Development of database of genes involved in Gastric Cancer

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Date: **ISHITA SOOD**

111504

CERTIFICATE

This is to certify that project report entitled "**Development of database of genes involved in Gastric Cancer**", submitted ISHITA SOOD (111504) in partial fulfillment for the award of degree of Bachelor of Technology in Bioinformatics to Jaypee University of Information Technology, Waknaghat, Solan has been carried out under my supervision.

This work has not been submitted partially or fully to any other University or Institute for the award of this or any other degree or diploma.

Date:

Supervisor's Name: Dr. Jayashree Ramanna

Designation: Assistant Professor (Senior Grade)

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Abstract

Carcinoma of the stomach is still the second most common cause of cancer death worldwide, although the incidence and mortality have fallen dramatically over the last 50 years in many regions. The incidence of gastric cancer varies in different parts of the world and among various ethnic groups. Despite advances in diagnosis and treatment, the 5-year survival rate of stomach cancer is only 20 per cent. There is no source available which integrates all the information of genes and miRNAs scattered in literature. So, we have done exhaustive research from published research articles and collected genes, and miRNA which can serve as a novel biomarker for diagnosis of gastric cancer. We have also provided attributes for these genes and miRNAs like pubmed id, location, chromosome number, mechanism of related gene or miRNA, transcription factors associated, technique used for the identification, reported in body fluid etc. These attributes will help in prioritizing and systematic testing of candidate biomarkers. We have constructed an integrated database with user friendly interface named as Gastric Cancer Database (GCDB). In addition, database provides various browse and search options for user to extraction or exploration of relevant information for all experimentally determined genes and miRNAs present in the database.

1. INTRODUCTION:

1.1 Gastric Cancer

The geographic incidence of gastric cancer has changed dramatically over the last few decades. Prior to 1950, it was the most common cause of cancer death in men, and the third leading cause of cancer death in women in the U.S. Mortality from gastric cancer in the United States has declined, perhaps due to dietary changes. This cancer is twice as common in men as women, twice as common in blacks than whites, and more common with advancing age. Gastric cancer is also seen in higher rates in Latin America, Northern Europe and the Far East. It remains the second leading cause of cancer death worldwide. Gastric cancer peaks in the seventh decade of life. Often, a delay in diagnosis may account for the poor prognosis. Fortunately, dedicated research into its pathogenesis and identification of new risk factors, treatment, and advanced endoscopic techniques has led to earlier detection of gastric cancer. Recognition that Helicobacter pylori infection causes most gastric ulcers has revolutionized the approach to gastric cancer today. Gastric tumors include adenocarcinoma, non-Hodgkin's lymphoma, and carcinoid tumors.

What is Gastric Cancer?

Gastric cancer consists of two pathological variants, intestinal and diffuse. The intestinal-type is the end-result of an inflammatory process that progresses from chronic gastritis to atrophic gastritis and finally to intestinal metaplasia and dysplasia. This type is more common among elderly men, unlike the diffuse type, which is more prevalent among women and in individuals under the age of 50. The diffuse-type, characterized by the development of linitis plastica, is associated with an unfavorable prognosis because the diagnosis is often delayed until the disease is quite advanced. Gastric H. pylori infection is highly associated with this type as with the intestinal-type.

Adenocarcinoma

Adenocarcinoma arising from gastric epithelium is the most common malignancies of the stomach (90% of cases). Malignancies arising from connective tissue (sarcoma) and from lymphatics (lymphoma) are less common. Adenocarcinoma are most often found in the gastric cardia (31%), followed by the antrum (26%), and body of the stomach (14%).

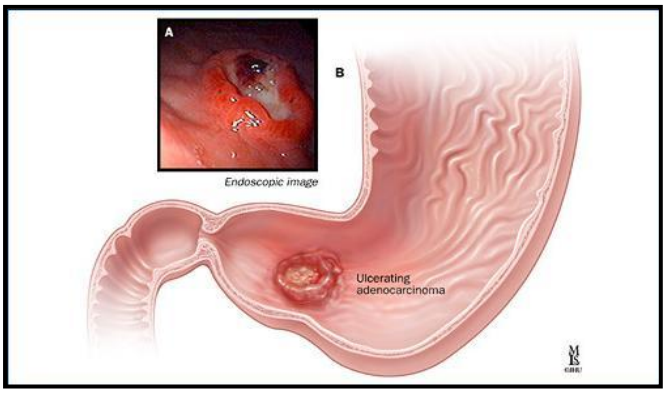

Figure 1. Endoscopic image of an ulcerating adenocarcinoma; B, ulcerating adenocarcinoma.

Adenocarcinoma is classified according to histology and location. Histologically, these malignancies may be divided into well-differentiated and poorly differentiated types, depending on the degree of gland formation and ability to secrete mucus. Most tumors are heterogeneous in histological appearance; therefore, classification is made by noting the predominant structures. Thus, well-differentiated tubular and poorly differentiated signet-ring cell carcinoma make up the majority of tumors. Less common types are mucinous, papillary and undifferentiated carcinoma.

Early Gastric Cancer

Early gastric cancers, where tumor cells are confined to the mucosa (the most superficial layer of the stomach), have been identified in Japan where there is active screening of patients at high-risk for gastric cancer. In these patients, early gastric cancer may appear as a subtle lesion, usually less than 2 cm in diameter. The identification of early gastric cancer is important because it is potentially amenable to endoscopic therapy and accompanied by an excellent prognosis.

1.2 Symptoms

Most patients are asymptomatic in early stages of gastric cancer and have advanced disease by the time of presentation. In a review of over 18,000 patients, the most common presenting symptoms included weight loss and abdominal pain. Epigastric fullness, nausea, loss of appetite, dyspepsia, and mild gastric discomfort may also occur. Dysphagia may be a prominent symptom for patients with tumors in the cardia or gastroesophageal junction. In patients with pyloric tumors and tumors located in the antrum, vomiting and gastric outlet obstruction may occur. Unusual presentations may include acute appendicitis, musculoskeletal pain, and the sudden appearance of seborrheic keratosis and freckles, accompanied by pruritis and dermatomyositis. Gastrointestinal bleeding is uncommon, and only seen in about 20% of cases.

Abdominal pain occurs in most patients with gastric lymphoma; however, symptoms may vary from those suggesting peptic ulcer diseases to advanced gastric cancer. Patients may complain of weight loss, nausea and vomiting. They may also present with overt gastrointestinal bleeding. Gastric lymphoma is more often found in younger females when compared to the incidence of gastric cancer.

1.3 Anatomy

The stomach is located in the upper part of the abdomen just beneath the diaphragm. The size, shape, and position may vary with posture and with content because it is distensible and on a free mesentery. An empty stomach is roughly the size of an open hand. It can fill much of the upper abdomen when distended with food and may descend into the lower abdomen or pelvis upon standing. The duodenum extends from the pylorus to the ligament of Treitz in a sharp curve that almost completes a circle. It is so named because it is about equal in length to the breadth of 12 fingers, or about 25 cm. It is largely retroperitoneal and the position is relatively fixed. The stomach and duodenum are closely related in function and in pathogenesis and manifestation of disease.

The stomach may be divided into seven major sections. The cardia is a 1–2 cm segment distal

to the esophagogastric junction. The fundus refers to the superior portion of the stomach that lies above an imaginary horizontal plane that passes through the esophagogastric junction. The antrum is the smaller distal, one-fourth to one-third of the stomach. The narrow, 1–2-cm channel that connects the stomach and duodenum is the pylorus. The lesser curve refers to the medial shorter border of the stomach, whereas the opposite surface is the greater curve. The angularis is along the lesser curve of the stomach where the body and antrum meet. This junction is accentuated during peristalsis.

Four vascular systems comprise the arterial supply of the stomach. The left gastric artery passes to the lesser curvature in the cardiac region. The right gastric artery, arising from the hepatic artery, passes in the lesser omentum to the lesser curvature. The right gastroepiploic artery branches off the gastroduodenal artery behind the upper portion of the duodenum, and extends along the greater curvature in the greater omentum. The left gastroepiploic artery, arising from the splenic artery, supplies the upper portion of the lesser curvature below the fundus. The splenic artery gives rise to short gastric arteries that course around the left margin of the omental bursa to the fundus and occasionally to a large posterior gastric artery. The regions of the hepatic artery and gastroduodenal artery have a variable arterial supply. Branches of the left gastric vein in the lesser curvature achieve venous drainage of the stomach and duodenum, though many anatomical variations occur. The greater curvature empties into the right gastroepiploic vein and then to the left gastric vein, or alternately into the splenic vein via the left gastroepiploic vein.

The lymphatic vessels form a dense, subperitoneal plexus on the anterior and posterior stomach surfaces that collect lymph from the gastric wall. Basically, there are four different areas into which the gastric lymph drains. Lymph from the upper left anterior and posterior wall filters through the lower left gastric and pericardial nodes. The pyloric segment filters lymph to the right suprapancreatic nodes via the suprapyloric nodes. The region of the fundus filters lymph along the gastrosplenic ligament and splits with lymph flowing to the left suprapancreatic nodes and the left gastroepiploic nodes via the splenic nodes. Lymph from the pyloric and distal portion of the corpus collects in the right gastroepiploic nodes and then flows to the subpyloric nodes. From all regions, the lymph stream continues to the celiac nodes (situated above the pancreas around the celiac artery), then to the gastrointestinal lymphatic trunk, and into the thoracic duct.

1.4 Causes

Environmental Risk Factors

The continued identification of risk factors for gastric cancer may one day lead to the global development of early detection programs that will change the clinical history of this disease. Environmental factors appear to be related to the intestinal type of gastric cancer. Socioeconomic status is inversely correlated with the incidence of this disease. Factors associated with low socioeconomic status, such as poor sanitation, poor nutrition, and inadequate handling and preservation of food and water, are involved. Diets high in fresh fruit, leafy vegetables, ascorbic acid, and beta-carotene are associated with reduced risk. The literature also reports that decreased use of nitrites in prepared foods has also resulted in a decreased incidence. Though cigarette smoking may increase pre-malignant lesions and gastric dysplasia, a clear relationship has not been demonstrated. Similarly, the relationship between alcohol consumption and gastric cancer is inconclusive.

Helicobacter pylori

The most important risk factor identified in the development of gastric cancer is infection of the stomach with the bacterial organism Helicobacter pylori. Studies with the Mongolian gerbil show that when infected with H. pylori, the gerbil develops gastritis that progresses to gastric cancer. Epidemiological studies further support the link between H. pylori and cancer of the distal stomach (i.e., antrum). The risk of developing gastric cancer is about 1 in 97 in infected individuals, compared to 1 in 750 in uninfected individuals, over a 30-year period. Thus, the risk of developing gastric cancer in H. pylori-infected individuals is about 8 times higher than in uninfected individuals. Despite this, the 1996 NIH consensus panel on H. pylori recommended that treatment not be initiated in asymptomatic infected individuals.

Treatment of asymptomatic individuals remains a controversial issue, particularly because it takes more than 30 years before one-third of these individuals develop atrophic gastritis. The matter of treatment is even more confusing, because recent data suggest the eradication of H. pylori predisposes individuals to cancer of the proximal stomach (cardia) and esophagus. The overall incidence of gastric cancer is diminishing in western countries, but the incidence of

proximal gastric cancers compared to distal is rising, and coincides with the widespread treatment of H. pylori. Some have proposed that H. pylori exert a protective effect in the proximal stomach and esophagus by inducing achlorhydria and atrophic gastritis. Eradication of H. pylori restores gastric acid production and, in individuals predisposed to gastroesophageal reflux, could possibly contribute to cancers of the distal esophagus and cardia. Additional data is needed before treatment recommendations can be made in asymptomatic individuals. H. pylori leads to atrophic gastritis through direct and indirect mechanisms The organism itself induces a host-inflammatory response within the gastric mucosa. This in turn leads to the production of reactive oxygen species, which can induce DNA damage and alterations to the genetic controls of normal cell proliferation. The host-immune response leads to the T-cell release of cytokines, such as interferon-gamma and interleukin-8, which recruit more inflammatory cells.

H. pylori also appear to play a role in the pathogenesis of gastric MALT lymphomas, which arise as a reaction to infection of the stomach. Eradication of this organism has demonstrated complete or partial regression of low-grade lymphoma lesions.

Hereditary (Familial) Gastric Cancer

The study of familial gastric kindreds has led to the identification of a germline mutation of the CDH1 gene in one third. CDH1 encodes E-cadherin, a cell adhesion molecule that participates in normal cell differentiation and tissue architecture. Mutation of CDH1 diminishes the availability of normal E-cadherin protein, thus perturbing normal cell differentiation and cell adhesiveness. Mutations of CDH1 in gastric cancer families may occur anywhere throughout the gene, in contrast to CDH1 mutations occuring almost exclusively in exons 7-9 in individuals with sporadic gastric cancer. A germline mutation of CDH1 has a 70% penetrance, increasing the susceptibility to gastric cancer. CDH1 is a tumor suppressor gene, since mutation of the second CDH1 allele, perhaps as the result of environmental influences such as H. pylori infection or diet, is required for full penetrance. Affected female family members are at higher risk for breast cancer as well and should be screened accordingly.

How affected family members should be screened for gastric cancer remains a dilemma. Since familial gastric cancer is the diffuse type, superficial endoscopic mucosal biopsies lack sufficient

sensitivity to identify dysplasia or early gastric cancer. Further studies are needed to determine the role of endoscopic ultrasound and PET scanning surveillance of family members. Occult gastric cancer has been found in the surgical specimens of asymptomatic family members with negative endoscopic screening who elected to undergo prophylactic total gastrectomy. Whether all affected family members should consider prophylactic gastrectomy remains unclear, but with a 70% chance of developing gastric cancer and limited surveillance methods, many individuals may opt for this radical procedure.

Molecular Biology

The development of gastric cancer is thought to occur through a multi-step process, in which the earliest lesion is atrophic gastritis, followed by the development of dysplasia, adenoma, and then adenocarcinoma. Progression from the preceding lesion to the next developmental stage is accompanied by molecular genetic events.

Abnormalities in protein-encoding genes that regulate normal cell growth have been detected in gastric cancers. Alterations to growth factor receptors like c-met and K-sam are often over-expressed in gastric cancers of the scirrhous type. Proteins such as cyclin E that regulate the cell cycle, critical for the control of normal cell proliferation, are also over-expressed. Mutation to p53, a tumor suppressor gene, is found in 64% of gastric cancers. The detection of replication errors in microstellate loci is an indication that genetic instability is involved.

1.5 Diagnosis

Radiological Diagnosis

Radiography has limited diagnostic value in the diagnosis of gastric cancer. Although better studies (using state-of-the-art techniques performed by practiced technicians) suggest a high sensitivity of x-rays (80–95%), there are limitations. Upper gastrointestinal series may show thickened or enlarged gastric folds, filling defects that correspond to a mass or ulcer, or may demonstrate a failure of the stomach to distend normally to air and instilled barium. These contrast studies do not aid in accurate disease staging and do not allow differentiation of benign from malignant lesions.

CT scan

Abdominal computed tomography (CT) has been used in gastric cancer tumor staging. The CT scan (Figure 12) can demonstrate the size and location of the cancer, wall thickness, presence or absence of fat between the mass and adjacent organs, as well as nodal, vascular, or visceral spread of tumor. The CT scan is unable to distinguish different layers of the gastric wall; hence, it cannot differentiate early from more advanced lesions.

Additionally, CT scanning does not provide tissue confirmation for grading and typing. The ability to distinguish carcinoma from lymphoma is crucial to provide therapy in a timely fashion.

Endoscopic Diagnosis

Endoscopy provides the most specific and sensitive means of diagnosis of gastric cancers. Gastrointestinal endoscopy allows the physician to visualize and biopsy the mucosa of the esophagus, stomach, duodenum, and most of the jejunum (Figure 2).

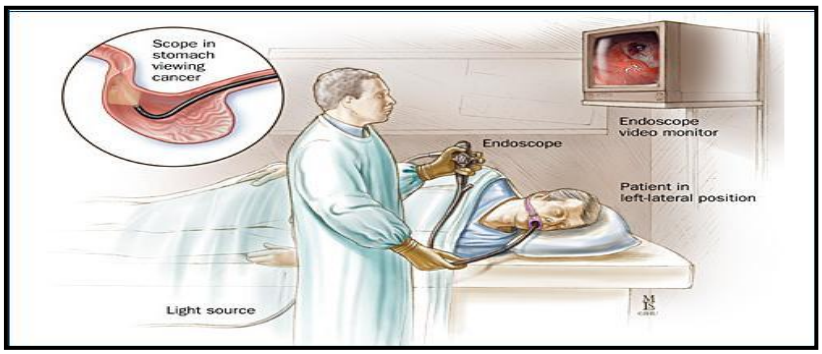

Figure 2. Room set-up and patient positioning for endoscopy.

The endoscope (a thin, flexible, lighted tube) is passed through the mouth and pharynx and into the esophagus. It transmits an image of the esophagus, stomach, and duodenum to a monitor visible to the physician. Air may be introduced into the stomach through the scope to expand the folds of tissue and enhance examination.

Staging

The most significant prognostic factor is depth of tumor invasion at the time of diagnosis. There are three classifications of gastric tumors. The Boorman classification is based on the macroscopic appearance of the tumor; the Lauren classification divides tumors into intestinal and diffuse types; and the TNM classification reflects the depth of tumor infiltration (T) (Figure 3), node involvement (N).

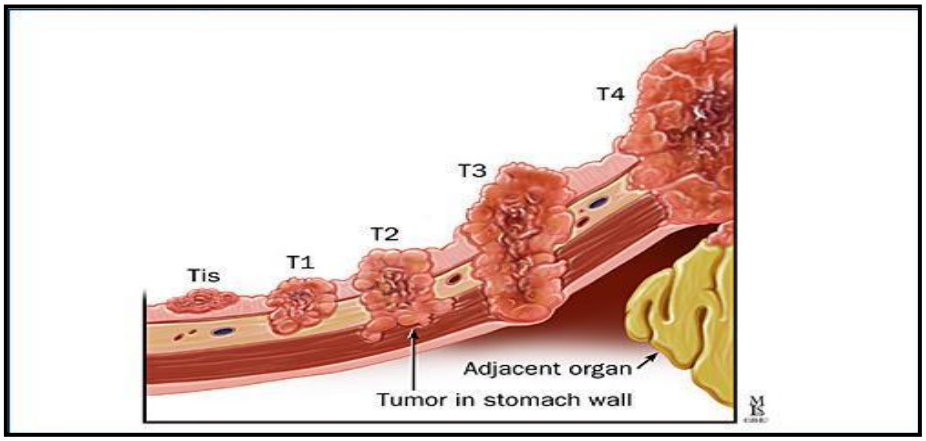

Figure 3. TNM staging of gastric cancer, showing depth of invasion.

Advanced TNM stages are associated with worse prognoses. Most patients present with stage III and IV disease, though the number of patients with stage IV disease at presentation at some U.S. centers has declined during the past 30 years. The five-year survival rate for patients without nodal involvement is about 40%, and is only 10% for those with metastatic disease. These figures are unchanged over the past several decades despite advances in medical and surgical therapy.

TNM System for Staging Gastric Cancer

Stages	T	N	M
Stage 0	Tis	N0	M0
Stage IA	T1	N0	M0
Stage IB	T1	N1	M0
	T2	N0	M0
Stage II	T1	N2	M0
	T2	N1	M0
	T3	N0	M0
Stage IIIA	T2	N2	M0
	T3	N1	M0
	T4	N0	M0
Stage IIIB	T3	N2	M0
	T4	N1	M0
	T4	N2	M0
Stage IV	T4	N1	M0
	T1	N3	M0
	T2	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
	Any T	Any N	M1

Table 1. TNM System for Staging Gastric Cancer

1.6 Therapy

Overview

There are essentially three modes of therapy for the treatment of gastric cancer. Curative resection, including endoscopic resection, appears the most effective. Surgical resection entails the removal of the primary tumor and regional lymph nodes with resection margins free of tumor. Gastric cancer has not been shown to respond successfully to radiation alone. Chemotherapy has demonstrated limited success with multi-drug regimens.

Surgical Therapy

The prognosis following surgical resection depends on the stage at presentation. Early tumors confined to the stomach lining have higher cure rates than cases in which disease has already spread to distant sites or regional lymph nodes. Cure rates have improved in the past 30 years, particularly in Japan. These improvements can be attributed mainly to an increase in early detection rates.

The type of surgery performed depends on the extent and location of tumor; therefore, preoperative evaluation is critical. Initial staging may be established by endoscopy with biopsy. Endoscopic ultrasound should follow. Endoscopic Ultrasound (EUS) has a sensitivity of 85% in assessing depth of tumor invasion and detecting nodal involvement prior to surgery. Laparoscopic staging prior to surgical resection is also advocated and has impacted preoperative treatment decisions.

There are two principle types of gastric resection—the subtotal gastrectomy and the total gastrectomy . Determination of the type of resection depends on various factors including: 1) the location of the tumor, 2) the size and the extent of the tumor, and 3) the histology pattern.

Endoscopic Therapy

Therapeutic endoscopy may be curative for early gastric cancer or palliative for more advanced disease. The decision to use endoscopic treatment as opposed to surgical resection is affected by tumor stage, location, morphology, prognosis of the disease, risk factors, assessment of resectability versus cure, and the associated morbidity with each procedure. The role of adjuvant systemic or regional therapy is also of importance. EUS provides valuable information regarding the stage and the feasibility of endoscopic therapy. Patients with more superficial lesions may be candidates for endoscopic (or surgical) resection, while patients with more advanced disease may require palliative therapy. Tissue resection or ablation, dilation of strictures, stent placement, palliation of bleeding, and the placement of feeding or decompression tubes may all be accomplished endoscopically.

Endoscopic Mucosal Resection

Endoscopic mucosal resection has been advocated for early gastric cancers, those that are superficial and confined to the mucosa. Endoscopic mucosal resection may be attempted in patients without evidence of nodal or distant metastases, with differentiated tumors that are slightly raised and less than 2 cm in diameter, or in differentiated tumors that are ulcerated and less than 1 cm in diameter. The most commonly employed methods of endoscopic mucosal resection include strip biopsy, double-snare polypectomy, resection with combined use of highly concentrated saline and epinephrine, and resection using a cap. The prognosis after treatment is comparable to that of surgical resection for early gastric cancer. Five-year survival rates for individuals undergoing endoscopic mucosal resection of early gastric cancers have been reported to be as high as 95%.

Chemotherapy

Adenocarcinoma of the stomach is relatively sensitive to chemotherapy. Fluorouracil (5-FU) is the most commonly used drug in the treatment of gastric cancer, with a response rate around 21%. In an attempt to improve this rate, drug combinations have been tried; the most common is 5-FU, doxorubicin, and mitomycin C (FAM) with a response rate of 33% and an acceptable degree of toxicity. Other drug combinations have been tried, although the response duration and overall survival, when compared with 5-FU alone, were not significantly different. In addition, the combination groups had a higher toxicity rate. Newer investigational modalities employ tumor antigen-specific immunochemotherapy. Antibodies to tumor antigens are conjugated with chemotherapeutic drugs; in this way, the drugs can be delivered to the tumor directly.

Bleeding

Bleeding may be controlled by endoscopic thermal techniques such as laser and multipolar electro coagulation. After resuscitation and stabilization of the patient, endoscopy is the preferred procedure for treating hemorrhage. Gastric lavage is usually performed to remove blood from the stomach prior to endoscopy. The goal of endoscopic therapy is to stop the bleeding and/or oozing from the surface of the tumor. This may be achieved using laser, MPEC, or cauterization.

2. Objective

Development of database of genes involved in Gastric Cancer

Ongoing researches globally, are producing huge data related to genes or miRNAs which are involved in causing Gastric Cancer, individually at different places by different scientists and researchers. There has been no such database till date, which catalogs information of genes and miRNAs along with their various attributes specific to Gastric Cancer Database. This genomic and miRNAomic data collected from the literature can be used for identification of biomarkers that can be used for experimental verification, for identifying the novel drug targets and it can also be helpful to the researchers and the scientific community.

3. What is a Biological Database ?

A biological database is a large, organized body of persistent data, usually associated with computerized software designed to update, query, and retrieve components of the data stored within the system. A simple database might be a single file containing many records, each of which includes the same set of information. For example, a record associated with a nucleotide sequence database typically contains information such as contact name; the input sequence with a description of the type of molecule; the scientific name of the source organism from which it was isolated; and, often, literature citations associated with the sequence.

For researchers to benefit from the data stored in a database, two additional requirements must be met:

1.Easy access to the information; and

2.A method for extracting only that information needed to answer a specific biological question.

4. Methodology

Gone through databases like NCBI (National Center for Biotechnology Information), which contain information about Gene and miRNAs, and got some information about each gene in the other databases and also consider the PMC and the Pubmed database for the selection of new potential genes and miRNAs which are playing a major role in causing Gastric Cancer.

4.1Data Retrieval

The Gastric Cancer causing genes or the miRNAs involved in causing the Gastric Cancer from Homo sapiens were retrieved from the NCBI (National Center for Biotechnology Information) literature sources like the Pubmed (A database of citations and abstracts for biomedical literature from MEDLINE and additional life science journals) or the PMC (Pubmed Central-A digital archive of full-text biomedical and life sciences journal literature, including clinical medicine and public health)

4.2Data Collection

The retrieved genes and the miRNAs were collected in an excel sheets along with their various attributes like the gene id, gene symbol, location, chromosome number, their mechanism in gastric cancer**,** transcription factors involved for their regulation, techniques for their extraction etc. like the figure given below. These attributes of genes and the miRNAs were retrieved from the NCBI database and the details were also found out by searching it through web**.**

A	B	C	D	E	F	G	H
S.no	**Gene name**	**Gene Symbol**	**gene id**	**pubmed id**	**location**	**chromosome**	**Mechanism**
1	29	MUC5AC		25166306			upstream of the coding reg
2	interleukin 1, beta	IL-1β	3553	25154996	2q14	2	up-regulation-PMC276132
3	estrogen receptor 1 (121)	ESR1	2099	25154989	6q25.1	6	down regulation-PMC2703
4	progesterone receptor	PGR	5241	25154989	11q22-q23	11	down regulation-PMC2703
5	Heat Shock Protein 60	HSP60	3329	25207654	2q33.1	2	RNA degradation
6	lectin, galactoside-binding, soluble, 3	LGALS3	3958	25222780	14q22.3	14	up-regulation
7	cyclin-dependent kinase 6	CDK6	1021	25202363	7q21-q22	7	down-regulation-PMC4156
8	Interleukin-17	IL-17	3605	25197971	6p12	6	tumor supressor
9	gastrokine 2	GKN2	200504	24408014	2p13.3	2	tumor supressor
10	Pleiotrophin	PTN	5764	25436328	7q33	7	up-regulation
11	spalt-like transcription factor 4	SALL4	57167	25436325	20q13.2	20	up-regulation
12	RAB guanine nucleotide exchange factor (GEF) 1	RABGEF1	27342	25427001	7q11.21	7	up-regulation
13	Interleukin-17A	IL17A	3605	25422215	6p12	6	up-regulation
14	natriuretic peptide receptor 1	NPR1	4881	2541935	1q21-q22	1	up-regulation
15	protein tyrosine phosphatase, receptor type, D	PTPRD	5789	25412184	9p23-p24.3	9	tumor supressor
16	toll-like receptor 4	TLR4	7099	25400780	9q33.1	9	up-regulation
17	toll-like receptor 9	TLR9	54106	25400780	3p21.3	3	up-regulation
18	major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	25400751	6p21.3	6	up-regulation

Fig.4: Data collected in excel sheet

4.3 Database Development

The database was built for the genes and the miRNAs which where collected or stored in the excel sheet along with their various attributes. The database was made by using the HTML, CSS, JavaScript as well as PHP languages and it will be openly accessible to all the research community. The database is containing the Home Page, the Statistics for Gastric Cancer, page for Gastric Cancer Gene Database as well as Gastric Cancer miRNAs Database and the Contact Us page which also includes the feedback form.

5 Tools and Techniques

5.1 Tools for the Data Collection:

5.1 NCBI(www.ncbi.nlm.nih.gov/)

The **National Center for Biotechnology Information** (**NCBI**) is part of the United States National Library of Medicine (NLM), a branch of the National Institutes of Health. The NCBI houses a series of databases relevant to biotechnology and biomedicine. Major databases include GenBank for DNA sequences and Pubmed, a bibliographic database for the biomedical literature. Other databases include the NCBI Epigenomics database. All these databases are available online through the Entrez search engine.

5.2 Pubmed(www.ncbi.nlm.nih.gov/pubmed)

Pubmed is a free search engine accessing primarily the MEDLINE database of references and abstracts on life sciences and biomedical topics. The United States National Library of Medicine (NLM) at the National Institutes of Health maintains the database as part of the Entrez system of information retrieval.

5.3 PMC(www.ncbi.nlm.nih.gov/pmc/)

Pubmed Central (PMC) is a free digital repository that archives publicly accessible full-text scholarly articles that have been published within the biomedical and life sciences journal literature. As one of the major research databases within the suite of resources that have been developed by the National Center for Biotechnology Information (NCBI), PubMed Central is much more than just a document repository.

5.2 Techniques for Web Interface Building:

a. HTML/CSS

HTML- **Hypertext Markup Language** is the standard markup language used to create web pages.[1] It is written in the form of HTML elements consisting of *tags* enclosed in angle brackets (like <html>). HTML tags most commonly come in pairs like <h1> and </h1>, although some represent *empty elements* and so are unpaired, for example <img>. The first tag in such a pair is the *start tag*, and the second is the *end tag* (they are also called *opening tags* and *closing tags*).

CSS- **Cascading Style Sheets** is a style sheet language used for describing the look and formatting of a document written in a markup language. While most often used to change the style of web pages and user interfaces written in HTML and XHTML, the language can be applied to any kind of XML document, including plain XML, SVG and XUL. Along with HTML and JavaScript, CSS is a cornerstone technology used by most websites to create visually engaging web pages, user interfaces for web applications, and user interfaces for many mobile applications.

b. Macromedia Dreamweaver 8

It is a proprietary web development tool developed by Adobe Systems. Dreamweaver was created by Macromedia in 1997, and was maintained by them until Macromedia was acquired by Adobe Systems in 2005. Adobe Dreamweaver is available for OS X and for Windows. Following Adobe's acquisition of the Macromedia product suite, releases of Dreamweaver subsequent to version 8.0 have been more compliant with W3C standards.

c. Wamp Server (Version 2.4- x86)

Wamp Server is a Windows web development environment. It allows you to create web applications with Apache2, PHP and a MySQL database. Alongside, PhpMyAdmin allows you to manage easily your databases.

d. phpMyAdmin

PhpMyAdmin is a free and open source tool written in PHP intended to handle the administration of MySQL with the use of a web browser. It can perform various tasks such as creating or deleting databases, tables, fields or rows; executing SQL statements; or managing users and permissions.

5.3Codes Used in Developing Databases and GUIs

a. For the styling

```
html

*
{ margin: 0;
  padding: 0;}

  body
{
width:1270px;
font: normal 85% Arial, Helvetica, sans-serif;
color: #000;
text-shadow: 1px 1px #FFF;
 background: #FFF url(../images/pattern_light.png) repeat;

}

h1, h2, h3, h4, h5, h6
```

```
{ font: bold 150% 'Open Sans Condensed', sans-serif;
  color: #284020;
 letter-spacing: -1px;
 margin: 0 0 10px 0;
}

h2
{ font: normal 165% 'Open Sans Condensed', sans-serif;}

h3
{ font: normal 150% 'Open Sans Condensed', sans-serif;}
h4, h5, h6
{
  font: normal 150% 'Open Sans Condensed', sans-serif;
  line-height: 1.5em;}

  h5, h6
{ font: normal 95% 'Open Sans Condensed', sans-serif;
  padding-bottom: 15px;}

  a
{ color: #000;
  text-shadow: 1px 1px #FFF;
  font-weight: bold;
  background: transparent;
  outline: none;
  text-decoration: underline;}

a:hover
{ text-decoration: none;}
```

```
 ul
{

 font-style: normal;
 font-size: 90%;}



 #main, #header, #banner, #menubar, #site_content, #footer
{ margin-left: auto;
 margin-right: auto;}
 #header
{ height: 110px;
 width: 1270px;
 background: #284020;
 background: -moz-linear-gradient(#437133, #284020);
 background: -o-linear-gradient(#437133, #284020);
 background: -webkit-linear-gradient(#437133, #284020);}

 #menubar_container
{ height: 100px;}

#menubar
{ width: 1220px;
 height: 160px;}

 #welcome
{ width: 940px;
 height: 50px;

 text-align: center;
```

```
  margin: 0 auto;}

  #welcome h1 a
{ font: bold 190% 'Open Sans Condensed', sans-serif;


  text-shadow: 1px 1px #350B39;}

  #menu_items
{ float: left;

  padding: 10px 0;
  width: 1200px;
  background: #437133;
  background: -moz-linear-gradient(#437133, #284020);
  background: -o-linear-gradient(#437133, #284020);
  background: -webkit-linear-gradient(#437133, #284020);
  border-bottom: 2px solid #1D2D17;
  border-radius: 30px 0px 30px 0px;

  }


ul#menu
{ margin:0;
  float: left;}
ul#menu li
{ padding: 0 0 0 0px;
  list-style: none;

  display: inline;
```

```
  background: transparent;}

  ul#menu li a
{ float: left;
  font: bold 120% 'Open Sans Condensed', sans-serif;
  text-align: center;
  color: #FFF;
  text-shadow: 1px 1px #000;
  text-decoration: none;
  margin: 0px 0 0 10px;
  padding: 3px 12px 3px 12px;
  background: transparent; }

  ul#menu li.current a
{ text-shadow: 1px 1px #323232;
  background: #284020;
  background: -moz-linear-gradient(#437133, #284020);
  background: -o-linear-gradient(#437133, #284020);
  background: -webkit-linear-gradient(#437133, #284020);
  border-radius: 15px 0px 15px 0px;

   }

  ul#menu li:hover a
{ text-shadow: 1px 1px #000;
  background: #284020;
  background: -moz-linear-gradient(#284020, #437133);
  background: -o-linear-gradient(#284020, #437133);
  background: -webkit-linear-gradient(#284020, #437133);
  border-radius: 15px 0px 15px 0px;
   }
```

```
 #site_content
{ width: 1200px;
  overflow : hidden;
  height: 280px;
  background: #FFF url(../images/pattern_light.png) repeat;
  }



  .sidebar_container
{ float: left;
  margin: 15px 0 0 0;
  width: 220px;
  }

  .sidebar
{ float: left;
  width: 1200px;
  padding: 0;
  }

  .sidebar_item
{ width: 215px;}

.sidebar h2
{ font: bold 200% 'Open Sans Condensed', sans-serif;}

#content
{ width: 1200px;
```

```
 float: left;}

 #content h1
{ margin-top: 20px;}

.content_item_left
{ width: 460px;
 float: left;
 margin: 0 0 20px 0;}

.content_item_right
{ width: 460px;
 float: right;
 margin: 0 0 20px 0;}


 .content_item_left h3, .content_item_right h3
{ font-size: 200%;
 font-weight: bold;
 color: #F4FB3B;}

.content_container
{ width: 310px;
 padding: 5px 5px 10px 5px;
 margin: 0 10px 10px 0;
 text-align: center;
 float: left;}

.content_container h3
{ font-size: 200%;
 font-weight: bold;}
```

```
#footer_container
{
height: 270px;
padding-top: 20px;
   margin:10px auto;
  color: #FFF;
  text-shadow: none;
  background: #000;
  }

#footer
{ width: 1060px;

  padding-top: 20px;
  text-align: center;
  }

#footer a, #footer a:hover
{ text-decoration: none;
  padding-bottom: 40px;
  color: #FFF;
  text-shadow: none;}

#footer a:hover
{ text-decoration: underline;}

.copyright
{  width: 1060px;
   padding-top: 20px;
```

```
   float: left;
}
.button_small
{ font: normal 110% 'Open Sans Condensed', sans-serif;
  text-align: center;
  margin-left: 95px;
  float: left;
  padding: 5px 15px 10px 10px;
  background: #284020;
  background: -moz-linear-gradient(#437133, #284020);
  background: -o-linear-gradient(#437133, #284020);
  background: -webkit-linear-gradient(#437133, #284020);
  border-radius: 15px 0px 15px 0px;
  -moz-border-radius: 15px 0px 15px 0px;
  -webkit-border: 15px 0px 15px 0px;
  -webkit-box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;
  -moz-box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;
  box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;}

  .button_small a
{ color: #FFF;
  text-shadow: 1px 1px #574303;
  padding-left: 5px;}

  .form_settings
{ margin: 0 0 0 0;}

.form_settings p
{ padding: 0 0 4px 0;}

.form_settings span
```

```
{ float: left;
  width: 280px;
  text-align: left;}

.form_settings input, .form_settings textarea
{ padding: 2px;
  width: 299px;
  font: 100% arial;
  border: 1px solid #BBB;
  background: #FFF;
  color: #47433F;}

.form_settings input[type="checkbox"]
{ padding: 2px 0;
  width: 15px;
  font: 100% arial;
  border: 0;
  background: #FFF;
  color: #47433F;
  margin: 28px 0;}

.form_settings .submit
{ font: bold 100% 'Open Sans Condensed', sans-serif;
  width: 99px;
  margin: 0 0 0 206px;
  height: 26px;
  padding: 2px 0 3px 0;
  cursor: pointer;
  background: #284020;
  background: -moz-linear-gradient(#437133, #284020);
  background: -o-linear-gradient(#437133, #284020);
```

```
background: -webkit-linear-gradient(#437133, #284020);
border-radius: 15px 0px 15px 0px;
-moz-border-radius: 15px 0px 15px 0px;
-webkit-border: 15px 0px 15px 0px;
-webkit-box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;
-moz-box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;
box-shadow: rgba(0, 0, 0, 0.5) 0px 0px 5px;
color: #FFF;
text-shadow: 1px 1px #000;}
```

b. For Table Creation in database 'gastric' through GUI

```
Table structure for table `genes`
--

CREATE TABLE IF NOT EXISTS `genes` (
  `id` varchar(50) NOT NULL,
  `name` varchar(50) NOT NULL,
  `symbol` varchar(50) NOT NULL,
  `pubmed` varchar(50) NOT NULL,
  `location` varchar(50) NOT NULL,
  `chromosome` varchar(50) NOT NULL,
  `mechanism` varchar(50) NOT NULL,
  `tf` varchar(50) NOT NULL,
  `technique` varchar(50) NOT NULL,
  `reportedinbodyfluid` varchar(50) NOT NULL,
  `presentinplasmamembrane` varchar(50) NOT NULL,
  PRIMARY KEY (`id`)
) ENGINE=InnoDB DEFAULT CHARSET=latin1;

--
-- Dumping data for table `genes`
--

INSERT INTO `genes` (`id`, `name`, `symbol`, `pubmed`, `location`, `chromosome`, `mechanism`, `tf`,
`technique`, `reportedinbodyfluid`, `presentinplasmamembrane`) VALUES
('', '29', 'MUC5AC', '25166306', '', '', ' upstream of the coding region', 'Gli-binding site', '', '', '\r\n'),
('10076', 'protein tyrosine phosphatase, receptor type, U', 'PTPRU', '25337216', '1p35.3', '1', 'tumor
suppressor', 'Pitx3-19515692', 'Fluorescent Antibody Technique-15016823', 'plasma, serum', 'yes-
PMC4203187\r\n'),
```

('1021', 'cyclin-dependent kinase 6', 'CDK6', '25202363', '7q21-q22', '7', 'down-regulation-PMC4156198', 'E2F-NBK21497', 'western blot analyses-PMC4156198', 'serum', 'yes -NBK21497\r\n'),
('10855', 'Heparanase', 'HPSE', '25337202', '4q21.3', '4', 'up-regulation', 'EGF-like growth factor-10855', 'ELISA technique-12602584', 'Cerebrospinal Fluid-PMC193904', 'yes-11936\r\n'),
('150094', 'salt-inducible kinase 1', 'SIK1', '25384047', '21q22.3', '21', 'tumor supressor', 'MEF2C-21954104', 'RT-PCR', 'cerebrospinal fluid', 'yes\r\n'),
('1894', 'epithelial cell transforming 2', 'ECT2', '25674238', '3q26.1-q26.2', '3', 'up-regulation', 'E2F1 -1894(gene)', 'qRT-PCR', 'salaiva and urine', 'cell membrane\r\n'),
('200504', 'gastrokine 2 ', 'GKN2 ', '24408014', '2p13.3', '2', 'tumor supressor', 'NF-KappaB-15774165', 'immunohistochemistry-PMC2993229', 'plasma-12921637', 'yes-12921637\r\n'),
('2064', 'v-erb-b2 avian erythroblastic leukemia viral oncog', 'HER2', '25327797', '17q12', '17', 'up-regulation', 'E2F-24362522', 'immunohistochemistry', 'serum and plasma-PMC3084889', 'yes-21206005\r\n'),
('207', 'v-akt murine thymoma viral oncogene homolog', 'AKT', '25282897', '14q32.32', '14', 'up-regulation', 'FOXO1-24552152', 'RT-PCR', 'alveolar fluid', 'yes-15859947\r\n'),
('2072', 'excision repair cross-complementation group 4', 'ERCC4', '25342505', '16p13.12', '16', 'tumor supressor', 'TFIIH-2072(gene)', 'Fluorescent In Situ Hybridization Technique', 'Cerebrospinal Fluid-PMC2758086', 'yes\r\n'),
('2073', 'Xeroderma pigmentosum group G', 'XPG', '25268735', '13q33', '13', 'tumor supressor', 'TFIIH-11259578', 'immunohistochemistry', 'cerebrospinal fluid-10841992', 'nitrocellulose membrane\r\n'),
('2099', 'estrogen receptor 1 (121)', 'ESR1', '25154989', '6q25.1', '6', 'down regulation-PMC2703551', 'NF-kappaB', 'RT-PCR', '', 'yes -NBK21517\r\n'),
('23411', 'Sirtuin-1', 'SIRT1', '25664004', '10q21.3', '10', 'up-regulation', 'STAT3 and NF-?B', 'qRT-PCR', 'cerebrospinal fluid', 'plasma membrane\r\n'),
('2520', 'gastrin', 'GAST', '25227854', '17q21', '17', 'up-regulation', 'STAT2-16689942', 'immunohistochemistry', 'synovial fluid', 'yes\r\n'),
('27342', 'RAB guanine nucleotide exchange factor (GEF) 1', 'RABGEF1', '25427001', '7q11.21', '7', 'up-regulation', 'Dlx5', 'immunoassay technique', 'Synovial fluid ', 'yes- 27342\r\n'),
('29126', 'programmed death ligand-1', 'PD-L1', '25733810', '9p24', '9', 'up-regulation', 'STAT6-14515254', 'immunohistochemistry-25733810', 'bronchoalveolar lavage fluid ', 'cell membrane-25600565\r\n'),
('3119', 'major histocompatibility complex, class II, DQ bet', 'HLA-DQB1', '25400751', '6p21.3', '6', 'up-regulation', 'SOX-2', 'PCR-SSP technique-8316943', 'cerebrospinal fluid-12405608', 'yes-12405608\r\n'),
('324', 'Adenomatosis Polyposis Coli', 'APC', '25210923', 'NC_000005.10 (112707505..112846239)', '5', 'up-regulation', '9.0 kb mRNA; 8538 bp ORF', 'Otorhinolaryngology', 'cerebrospinal fluid-9836773', 'yes\r\n'),
('328', 'apurinic/apyrimidinic endonuclease 1', 'APE1', '25733810', '14q11.2', '14', 'up-regulation', 'STAT3-23094050', 'immunohistochemistry-25733810', 'serum', 'plasma membrane'),
('3329', 'Heat Shock Protein 60', 'HSP60', '25207654', '2q33.1', '2', 'RNA degradation', 'NF-?B', 'immunohistochemistry-PMC3265716', 'Saliva and Urine', 'yes\r\n'),
('3553', 'interleukin 1, beta', 'IL-1ÃŸ', '25154996', '2q14', '2', 'up-regulation-PMC2761322', 'interferon-regulatory factor 1', 'RT-PCR', 'cerebrospinal fluid-2787856', 'yes\r\n'),
('3605', 'Interleukin-17', 'IL-17', '25197971', '6p12', '6', 'tumor supressor', 'NF-KappaB-3605', 'RT-PCR-PMC2849293', 'synovial fluids-PMC408356', 'yes-PMC408356\r\n'),
('3958', 'lectin, galactoside-binding, soluble, 3', 'LGALS3', '25222780', '14q22.3', '14', 'up-regulation', 'IFN-?R 1-20980634', 'immunohistochemistry-10225438', 'serum-PMC327869', 'yes-16478649\r\n'),
('4288', 'marker of proliferation Ki-67', 'Ki-67', '25339008', '10q26.2', '10', 'up-regulation', 'TTF-1-12923324', 'immunohistochemistry-16608796', 'cerebrospinal fluid-PMC3646137', 'cell membrane-17525638\r\n'),
('4363', 'ATP-binding cassette, sub-family C (CFTR/MRP), mem', 'ABCC1', '25329677', '16p13.1', '16', 'up-regulation', 'E2A,OCT4', 'Nothern blotting-PMC3952141', 'blood-cerebrospinal fluid-4363', 'yes-4363\r\n'),

('440823', 'Long non-coding RNAs', 'lncRNAs', '25674261', '22q12.1', '22', 'down-regulation', 'HOTTIP-PMC3702037', 'High-throughput RNA-sequencing techniques ', 'serum and urine', 'yes\r\n'),
('4486', 'macrophage stimulating 1 receptor (c-met-related t', 'RON-160', '25685065', '3p21.3', '3', 'up-regulation', 'Nrf2-21799005', 'RT-PCR-25685065', 'cells of epithelial origin', 'cell membrane-PMC4102433\r\n'),
('4582', 'mucin 1, cell surface associated', 'MUC1', '25332893', '1q21', '1', 'tumor supressor', 'TCF7L2-22318732', 'immunohistochemistry-22624465', 'serum-11034378', 'yes-19415654\r\n'),
('4680', 'carcinoembryonic antigen-related cell adhesion mol', 'CEACAM6', '25398131', '19q13.2', '19', 'up-regulation', 'TTF-1-19329538', 'immunohistochemistry', 'lung-lining fluid-22037359', 'yes-22037359\r\n'),
('4831', 'NME/NM23 nucleoside diphosphate kinase 2', 'NME2', '25700270', '17q21.3', '17', 'up-regulation', 'c-myc', 'immunohistochemistry- 25700270', 'serum', 'yes-4830\r\n'),
('4869', 'nucleophosmin', 'NPM', '25279197', '5q35.1', '5', 'up-regulation', 'AP-1-17690253', 'immunohistochemistry', 'cerebral spinal fluid.', 'cytosol\r\n'),
('4881', 'natriuretic peptide receptor 1', 'NPR1', '2541935', '1q21-q22', '1', 'up-regulation', ' TGA/OBF-10659709', 'cDNA-AFLP-16307367', 'plasma', 'yes\r\n'),
('5037', 'phosphatidylethanolamine binding protein 1', 'RKIP', '25337233', '12q24.23', '12', 'tumor supressor', 'STAT3', 'immunohistochemistry', 'BAL fluid-PMCID: PMC3391234', 'yes\r\n'),
('51561', 'interleukin 23, alpha subunit p19', 'IL-23A', '25349535', '12q13.3', '12', 'up-regulation', 'NF-KappaB-25349535', 'RT-PCT-16769867', 'cerebrospinal fluid-16769867', 'yes\r\n'),
('5225', 'pepsinogen', 'PGC', '25292040', '6p21.1', '6', 'up-regulation', 'IRF4-24995979', 'Fluorescent Antibody Technique-19350678', 'amniotic fluid', 'yes\r\n'),
('5241', 'progesterone receptor', 'PGR', '25154989', '11q22-q23', '11', 'down regulation-PMC2703551', 'NF-kappaB', 'RT-PCR', '', 'yes -NBK21517\r\n'),
('5243', 'ATP-binding cassette, sub-family B (MDR/TAP), memb', 'ABCB1', '25276252', '7q21.12', '7', 'down-regulation', 'Mrr1p-17983269', 'RT-PCR', 'cerebrospinal fluid-5243', 'yes-10574703\r\n'),
('5290', 'phosphatidylinositol-4,5-bisphosphate 3-kinase', 'PI3K', '25298748', '3q26.3', '3', 'tumor supressor', 'Runx2-23389849', 'immunohistochemistry-19671839', 'alveolar fluid', 'yes-15859947\r\n'),
('5335', 'phospholipase C, gamma 1', 'PLC?1', '25308733', '20q12-q13.1', '20', 'up-regulation', 'NFATC-23028325', 'immunohistochemistry-PMC2173518', 'cerebrospinal fluid', 'yes-24899266\r\n'),
('54106', 'toll-like receptor 9', 'TLR9', '25400780', '3p21.3', '3', 'up-regulation', 'XBP1-20351694', 'RT-PCR-16303959', 'Synovial fluid -22037282', 'yes-22037282\r\n'),
('5594', 'mitogen-activated protein kinase 1', 'ERK', '25337564', '22q11.21', '22', 'up-regulation', 'NF-KappaB', 'Western blot analyses', 'cerebrospinal fluid-20847405', 'yes\r\n'),
('57142', 'reticulon 4', 'RTN4', '25683937', '2p16.3', '2', 'up-regulation', 'ATF6-57142(gene)', 'immunohistochemistry', 'cerebrospinal fluid', 'NE membrane\r\n'),
('57167', 'spalt-like transcription factor 4', 'SALL4', '25436325', '20q13.2', '20', 'up-regulation', 'SOX2-23269686', 'RT-PCR-21756254', 'serum-22298374', 'yes-22298374\r\n'),
('5734', 'prostaglandin E receptor 4', 'PGE2', '25337570', '5p13.1', '5', 'down-regulation', 'NFkappaB-12349897', 'Fluorescent Antibody Technique-2186409', 'gingival crevicular fluid-8034777', 'yes-10323681\r\n'),
('5764', 'Pleiotrophin', 'PTN', '25436328', '7q33', '7', 'up-regulation', 'SOX2-23686309', 'immunohistochemistry- 25436328', 'follicular fuild-7859927', 'yes-11546745\r\n'),
('5789', 'protein tyrosine phosphatase, receptor type, D', 'PTPRD', '25412184', '9p23-p24.3', '9', 'tumor supressor', 'STAT3-24843164', 'microarray analysis-PMC2426828', 'cerebrospinal fluid-PMC3032368', 'yes-PMC3032368\r\n'),
('5820', 'Pvt1 oncogene (non-protein coding)', 'PVT1', '25258543', '8q24', '8', 'up-regulation', 'p53-PMC3268411', 'Microarray Analysis-22869583', 'spinal fluid', 'yes\r\n'),
('64083', 'golgi phosphoprotein 3 (coat-protein)', 'GOLPH3', '25286393', '5p13.3', '5', 'up-regulation', 'FOXO1-PMC4133629', 'immunohistochemistry', 'interstitial fluid-PMC3404881', 'yes\r\n'),

('6648', 'Manganese superoxide dismutase', 'MnSOD', '25684475', '6q25.3', '6', 'up-regulation', 'AP-2-11491651', 'PCR-RFLP-25684475', 'blood', 'plasma membrane\r\n'),
('6775079', 'cyclooxygenase-2', 'COX-2', '25371669', 'NC_011137.1', '7581..8264', 'up-regulation', 'ESE-1-15794755', 'RT-PCR-11427038', 'cerebrospinal fluid-9836773', 'yes-9836773\r\n'),
('7033', 'trefoil factor 3 (intestinal)', 'TFF3', '25279197', '21q22.3', '21', 'up-regulation', 'NF?B-PMC1773791', 'immunohistochemistry', 'cerebrospinal fluid-10834934', 'yes\r\n'),
('7099', 'toll-like receptor 4', 'TLR4', '25400780', '9q33.1', '9', 'up-regulation', 'XBP1-20351694', 'RT-PCR-16303959', 'Synovial fluid -22037282', 'yes-22037282\r\n'),
('7515', 'X-ray repair complementing defective repair in Chi', 'XRCC1', '25335737', '19q13.2', '19', 'tumor supressor', 'E2F1-19031698', 'RFLP-12151350', 'plasma ', 'yes\r\n'),
('8000', 'prostate stem cell antigen', 'PSCA', '25709466', '8q24.2', '8', 'up-regulation', 'YY1', 'RT-PCR', 'blood and serum', 'cell membrane\r\n'),
('85320', 'ATP-binding cassette, sub-family C (CFTR/MRP), mem', 'ABCC11', '25320405', '16q12.1', '16', 'tumor supressor', 'OTX2', 'western blot analyses-PMC4156198', 'amniotic fluid', 'yes- PMC4164699\r\n'),
('857', 'caveolin 1, caveolae protein, 22kDa', 'Cav-1', '25339030', '7q31.1', '7', 'up-regulation', 'GATA-6-21514437', 'Patch-Clamp Techniques-18923542', 'serum', 'yes-857(gene)\r\n'),
('8738', 'CASP2 and RIPK1 domain containing adaptor with dea', 'CRADD', '25360218', '12q21.33-q23.1', '12', 'up-regulation', 'TSA-25360218', 'T-RFLP-16891498', 'spinal fluid- PMC540195', 'yes\r\n'),
('8838', 'WNT1 inducible signaling pathway protein 3', 'WISP3', '25400723', '6q21', '6', 'tumor supressor', 'SOX family-14872491', 'RT-PCR-PMC3366172', 'Synovial fluid-PMC3366172', 'yes-PMC3366172\r\n'),
('8842', 'prominin 1', 'CD133', '25339008', '4p15.32', '4', 'up-regulation', 'PROM1-22945648', 'immunohistichemistry-24375541', 'neural tube fluid- PMC3701589', 'yes-15917475\r\n'),
('9314', 'Kruppel-like factor 4 (gut)', 'KLF4', '25292057', '9q31', '9', 'up-regulation', 'OCT4-24792165', 'Gene Knockdown technique-24599951', 'amniotic fluid-PMC3471036', 'yes-19147802\r\n'),
('942', 'important member of the B7-CD28', 'B7-H1', '25337246', '2q33', '2', 'tumor supressor', 'STAT3-21267998', 'RT-PCR-PMC2802396', 'serum-25120686', 'yes\r\n'),
('9474', 'autophagy related 5', 'ATG-5', '25329677', '6q21', '6', 'up-regulation', 'ATF4-20038797', 'Gene Knockdown Technique-23075929', 'cerebrospinal fluid-7735128', 'yes-11793\r\n'),
('9582', 'apolipoprotein B mRNA editing enzyme, catalytic po', 'APOBEC3B', '25296601', '22q13.1-q13.2', '22', 'up-regulation', 'OTX2', 'Gene Knockdown Techniques-24154874', 'cerebrospinal fluid-PMC4144122', 'yes-PMC3934647\r\n'),
('960', 'Cluster of differentiation 44', 'CD44', '25664005', '11p13', '11', 'up-regulation', 'NF-kappa B-23226410', 'qRT-PCR', 'body cavity fluids', 'plasma membrane\r\n'),
('9734', 'histone deacetylase', 'HDAC', '25337229', '7p21.1', '7', 'up-regulation', 'GATA-2-11567998', 'cDNA microarray', 'BAL fluid-PMC2212744', 'yes-23167260\r\n'),
('9966', 'tumor necrosis factor (ligand) superfamily, member', 'TNFSF15', '25251497', '9q32', '9', 'up-regulation', 'STAT4-23000144', 'enzyme-linked immuno-sorbent assay', 'synovial fluid-9966', 'yes\r\n');

Structure of table in Database

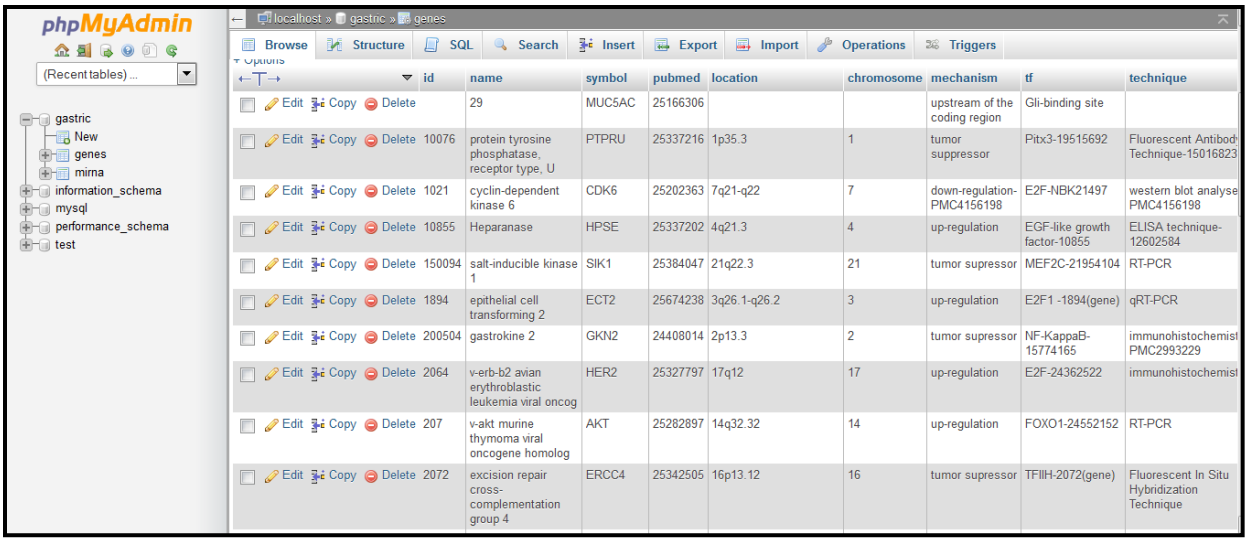

Figure. 5: Structure of table in database

c. For database connectivity

```
<?php
        $mysql=mysql_connect("localhost","root","");
                mysql_select_db("gastric");
                $query="SELECT * FROM genes ";
                $results=mysql_query($query);
                echo '<center>   <table border="0" cellpadding="100" cellsapcing="10" > ';
                echo '     <tr width="40%" height="50%">';
                $ish=0;
                while($result=mysql_fetch_assoc($results))
                {
```

```
                    echo          '

            <td width="40%" height="45" cellspacing="20"
cellpadding="100"                                                    ><a
href="search.php?submit='.$result['name'].'">'.$result['name'].'</a></td>

                                                                      ';

                                                                    $ish++;

                                                                    if($ish==3)

                                                                    {

                                                                            echo
'    </tr><tr>';

                                                                            $ish=0;

                                                                    }

                                                }

                                                echo      '    </tr></table>
</center>';

                                /*              else

                                                {

                                                        echo 'Nothing Found!';

                                                }       */



                                ?>
```

```
                    </div>
</div>
</div><!--close main-->
</body> </html>
```

6 Results

The Gastric Cancer Database was formed for the genes or the miRNAs which are responsible for causing the stomach cancer. HTML, CSS, JavaScript, PHP are the languages which are mainly used for this Database development. It includes:

6.1 The Home Page

The Home Page is having the basic introduction about the Gastric Cancer followed by the various causes of the Gastric Cancer, the signs and the symptoms of the gastric cancer, the various diagnosis processes for the Gastric Cancer, the various prevention measures that can be undertaken to get rid of the Gastric Cancer and the prognosis process for the cancer.

Figure 6: Home page

6.2 The Statistics Page

This page gives idea about the recent statistics of the Gastric Cancer across the world, the total cases of the cancer diagnosed, number of deaths, and the survival rates.

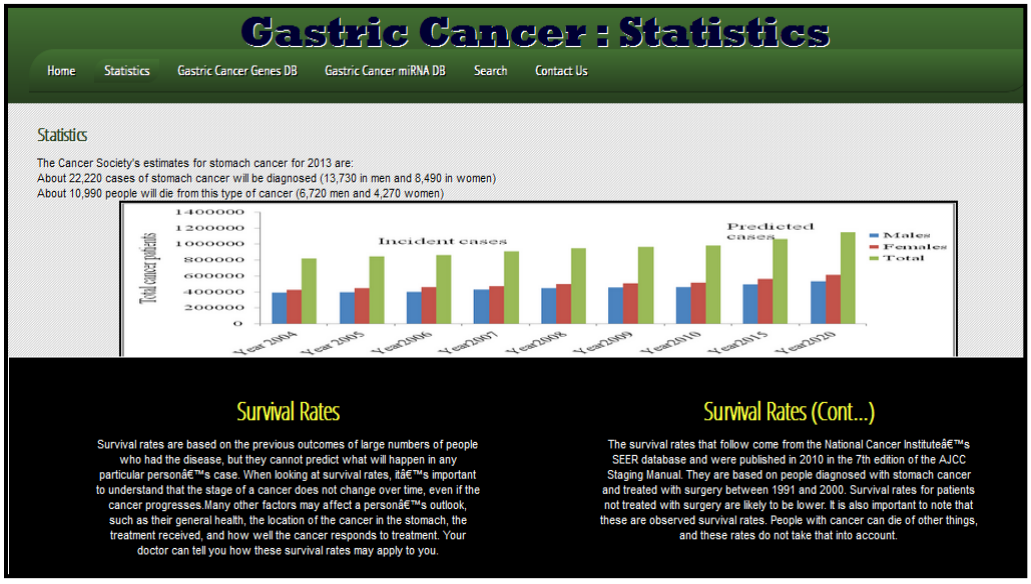

Figure 7: Statistics page

6.3 The Gastric Cancer Gene Database

The following page involves all the Gastric Cancer causing genes. By clicking on these genes you will able to get all the information or the various attributes of that gene like the gene id, the Pubmed id from which we concluded that this gene is responsible in causing the Gastric Cancer, the gene number, the chromosome number, the location where this gene is located, the transcription factors for that gene, the techniques which can be used for the extraction and also whether that gene is present in plasma membrane or not.

Figure 8: Gastric Cancer Gene Database

6.4 The Gastric Cancer miRNA Database

This page involves all the Gastric Cancer causing miRNAs. By clicking on these miRNAs you will able to get all the information or the various attributes of that miRNA like the gene id, the Pubmed id, the gene number, the chromosome number, the location where this miRNA is located, the transcription factors for that miRNA, the techniques which can be used for the extraction and also whether that miRNA is present in plasma membrane or not.

6.5 The Search Page

This page involves the search options for the Gastric Cancer causing Genes as well as the Gastric Cancer causing miRNAs. We can search by different attributes like Gene Symbol, Gene-ID, Pubmed ID and Gene Name in case of the Gene search and Gene Symbol, Gene-ID and Gene Name in case of the miRNA search.

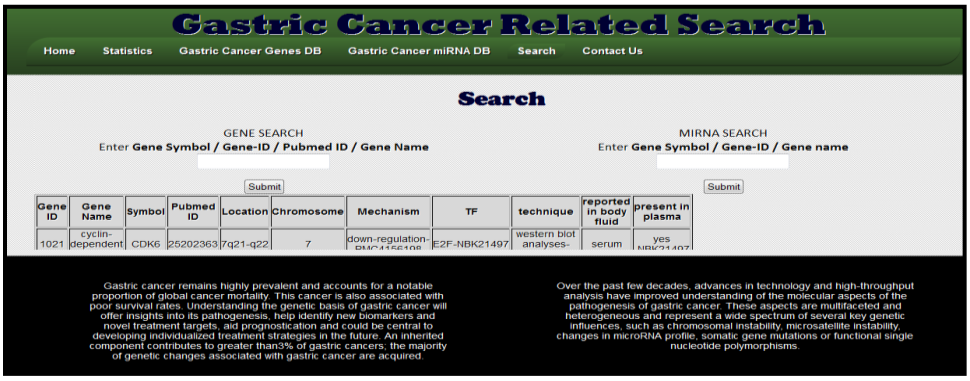

Figure 9: Search page

6.6 The Contact Page

This page includes the contact information for the developers of this database. This page also provides the feedback form for the users who will use this database which involves their name, email id and their comments for this database.

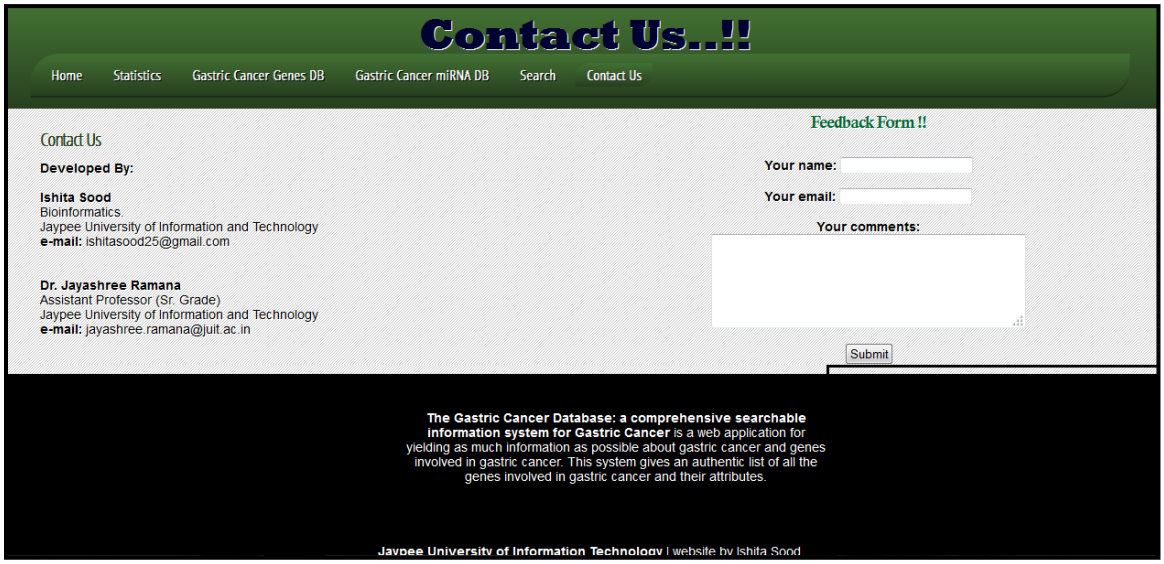

Figure 10: Contact page

7. Conclusion & Future Prospects

This web repository will be comprehensive resource for scientists and academicians working in the area of Gastric Cancer. Database developed and integrated in the background will provide users information as per their need and will help them to extract information regarding genes or miRNAs associated with Gastric Cancer.

Basic information has been collected that contains the genes and the miRNAs information along with their attributes.

We will extend the functionality and storage of this repository by the inclusion of more data sets in near future**.**

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