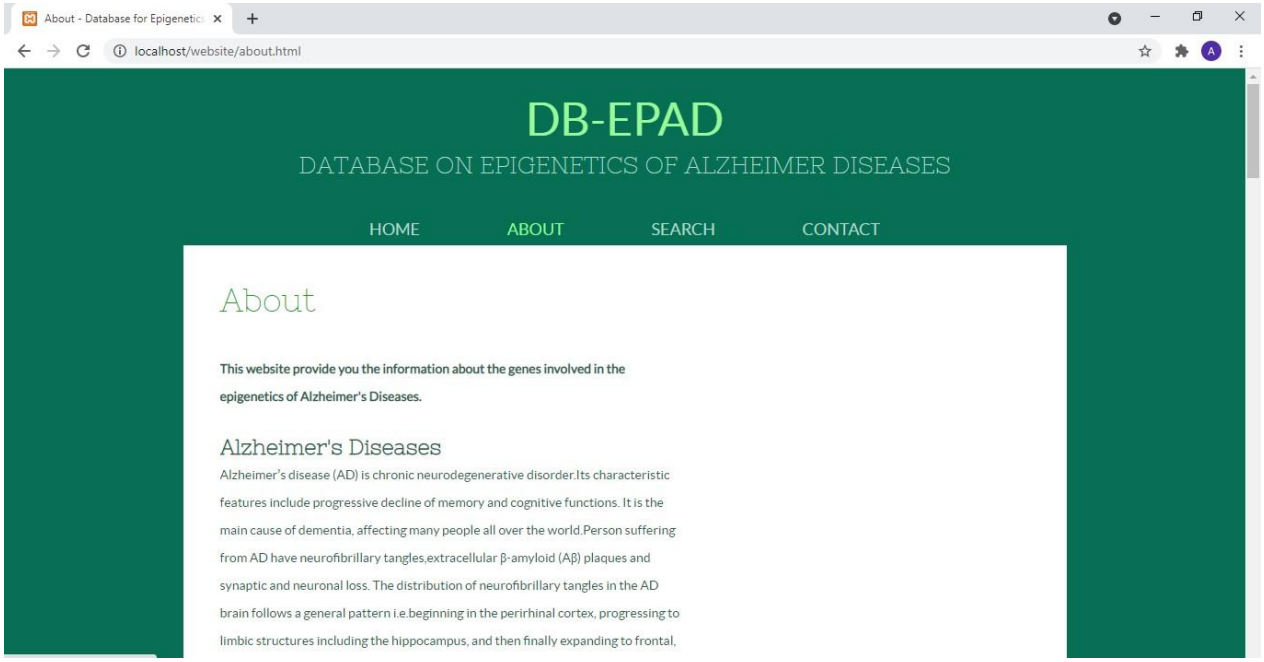

Figure 15.About page of the website.

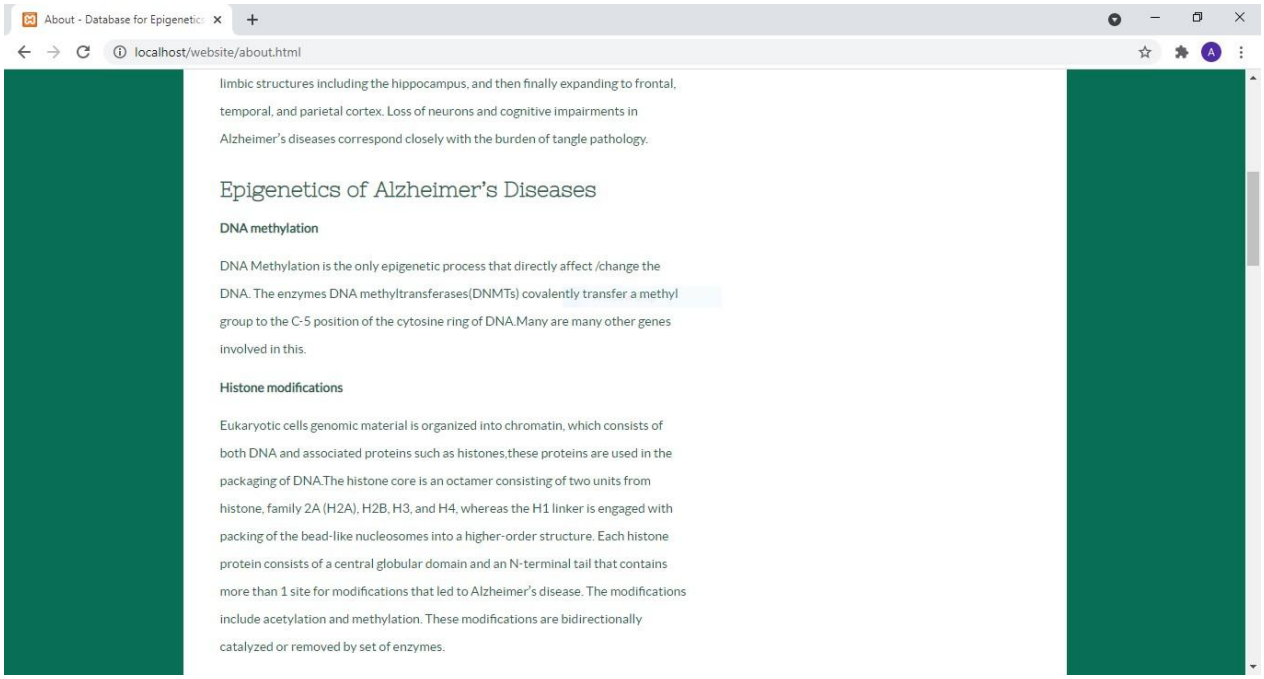

Figure 16.About page of the website showing information related to DNA Methylation and histone modifications.

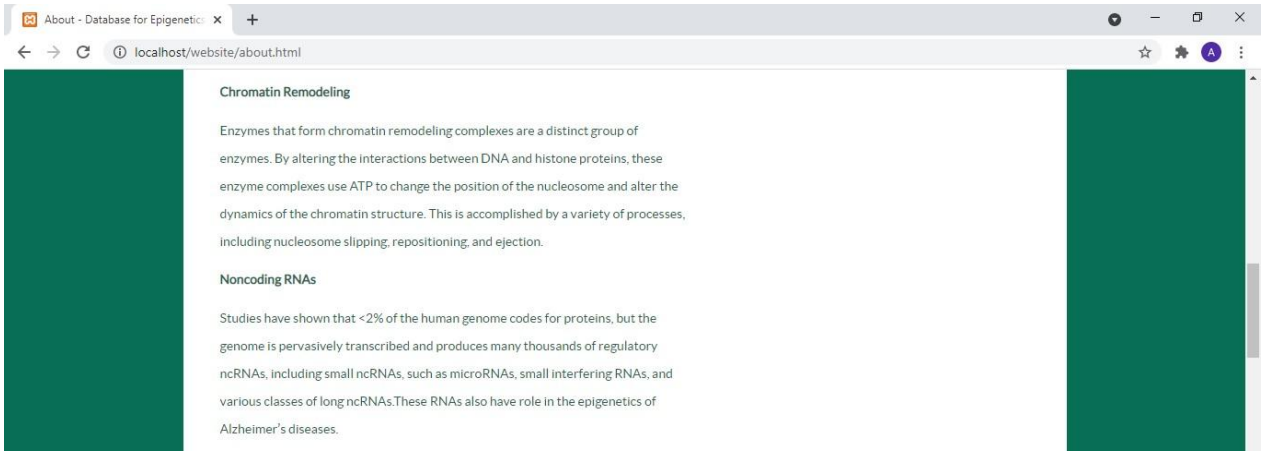

Figure 17.About page showing information about Chromatin remodeling and Non-Coding DNA.

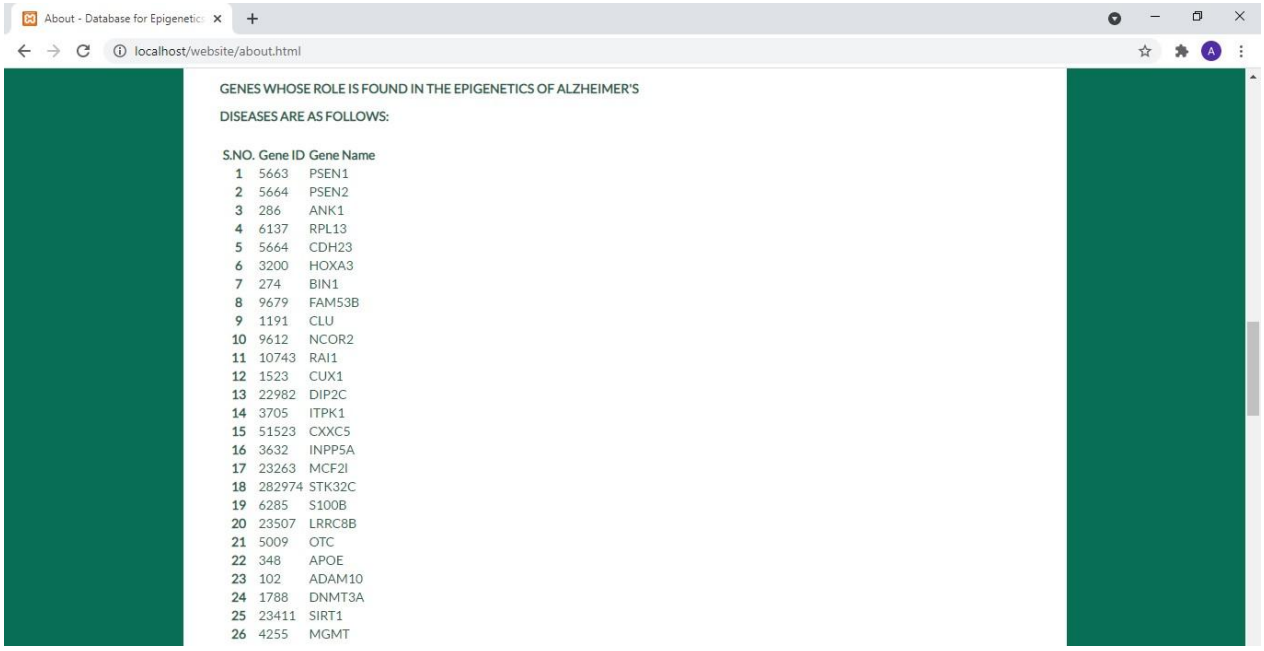

Figure 18. About page showing information about genes involved.

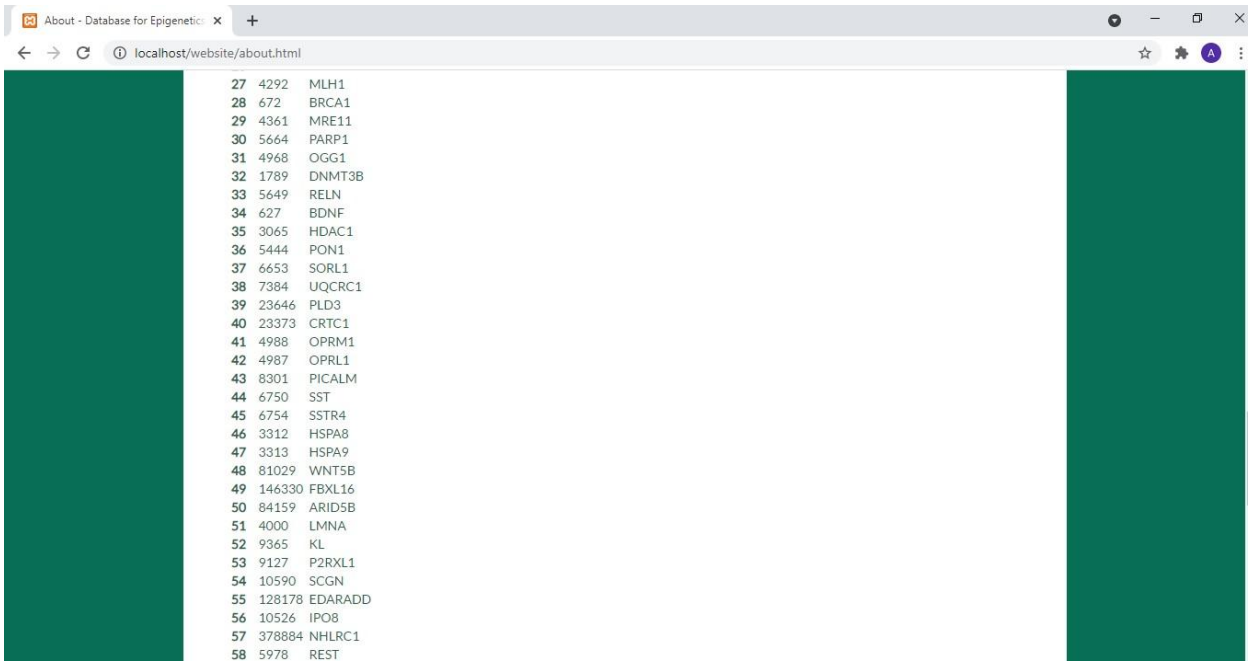

Figure 19.About page showing set of genes and their gene ids.

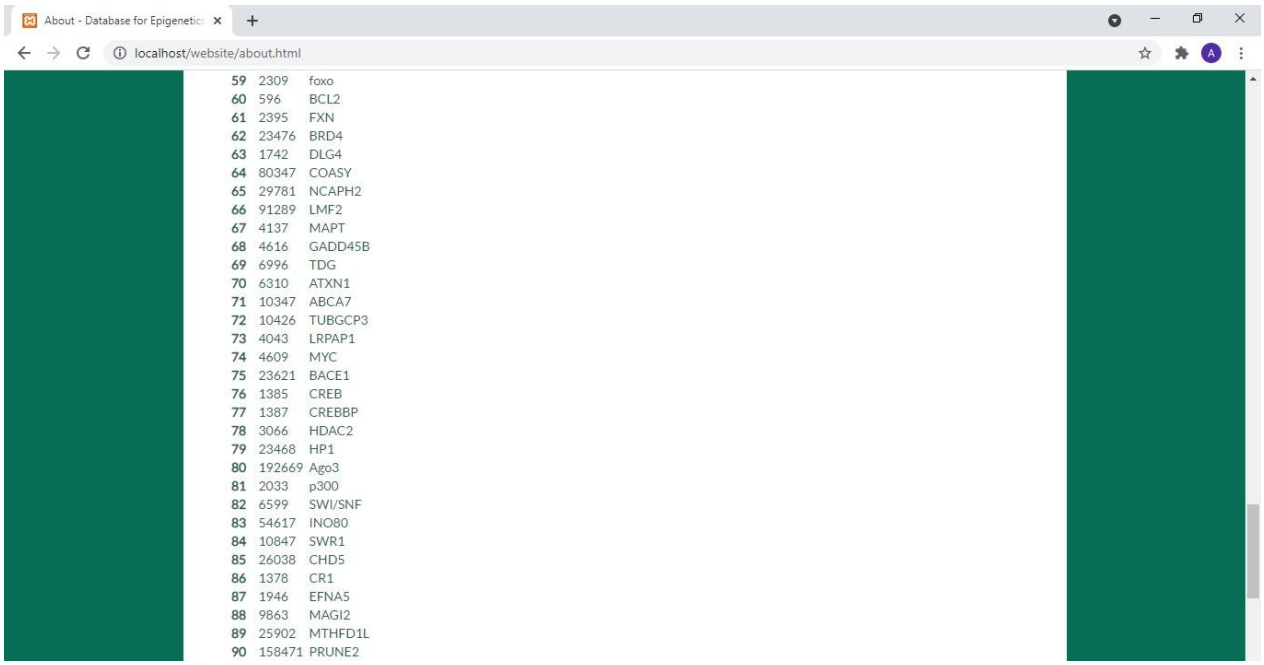

Figure 20.About page showing set of genes and their gene ids which are responsible for Alzheimer's epigenetics.

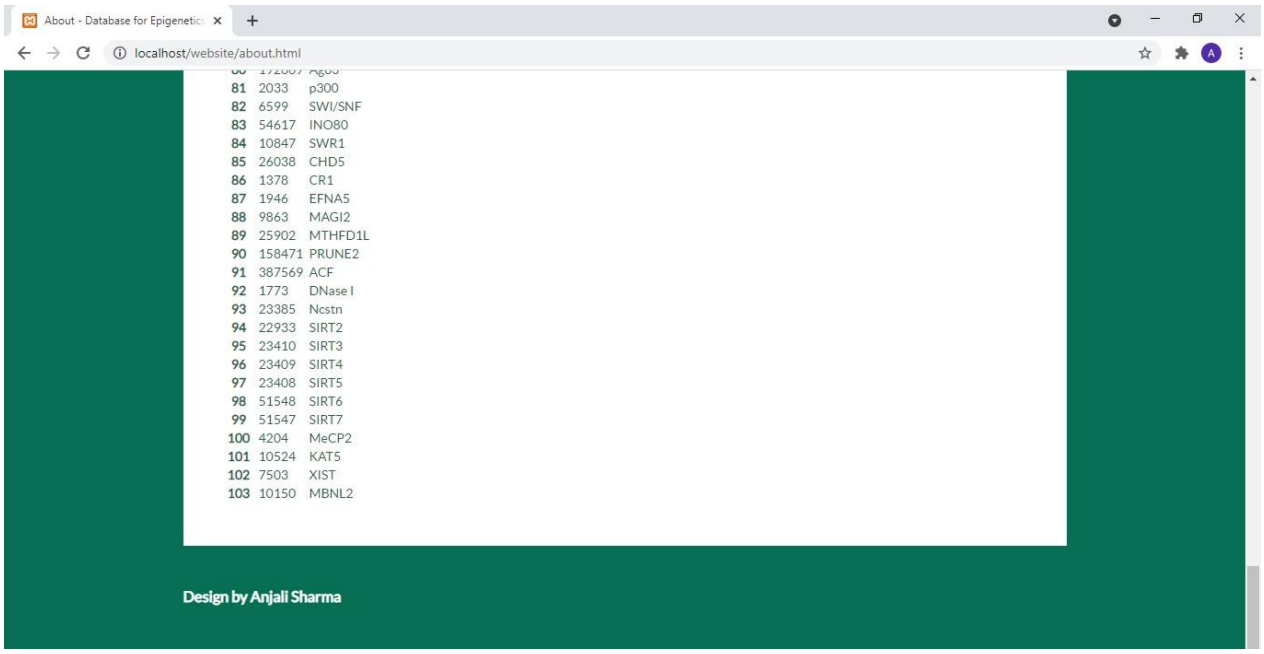

Figure 21. Bottom part of about page.

SEARCH PAGE:-

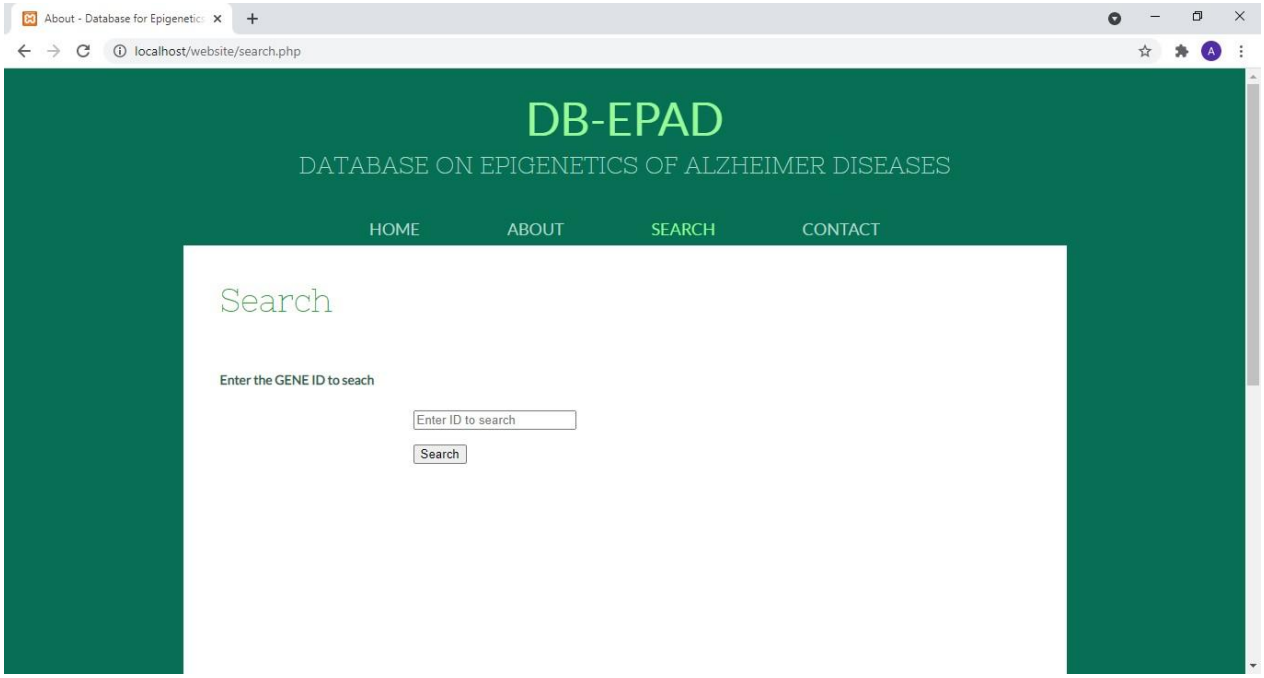

Figure 22. Search page of the website.

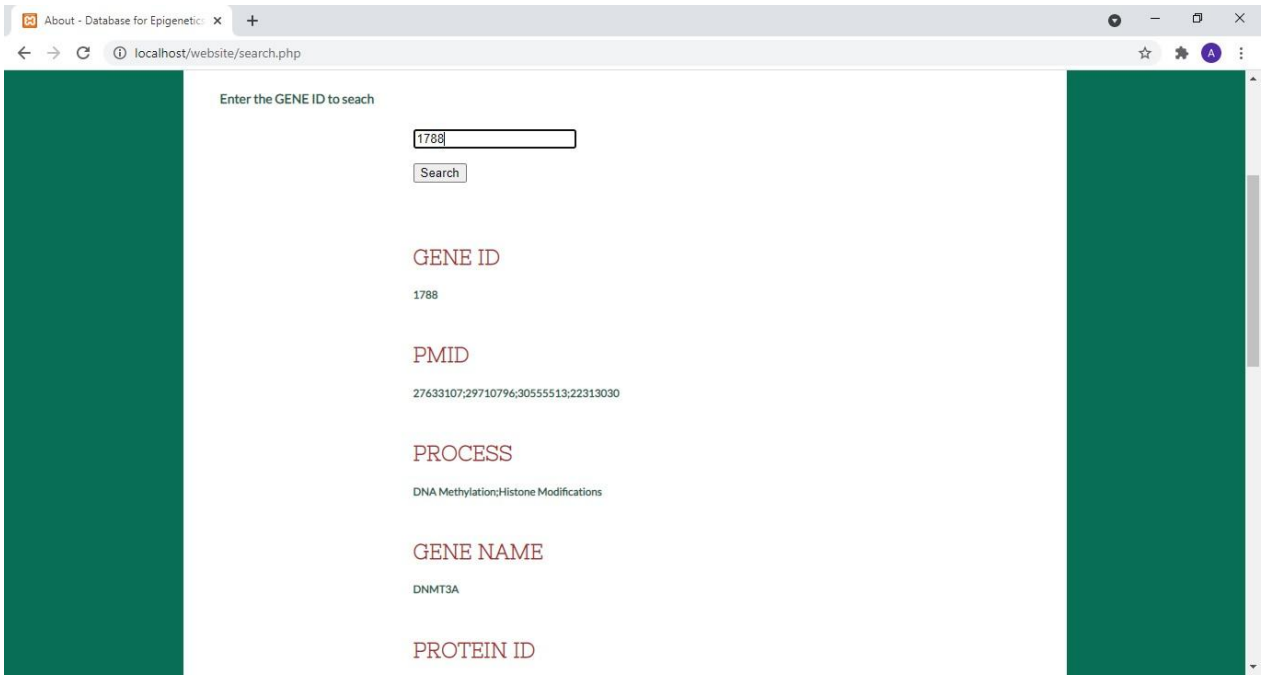

Figure 23.Search page showing results.

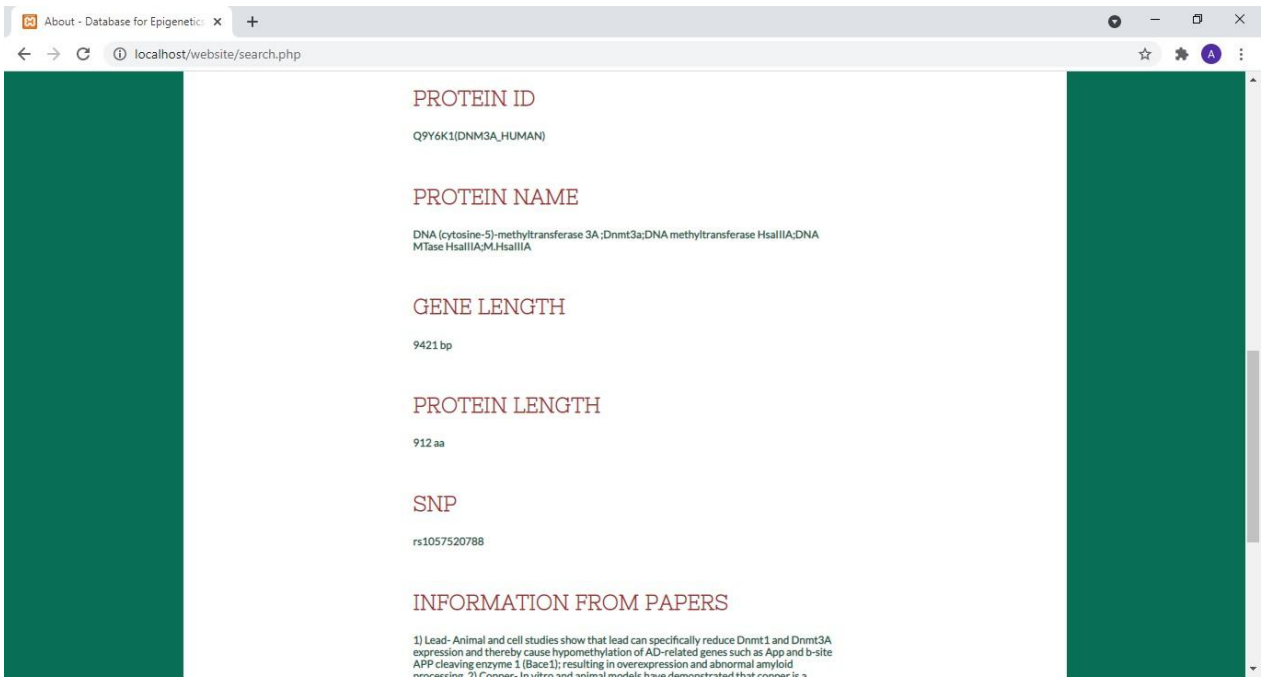

Figure 24.Search page showing results for the Gene id 1788.

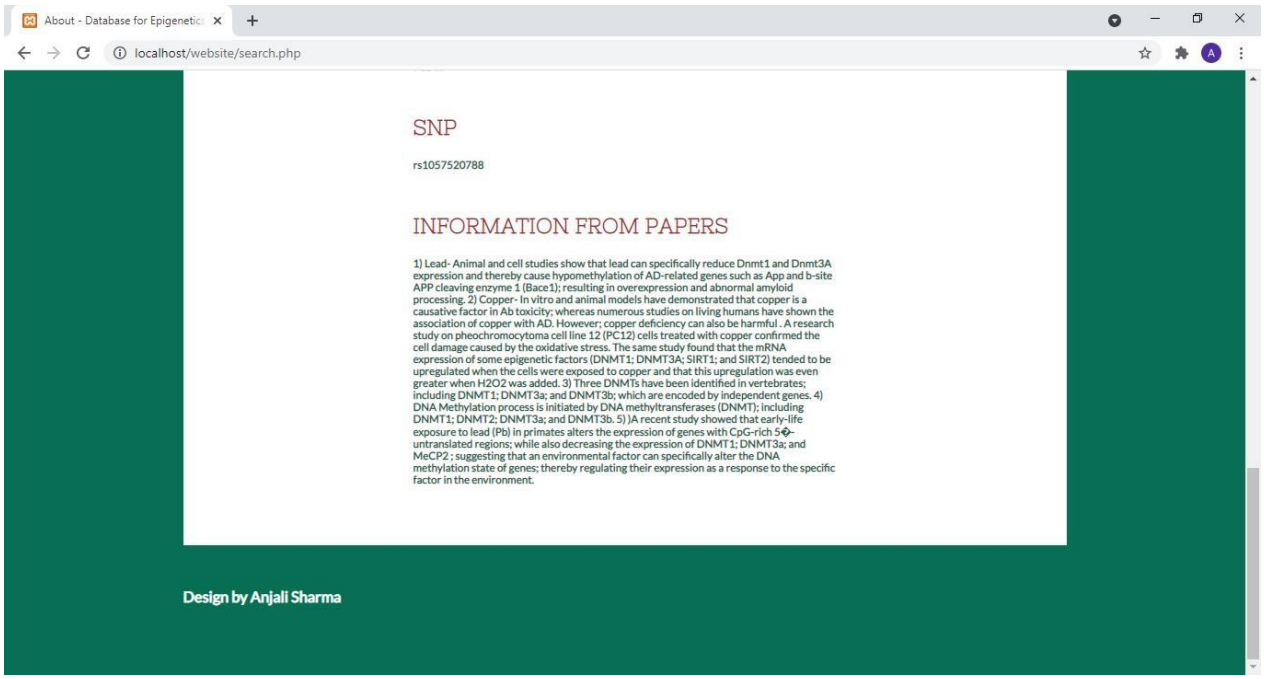

Figure 25.Search page showing results for gene id 1788, in this particular case information about that gene which is present in research papers is showing.

CONTACT PAGE:-

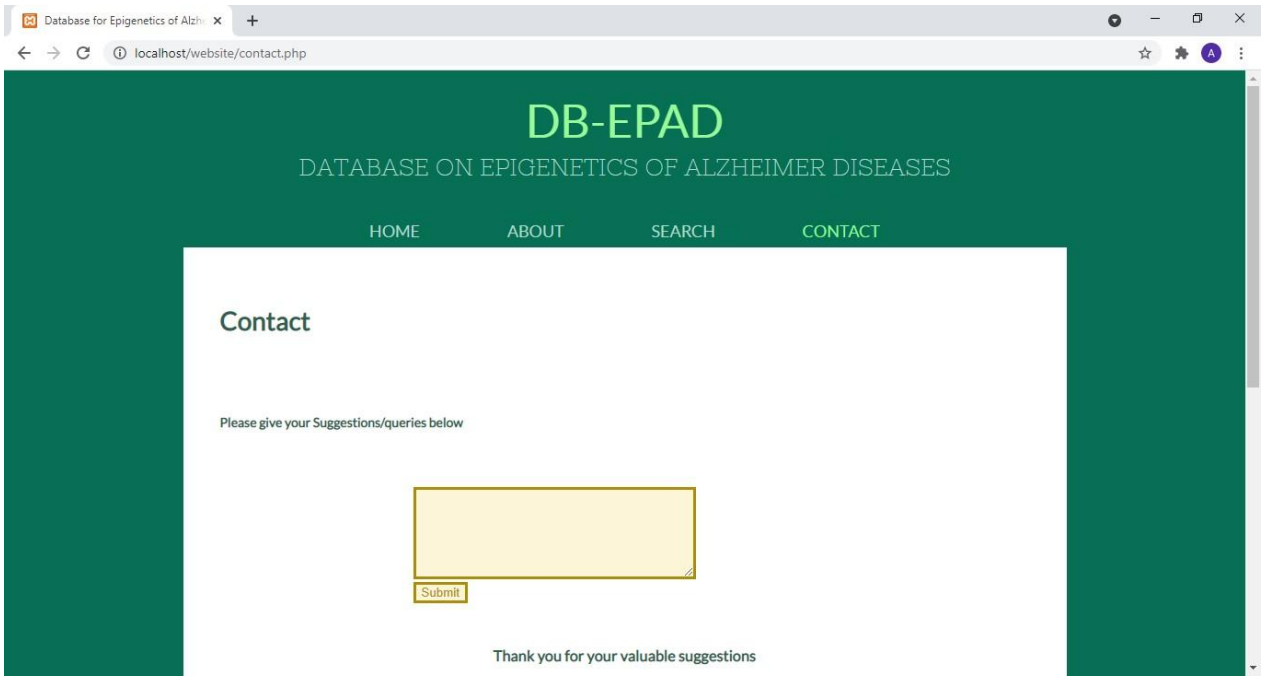

Figure 26. Contact page of the website.

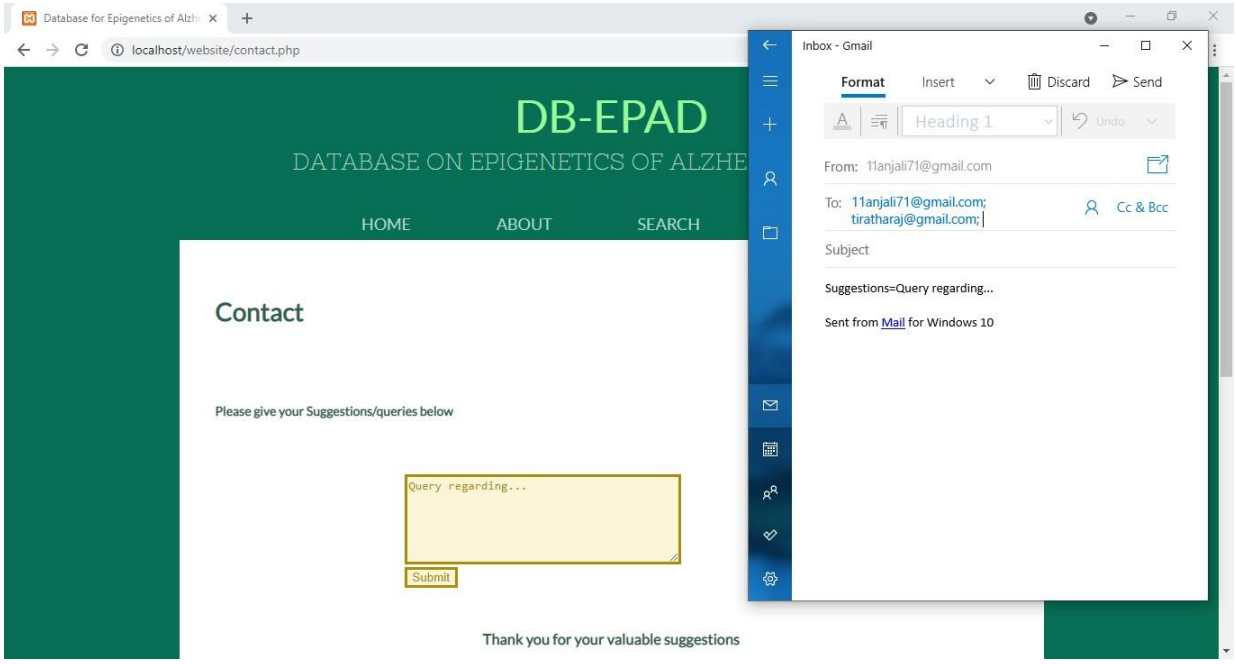

Figure 27. Screenshot of contact page, when submit button is pressed it will redirect to email.

5. CONCLUSION

Alzheimer's disease is a neurodegenerative disease which causes memory losses. It is affecting many people worldwide. Nerve cells progressively deteriorate in this disease. The main features characterized by the diseases involve the accumulation of plaques in the brain.Many factors like genetic, environmental and epigenetic factors can lead to this diseases. Our study includes studying epigenetics of Alzheimer's diseases and make a database on the involved genes and information related to this gene. In the future this database can be further updated with more genes, and other fields/parameters.

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7.APPENDIX

Common CSS Code for each page i.e,(index.html,about.html,search.php,contact.php):

(style.css):-

```
body {
	background: #077054;
	color: #315f52;
	font-family: 'latoregular';
	font-size: 14px;
	margin: 0;
	padding: 0;
}
@font-face {
	font-family: 'latoregular';
	src: url('../fonts/lato-regular-webfont.eot');
	src: url('../fonts/lato-regular-webfont.eot?#iefix') format('embedded-opentype'),
		url('../fonts/lato-regular-webfont.woff') format('woff'),
		url('../fonts/lato-regular-webfont.ttf') format('truetype'),
		url('../fonts/lato-regular-webfont.svg#latoregular') format('svg');
	font-weight: normal;
```

```
	font-style: normal;
}
@font-face {
	font-family: 'nixie_oneregular';
	src: url('../fonts/nixieone-regular-webfont.eot');
	src: url('../fonts/nixieone-regular-webfont.eot?#iefix') format('embedded-opentype'),
		url('../fonts/nixieone-regular-webfont.woff') format('woff'),
		url('../fonts/nixieone-regular-webfont.ttf') format('truetype'),
		url('../fonts/nixieone-regular-webfont.svg#nixie_oneregular') format('svg');
	font-weight: normal;
	font-style: normal;
}
a {
	outline: none;
}
img {
	border: none;
}
p {
	line-height: 30px;
	margin: 0;
```

```
}
p a {
	color: #315f52;
}
p a:hover {
	color: #451374;
}
#header {
	margin: 0 auto;
	max-width: 960px;
}
#header h1 {
	font-size: 50px;
	font-weight: normal;
	line-height: 50px;
	margin: 0;
	padding: 30px 0;
	text-align: center;
}
#header h1 a {
	color: #99fa99;
```

```
        text-decoration: none;
}
#header h1 a span {
        color: #b6d8cf;
        display: block;
        font-family: 'nixie_oneregular';
        font-size: 26px;
        text-transform: uppercase;
}
#header ul#navigation {
        list-style: none;
        margin: 0;
        padding: 0;
        text-align: center;
}
#header ul#navigation li {
        display: inline;
        line-height: 30px;
        position: relative;
}
#header ul#navigation li a {
```

```
        color: #b6d8cf;
        font-size: 18px;
        padding: 0 46px;
        text-align: center;
        text-decoration: none;
        text-transform: uppercase;
}
#header ul#navigation li a:hover,
#header ul#navigation li.current ul li a:hover {
        color: #d3a3ff;
}
#header ul#navigation li.current a {
        color: #99fa99;
}
#header ul#navigation li ul {
        display: none;
        left: 0;
        list-style: none outside none;
        margin: 0;
        padding: 11px 0 0;
        position: absolute;
```

```
        top: 12px;
}
#header ul#navigation li:hover ul {
        display: block;
}
#header ul#navigation li ul li {
        background:  #077054;
        display: block;
        height: 46px;
        line-height: 46px;
}
#header ul#navigation li ul li a {
        padding: 0 20px;
}
#header ul#navigation li.current ul li a {
        color: #b6d8cf;
}
#body {
        background: #ffffff;
        margin: 1px auto 0;
        max-width: 880px;
```

```
        min-height: 827px;
        overflow: hidden;
        padding: 45px 40px 46px;
}
#body > h2 {
        color: #21a51e;
        font-family: 'nixie_oneregular';
        font-size: 35px;
        font-weight: normal;
        line-height: 30px;
        margin: 0;
        padding: 0 0 44px;
}
#body img.figure {
        display: block;
        float: right;
        margin: 74px 38px 46px 0;
        max-width: 100%;
        width: auto;
}
#body div#tagline {
```

```
        float: left;
        margin: 110px 0 0 25px;
        max-width: 510px;
}
#body div#tagline h1 {
        background: url(../images/bg-separator.png) no-repeat center bottom;
        color: #21a51e;
        font-family: 'nixie_oneregular';
        font-size: 100px;
        font-weight: normal;
        line-height: 100px;
        margin: 0;
        padding: 0 0 55px;
        text-align: center;
        text-transform: uppercase;
}
#body div#tagline p {
        color: #21a51e;
        font-family: 'nixie_oneregular';
        font-size: 100px;
        line-height: 100px;
```

```
        padding: 43px 0 0;
        text-align: center;
}
#body div.content {
        overflow: hidden;
}
#body div.content > div {
        float: left;
        width: 510px;
}
#body div.content h3,
#body form h3,
#body ul.blog li h3 {
        font-family: 'nixie_oneregular';
        font-size: 23px;
        font-weight: normal;
        line-height: 30px;
        margin: 0;
        padding: 25px 0 0;
}
#body div.content h3:first-child,
```

```
#body div.content div div.section:first-child {
	padding: 0;
}
#body div.content img.figure {
	margin: 0 38px 46px 0;
}
#body div.content div div.section {
	padding: 55px 0 0;
	width: 430px;
}
#body div.content div div.section span {
	display: block;
	line-height: 30px;
}
#body div.content div ul {
	list-style: none;
	margin: 0;
	overflow: hidden;
	padding: 0 0 65px;
}
#body div.content div ul li {
```

```
        float: left;
        margin: 0 0 0 83px;
        width: 207px;
}
#body div.content div ul li:first-child {
        margin: 0;
}
#body div.content div ul li img {
        display: block;
        max-width: 100%;
        width: auto;
}
#body div.content div ul li h4 {
        font-family: 'nixie_oneregular';
        font-size: 18px;
        font-weight: normal;
        margin: 0;
        padding: 12px 0 0;
        text-align: center;
}
#body form {
```

```
        margin: 25px auto 0;
        overflow: hidden;
        width: 460px;
}
#body form label {
        display: block;
        padding: 15px 0 0;
}
#body form label span {
        display: block;
        line-height: 27px;
        padding: 0 0 5px
}
#body form label input {
        background: #d1d3d4;
        border: 1px solid #b6d8cf;
        color: #315f52;
        display: block;
        font-family: 'latoregular';
        font-size: 14px;
        height: 46px;
```

```
        line-height: 46px;
        padding: 0 5px;
        width: 448px;
}
#body form label textarea {
        background: #d1d3d4;
        border: 1px solid #b6d8cf;
        color: #315f52;
        display: block;
        font-family: 'latoregular';
        font-size: 14px;
        height: 250px;
        line-height: 30px;
        overflow: auto;
        padding: 0 5px;
        resize: none;
        width: 448px;
}
#body form input#send {
        background: #077054;
        border: none;
```

```
        border-radius: 5px;
        color: #99fa99;
        cursor: pointer;
        font-family: 'latoregular';
        font-size: 14px;
        float: right;
        height: 30px;
        margin: 8px 0 0;
        width: 50px;
}
#body form input#send:hover {
        background: #d3a3ff;
        color: #000000;
}
#body ul.blog {
        list-style: none;
        margin: 0;
        padding: 0;
}
#body ul.blog li {
        overflow: hidden;
```

```
        padding: 104px 100px 0 0;
}
#body ul.blog li:first-child {
        padding: 0 100px 0 0;
}
#body ul.blog li img {
        display: block;
        float: left;
        margin: 0 20px 0 0;
        max-width: 100%;
        width: auto;
}
#body ul.blog li h3 {
        line-height: 20px;
        padding: 0 0 8px;
}
#body ul.blog li h3 a,
#body div.content div.sidebar ul li h4 a {
        color: #315f52;
        text-decoration: none;
}
```

```
#body ul.blog li h3 a:hover,
#body div.content div.sidebar ul li h4 a:hover {
	text-decoration: underline;
}
#body ul.blog li span,
#body div.content div.article span,
#body div.content div.sidebar ul li span {
	display: block;
	line-height: 30px;
}
#body div.content div.article {
	width: 570px;
}
#body div.content div.article img {
	display: block;
	margin: 0 0 9px;
	max-width: 100%;
	width: auto;
}
#body div.content div.article p {
	padding: 0 0 30px;
```

```
}
#body div.content div.sidebar {
	float: left;
	margin: 0 0 0 50px;
	width: 259px;
}
#body div.content div.sidebar ul {
	padding: 20px 0 0;
}
#body div.content div.sidebar ul li {
	border-top: 1px solid #88b4a8;
	float: none;
	margin: 0;
	padding: 18px 0 28px;
	width: auto;
}
#body div.content div.sidebar ul li:first-child {
	border: none;
	padding: 0 0 28px;
}
#body div.content div.sidebar ul li h4 {
```

```
        line-height: 30px;
        text-align: left;
}
#footer {
        margin: 0 auto;
        max-width: 960px;
        overflow: hidden;
        padding: 30px 0 60px;
}
#footer div {
        float: left;
        width: 500px;
}
#footer div span {
        color: #99fa99;
        display: block;
        font-size: 26px;
        line-height: 24px;
}
#footer div p {
        color: #b6d8cf;
```

```
        font-size: 12px;
        line-height: 30px;
}
#footer div#connect {
        float: right;
        overflow: hidden;
        width: auto;
}
#footer div#connect a {
        background: url(../images/icons.png) no-repeat;
        display: block;
        float: left;
        text-indent: -99999px;
}
#footer div#connect a#facebook {
        background-position: 0 0;
        height: 30px;
        width: 16px;
}
#footer div#connect a#twitter {
        background-position: 0 -30px;
```

```
        height: 30px;
        margin: 0 0 0 28px;
        width: 37px;
}
#footer div#connect a#googleplus {
        background-position: 0 -61px;
        height: 32px;
        margin: 0 0 0 19px;
        width: 32px;
}
#footer div#connect a#googleplus {
        background-position: 0 -61px;
        height: 32px;
        margin: 0 0 0 19px;
        width: 32px;
}
#footer div#connect a#pinterest {
        background-position: 0 -94px;
        height: 30px;
        margin: 0 0 0 23px;
        width: 30px;
```

```
}
```

CSS Styling for website when used in mobile phones:

(mobile.css):-

```
@media only screen and (max-width : 918px) {
	html {
		-webkit-text-size-adjust: none;
	}
	#mobile-navigation {
		background: url(../images/mobile/mobile-menu.png) no-repeat 0 0;
		display: block;
		height: 50px;
		margin: 0;
		padding: 0;
		position: absolute;
		right: 0;
		top: 20px;
		width: 50px;
		z-index: 1001;
	}
```

```
#header ul#navigation {
        background: url(../images/mobile/bg-mobile.png);
        border: 1px solid #99fa99;
        display: none;
        font-size: 1.5625em;
        height: auto;
        left: 0;
        margin: 0 auto;
        position: absolute;
        padding: 0;
        top: 71px;
        transition: all .5s ease-in-out;
        width: 100%;
        z-index: 1001;
}
#header ul#navigation li {
        background: none;
        display: block;
        float: none;
        height: auto;
        line-height: normal;
```

```
        margin: 0;
        padding: 0;
        text-align: center;
        width: 100%;
}
#header ul#navigation li:first-child,
#header ul#navigation li ul li:first-child {
        border: none;
        width: 100%;
}
#header ul#navigation li a {
        background: none;
        border-top: 1px solid #99fa99;
        color: #ffffff;
        display: block;
        font-family: Arial;
        font-size: 0.8125em;
        font-weight: normal;
        height: 49px;
        line-height: 49px;
        padding: 0 15px;
```

```
        text-align: left;
        width: auto;
}
#header ul#navigation li span {
        background: transparent url(../images/mobile/mobile-expand.png) no-repeat;
        border-left: 1px solid #99fa99;
        border-top: 1px solid #99fa99;
        display: block;
        height: 49px;
        position: absolute;
        right: 0;
        top: 0;
        width: 50px;
}
#header ul#navigation li.current span {
        background: url(../images/mobile/mobile-expand.png) no-repeat;
}
#header ul#navigation li.current ul li a {
        background: none;
        color: #ffffff;
}
```

```
#header ul#navigation li a:hover,
#header ul#navigation li.current ul li a:hover,
#header ul#navigation li.current a {
	background: rgba(153, 250, 153, 0.8);
	color: #ffffff;
}
#header ul#navigation > li:first-child > a {
	border: none;
}
#header ul#navigation li ul {
	border: 0;
	display: none;
	left: 0;
	margin: 0;
	opacity: 1;
	padding: 0;
	position: relative;
	top: 0;
	width: 100%;
}
#header ul#navigation li ul,
```

```
#header ul#navigation li:hover ul {
	display: none;
}
#header ul#navigation li ul li {
	background: none;
	height: auto;
	line-height: normal;
	padding: 0;
	text-align: left;
}
#header ul#navigation li ul li a {
	padding: 0 30px;
}
#header {
	position: relative;
	width: 90%;
}
#header h1 {
	padding: 74px 0 0;
}
#body {
```

```
        margin: 20px auto 0;
        padding: 45px 0 46px;
        width: 90%;
}
#body div#tagline {
        float: none;
        margin: 20px auto 0;
        width: 90%;
}
#body div#tagline h1 {
        background-size: 37% auto;
        line-height: 1em;
        padding: 0 0 50px;
}
#body div#tagline p {
        font-size: 5em;
        line-height: 1.25em;
        padding: 43px 10px;
}
#body img.figure {
        float: none;
```

```
        margin: 0 auto;
        width: 70%;
}
#body > h2 {
        padding: 0 20px 30px;
}
#body div.content {
        padding: 0 20px;
}
#body div.content div,
#footer div {
        float: none;
        width: auto;
}
#body div.content img.figure {
        margin: 0 auto;
}
#body div.content div div.section {
        padding: 30px 0 0;
        width: auto;
}
```

```
#body div.content div ul li {
	margin: 0 5%;
	width: 40%;
}
#body div.content div ul li:first-child {
	margin: 0 5%;
}
#body form {
	margin: 0 auto;
	padding: 0 20px;
	width: auto;
}
#body form h3,
#body ul.blog li:first-child {
	padding: 0;
}
#body form label input,
#body form label textarea {
	border-radius: 0;
	padding: 0 3%;
	-webkit-appearance: none;
```

```
        width: 93%;
}
#body form input#send {
        margin: 8px 2px 0 0;
        padding: 0;
        text-align: center;
        -webkit-appearance: none;
}
#body ul.blog {
        padding: 0 20px;
}
#body ul.blog li {
        padding: 30px 0 0;
}
#body ul.blog li img {
        margin: 0 0 20px;
        width: 100%;
}
#body ul.blog li h3 {
        line-height: 1.35em;
}
```

```
#body div.content div.article {
	width: auto;
}
#body div.content div.sidebar {
	float: none;
	margin: 0;
	width: auto;
}
#body div.content div.sidebar ul li:first-child {
	margin: 0;
}
#footer {
	padding: 20px 0;
	width: 90%;
}
#footer div span {
	line-height: 1.25em;
	text-align: center;
}
#footer div p {
	font-size: 1.125em;
```

```
            line-height: 1.65em;
            padding: 20px 0 0;
            text-align: center;
        }
        #footer div#connect {
            float: none;
            margin: 30px auto 0;
            max-width: 185px;
        }
}
@media screen
and (max-width : 320px) {
        #header h1 {
            font-size: 2.8125em;
        }
        #header h1 a span {
            font-size: 0.5em;
            line-height: 1.25em;
        }
        #body div#tagline h1 {
            font-size: 4.375em;
```

```
	}
	#body div#tagline p {
		font-size: 3.125em;
	}
	#footer div p {
		font-size: 1em;
	}
}
```

Code of Home page(index.html):-

```
<!DOCTYPE html>
<html>
<head>
	<meta charset="UTF-8">
	<meta name="viewport" content="user-scalable=0, width=device-width, initial-scale=1.0, maximum-scale=1.0, minimum-scale=1.0">
	<title>Database for Epigenetics of Alzheimer's Diseases</title>
	<link rel="stylesheet" type="text/css" href="css/style.css">
	<link rel="stylesheet" type="text/css" href="css/mobile.css">
	<script type='text/javascript' src='js/mobile.js'></script>
```

```
</head>
<body>
    <div id="header">
        <h1><a href="index.html">DB-EPAD<span>Database on Epigenetics Of Alzheimer Diseases</span></a></h1>
        <ul id="navigation">
            <li class="current">
                <a href="index.html">Home</a>
            </li>
            <li>
                <a href="about.html">About</a>
            </li>
            <li>
                <a href="search.php">Search</a>
            </li>
            <li>
                <a href="contact.php">Contact</a>
            </li>
        </ul>
    </div>
    <div id="body">
```

```
        <img src="images/photoalz.jpg" alt="epigenetics of Alz" class="figure">
    </div>
    <div id="footer">
        <div>
        <p>
                <h3><b><font color="white";> Design by Anjali Sharma</b></h3>
        </p>
        </div>
        </div>
</body>
</html>
```

Code of About page (about.html):-

```
<!DOCTYPE html>
<html>
<head>
    <meta charset="UTF-8">
    <meta name="viewport" content="user-scalable=0, width=device-width, initial-scale=1.0, maximum-scale=1.0, minimum-scale=1.0">
    <title>About - Database for Epigenetics of Alzheimer's Diseases</title>
    <link rel="stylesheet" type="text/css" href="css/style.css">
```

```
        <link rel="stylesheet" type="text/css" href="css/mobile.css">
        <script type='text/javascript' src='js/mobile.js'></script>
</head>
<body>
        <div id="header">
                <h1><a href="index.html">DB-EPAD<span>Database on Epigenetics Of Alzheimer Diseases</span></a></h1>
                <ul id="navigation">
                        <li>
                                <a href="index.html">Home</a>
                        </li>
                        <li class="current">
                                <a href="about.html">About</a>
                        </li>
                        <li>
                                <a href="search.php">Search</a>
                        </li>
                        <li>
                                <a href="search.php">Contact</a>
                        </li>
                      </ul>
```

```
</div>

<div id="body">

    <h2>About</h2>

    <div class="content">

        <div>

            <p><b> This website provide you the information about the genes involved in the epigenetics of Alzheimer's Diseases.</b></p>

<h3><strong>Alzheimer's Diseases</strong></h3>

<p>Alzheimer’s disease (AD) is chronic neurodegenerative disorder.Its characteristic features include progressive decline of memory and cognitive functions. It is the main cause of dementia, affecting many people all over the world.Person suffering from AD have neurofibrillary tangles,extracellular β-amyloid (Aβ) plaques and synaptic and neuronal loss. The distribution of neurofibrillary tangles in the AD brain follows a general pattern i.e.beginning in the perirhinal cortex, progressing to limbic structures including the hippocampus, and then finally expanding to frontal, temporal, and parietal cortex. Loss of neurons and cognitive impairments in Alzheimer’s diseases correspond closely with the burden of tangle pathology.<p>

<h3><strong>Epigenetics of Alzheimer’s Diseases</strong></h3>

  <h4>DNA methylation</h4>

<p>DNA Methylation is the only epigenetic process that directly affect /change the DNA. The enzymes DNA methyltransferases(DNMTs) covalently transfer a methyl group to the C-5 position of the cytosine ring of DNA.Many are many other genes involved in this.</p>

<h4>Histone modifications</h4>

<p>Eukaryotic cells genomic material is organized into chromatin, which consists of both DNA and associated proteins such as histones,these proteins are used in the packaging of DNA.The histone core is an octamer consisting of two units from histone, family 2A (H2A), H2B, H3, and
```

H4, whereas the H1 linker is engaged with packing of the bead-like nucleosomes into a higher-order structure. Each histone protein consists of a central globular domain and an N-terminal tail that contains more than 1 site for modifications that led to Alzheimer's disease. The modifications include acetylation and methylation. These modifications are bidirectionally catalyzed or removed by set of enzymes.

<h4>Chromatin Remodelling </h4>

Enzymes that form chromatin remodeling complexes are a distinct group of enzymes. By altering the interactions between DNA and histone proteins, these enzyme complexes use ATP to change the position of the nucleosome and alter the dynamics of the chromatin structure. This is accomplished by a variety of processes, including nucleosome slipping, repositioning, and ejection.

<h4>Noncoding RNAs</h4>

Studies have shown that <2% of the human genome codes for proteins, but the genome is pervasively transcribed and produces many thousands of regulatory ncRNAs, including small ncRNAs, such as microRNAs, small interfering RNAs, and various classes of long ncRNAs.These RNAs also have role in the epigenetics of Alzheimer's diseases.

GENES WHOSE ROLE IS FOUND IN THE EPIGENETICS OF ALZHEIMER'S DISEASES ARE AS FOLLOWS:

<table>

<tr><th>S.NO.</th> <th>Gene ID</th><th>Gene Name</th></tr>

<tr> <th>1</th> <td>5663</td> <td>PSEN1</td> </tr>

<tr> <th>2</th> <td> 5664</td> <td>PSEN2</td></tr>

<tr><th>3</th> <td> 286</td> <td>ANK1</td> </tr>

<tr><th>4</th><td> 6137</td><td>RPL13</td> </tr>

<tr> <th>5</th> <td> 5664</td><td>CDH23</td> </tr>

<tr> <th>6</th> <td> 3200</td><td>HOXA3</td></tr>

<tr> <th>7</th> <td> 274</td> <td>BIN1</td></tr>

<tr><th>8</th> <td> 9679</td> <td>FAM53B</td> </tr>

<tr><th>9</th><td>1191</td><td>CLU</td> </tr>

<tr><th>10</th><td> 9612</td> <td>NCOR2</td></tr>

<tr><th>11</th><td> 10743</td><td>RAI1</td> </tr>

<tr><th>12</th><td> 1523</td><td>CUX1</td></tr>

<tr><th>13</th><td>22982</td><td>DIP2C</td></tr>

<tr><th>14</th><td>3705</td><td>ITPK1</td></tr>

<tr><th>15</th><td> 51523</td><td>CXXC5</td></tr>

<tr><th>16</th><td>3632</td><td>INPP5A</td></tr>

<tr><th>17</th> <td> 23263</td><td>MCF2l</td></tr>

<tr><th>18</th><td> 282974</td><td>STK32C</td></tr>

<tr> <th>19</th><td> 6285</td><td>S100B</td></tr>

<tr><th>20</th><td> 23507</td><td>LRRC8B</td></tr>

<tr><th>21</th><td> 5009</td> <td>OTC</td> </tr>

<tr> <th>22</th><td>348</td><td>APOE</td></tr>

<tr><th>23</th><td>102</td> <td>ADAM10</td></tr>

<tr><th>24</th><td> 1788</td> <td>DNMT3A</td></tr>

<tr><th>25</th><td> 23411</td> <td>SIRT1</td></tr>

<tr><th>26</th><td>4255</td><td>MGMT</td></tr>

<tr><th>27</th> <td> 4292</td><td>MLH1</td></tr>

<tr> <th>28</th><td>672</td><td>BRCA1</td></tr>

<tr> <th>29</th><td>4361</td><td>MRE11</td></tr>

<tr><th>30</th><td> 5664</td><td>PARP1</td></tr>

<tr><th>31</th> <td>4968</td><td>OGG1</td></tr>

<tr><th>32</th><td>1789</td> <td>DNMT3B</td></tr>

<tr><th>33</th><td> 5649</td><td>RELN</td></tr>

<tr><th>34</th><td>627</td><td>BDNF</td></tr>

<tr><th>35</th> <td>3065</td> <td>HDAC1</td></tr>

<tr> <th>36</th><td>5444</td><td>PON1</td></tr>

<tr> <th>37</th><td>6653</td><td>SORL1</td></tr>

<tr><th>38</th><td>7384</td><td>UQCRC1</td> </tr>

 <tr><th>39</th><td>23646</td><td>PLD3</td></tr>

<tr><th>40</th> <td>23373</td><td>CRTC1</td></tr>

<tr><th>41</th> <td>4988</td><td>OPRM1</td></tr>

<tr> <th>42</th> <td>4987</td><td>OPRL1</td> </tr>

<tr><th>43</th><td>8301</td><td>PICALM</td></tr>

<tr><th>44</th><td>6750</td> <td>SST</td></tr>

<tr><th>45</th><td>6754</td><td>SSTR4</td></tr>

<tr><th>46</th> <td>3312</td><td>HSPA8</td> </tr>

<tr> <th>47</th><td>3313</td><td>HSPA9</td></tr>

<tr><th>48</th><td>81029</td> <td>WNT5B</td></tr>

<tr><th>49</th><td>146330</td><td>FBXL16</td></tr>

<tr><th>50</th><td>84159</td><td>ARID5B</td></tr>

<tr><th>51</th><td>4000</td><td>LMNA</td></tr>

<tr><th>52</th><td>9365</td><td>KL</td> </tr>

<tr><th>53</th><td>9127</td><td>P2RXL1</td> </tr>

<tr><th>54</th><td>10590</td> <td>SCGN</td></tr>

<tr><th>55</th><td>128178</td> <td>EDARADD</td></tr>

<tr><th>56</th><td>10526</td><td>IPO8</td> </tr>

<tr><th>57</th><td>378884</td><td>NHLRC1</td> </tr>

<tr><th>58</th><td>5978</td><td>REST</td></tr>

<tr><th>59</th><td>2309</td><td>foxo</td></tr>

<tr><th>60</th><td>596</td><td>BCL2</td></tr>

<tr><th>61</th><td>2395</td><td>FXN</td></tr>

<tr><th>62</th><td>23476</td><td>BRD4</td></tr>

<tr><th>63</th><td>1742</td><td>DLG4</td></tr>

<tr><th>64</th><td>80347</td><td>COASY</td> </tr>

<tr><th>65</th><td>29781</td><td>NCAPH2</td> </tr>

<tr> <th>66</th><td>91289</td><td>LMF2</td> </tr>

<tr> <th>67</th><td>4137</td><td>MAPT</td></tr>

<tr> <th>68</th><td>4616</td><td>GADD45B</td></tr>

<tr> <th>69</th><td>6996</td><td>TDG</td></tr>

<tr> <th>70</th><td>6310</td><td>ATXN1</td></tr>

<tr><th>71</th><td>10347</td><td>ABCA7</td></tr>

<tr><th>72</th><td>10426</td><td>TUBGCP3</td> </tr>

<tr><th>73</th><td>4043</td><td>LRPAP1</td></tr>

<tr><th>74</th><td>4609</td><td>MYC</td> </tr>

<tr><th>75</th><td>23621</td><td>BACE1</td> </tr>

<tr><th>76</th><td>1385</td><td>CREB</td> </tr>

<tr><th>77</th> td>1387</td><td> < CREBBP</td>

<tr> <th>78</th> <td>3066</td><td>HDAC2</td></tr>

<tr><th>79</th> <td>23468</td><td>HP1</td></tr>

<tr><th>80</th><td>192669</td><td>Ago3</td></tr>

<tr><th>81</th><td>2033</td><td>p300</td></tr>

<tr><th>82</th><td>6599</td> <td>SWI/SNF</td></tr>

<tr><th>83</th><td> 54617</td><td>INO80</td> </tr>

<tr><th>84</th><td>10847</td><td>SWR1</td></tr>

<tr><th>85</th><td>26038</td><td>CHD5</td></tr>

<tr><th>86</th><td>1378</td><td>CR1</td></tr>

<tr><th>87</th><td>1946</td><td>EFNA5</td></tr>

<tr><th>88</th><td>9863</td><td>MAGI2</td></tr>

<tr><th>89</th><td>25902</td><td>MTHFD1L</td></tr>

<tr><th>90</th><td>158471</td><td>PRUNE2</td></tr>

<tr><th>91</th> <td>387569</td> <td>ACF</td> </tr>

<tr><th>92</th><td>1773</td><td>DNase I</td> </tr>

<tr><th>93</th><td>23385</td><td>Ncstn</td></tr>

<tr><th>94</th><td>22933</td><td>SIRT2</td></tr>

<tr> <th>95</th><td>23410</td><td>SIRT3</td></tr>

<tr><th>96</th><td>23409</td><td>SIRT4</td> </tr>

<tr><th>97</th><td>23408</td><td>SIRT5</td></tr>

<tr><th>98</th><td>51548</td><td>SIRT6</td></tr>

<tr><th>99</th><td>51547</td><td>SIRT7</td></tr>

<tr><th>100</th> <td>4204</td> <td>MeCP2</td></tr>

<tr> <th>101</th><td>10524</td> <td>KAT5</td> </tr>

<tr><th>102</th><td>7503</td><td>XIST</td></tr>

<tr> <th>103</th> <td>10150</td> <td>MBNL2</td> </tr>

</table>

```
<div id="footer">
<div>
<p>
<h3><b><font color="white";> Design by Anjali Sharma</b></h3>
</p>
</div>
</div>
</body>
</html>
```

Code for search page (search.php):-

```
<!DOCTYPE html>
<html>
<head>
        <meta charset="UTF-8">
        <meta name="viewport" content="user-scalable=0, width=device-width, initial-scale=1.0, maximum-scale=1.0, minimum-scale=1.0">
        <title>About - Database for Epigenetics of Alzheimer's Diseases</title>
        <link rel="stylesheet" type="text/css" href="css/style.css">
        <link rel="stylesheet" type="text/css" href="css/mobile.css">
        <script type='text/javascript' src='js/mobile.js'></script>
  </head>
<body>
        <div id="header">
                <h1><a href="index.html">DB-EPAD<span>Database on Epigenetics Of Alzheimer Diseases</span></a></h1>
```

```
                <ul id="navigation">
                        <li>
                                <a href="index.html">Home</a>
                        </li>
    <li>
                        <a href="about.html">About</a>
                        </li>
                        <li>
      <li class="current">
                                <a href="search.php">Search</a>
                                </li>
                        <li>
                                <a href="contact.php">Contact</a>
                        </li>


                </ul>
            </div>
            <div id="body">
     <h2>Search </h2>
   <h4>Enter the GENE ID to seach </h4>
    <form action="" method="POST">
    <input type="text" name="GENE_ID" placeholder="Enter ID to search"/> <br/><br>
    <input type="submit" name="search" value="Search">
    </form><br>
 <?php
$connection =mysqli_connect("localhost","root","");
$db=mysqli_select_db($connection,'dead');
if(isset($_POST['search']))
{
    $id=$_POST['GENE_ID'];
    $query="SELECT*FROM mytable where GENE_ID='$id' ";
```

```
    $query_run=mysqli_query($connection,$query);
    while($row = mysqli_fetch_array($query_run))
    {
     ?>
     <form action="" method="POST">
    <h3><b><span style="color: brown">GENE ID</</b></h3><tab><h5><?php echo $row['GENE_ID'] ?></h5>
 <h3><b><span style="color: brown">PMID</</b></h3><tab><h5> <?php echo $row['PMID'] ?></h5>
 <h3><b><span style="color: brown">PROCESS</</b></h3><tab><h5> <?php echo $row['PROCESS'] ?></h5>
          <h3><b><span style="color: brown">GENE NAME</</b></h3><tab><h5> <?php echo $row['GENE_NAME'] ?></h5>
 <h3><b><span style="color: brown">PROTEIN ID</</b></h3><tab><h5> <?php echo $row['PROTEIN_ID'] ?></h5>
      <h3><b><span style="color: brown">PROTEIN NAME</</b></h3><tab><h5> <?php echo $row['PROTEIN_NAME'] ?></h5>
       <h3><b><span style="color: brown">GENE LENGTH</</b></h3><tab><h5> <?php echo $row['GENE_LENGTH'] ?></h5>
  <h3><b><span style="color: brown">PROTEIN LENGTH</</b></h3><tab><h5> <?php echo $row['PROTEIN_LENGTH'] ?></h5>
       <h3><b><span style="color: brown">SNP</</b></h3><tab><h5> <?php echo $row['SNP'] ?></h5>
        <h3><b><span style="color: brown">INFORMATION FROM PAPERS</</b></h3><tab><h5> <?php echo $row['INFORMATION_FROM_PAPERS'] ?></h5>
 </form>
  <?php
    }
}
?>
```

```
                    </div>
                    </div>
                   </div>
        <div id="footer">
                <div>
                <p>
                        <h3><b><font color="white";> Design by Anjali Sharma</b></h3>
                    </p>
                </div>
                </div>
</body>
</html>
```

Code for contact page(contact.php):-

```
<!DOCTYPE html>
<html>
<head>
        <meta charset="UTF-8">
        <meta name="viewport" content="user-scalable=0, width=device-width, initial-scale=1.0, maximum-scale=1.0, minimum-scale=1.0">
        <title>Database for Epigenetics of Alzheimer's Diseases</title>
        <link rel="stylesheet" type="text/css" href="css/style.css">
        <link rel="stylesheet" type="text/css" href="css/mobile.css">
        <script type='text/javascript' src='js/mobile.js'></script>
</head>
<body>
        <div id="header">
                <h1><a href="index.html">DB-EPAD<span>Database on Epigenetics Of Alzheimer Diseases</span></a></h1>
```

```
                <ul id="navigation">
                        <li>
                                <a href="index.html">Home</a>
                        </li>
                        <li>
                                <a href="about.html">About</a>
                        </li>
                        <li>
                                <a href="search.php">Search</a>
                         </li>
                        <li class="current">
                                <a href="contact.php">Contact</a>
                        </li>

                </ul>
        </div>
        <div id="body">
        <h1>Contact</h1>
<p style="font-size:100%;"><b><br><br>Please give your Suggestions/queries below </br></br></b> </p>
<?php
$Suggestions= "";
if ($_SERVER["REQUEST_METHOD"] == "POST") {
 if (empty($_POST["Suggestions"])) {
   $Suggestions = "";
  } else {
   $Suggestions = test_input($_POST["Suggestions"]);
  }
}
function test_input($data) {
  $data = trim($data);
```

```
  $data = stripslashes($data);
  $data = htmlspecialchars($data);
  return $data;
}
?>
<form action="mailto:11anjali71@gmail.com;tiratharaj@gmail.com" method="post" enctype="text/plain">

<textarea name="Suggestions" rows="6" cols="40"style="background-color:#FCF5D8;color:#AD8C08;border:3px solid #AD8C08;"><?php echo $Suggestions;?></textarea><br>
<input type="submit"style="background-color:#FCF5D8;color:#AD8C08;border:3px solid #AD8C08; value="Submit!" >
  <br><br>
</form>
<?php
echo "<br>";
echo $Suggestions;
?>
<H3><center>Thank you for your valuable suggestions</center></H3>
        </div>
        <div id="footer">
                <div>

                        <p>
                                <h3><b><font color="white";> Design by Anjali Sharma</b></h3>
                        </p>
                </div>

        </div>
```

```
</body>
</html>
```