User Manual

Table of Contents

Introduction

Genetic disease genes are considered a promising source of drug targets. Most diseases are caused by more than one pathogenic factor; thus, it is reasonable to consider that chemical agents targeting multiple disease genes are more likely to have desired activities. This is supported by a comprehensive analysis on the relationships between agent activity/druggability and target genetic characteristics. The therapeutic potential of agents increases steadily with increasing number of targeted disease genes, and can be further enhanced by strengthened genetic links between targets and diseases. By using the multi-label machine-learning models for genetics-based drug activity prediction, we provide universal tools for prioritizing drug candidates.

To facilitate the use of the machine-learning prediction models, we developed a web server SCG-Drug (Systems Chemical Genetics-Drug, http://zhanglab.hzau.edu.cn/scgdrug) that allows a quick and intuitive access to the background information and predicted results.

Using the website

SCG-Drug is a web service that can help researchers to predict potential activities of drugs of interest with respect to their genetic information using the systems chemical genetics method.

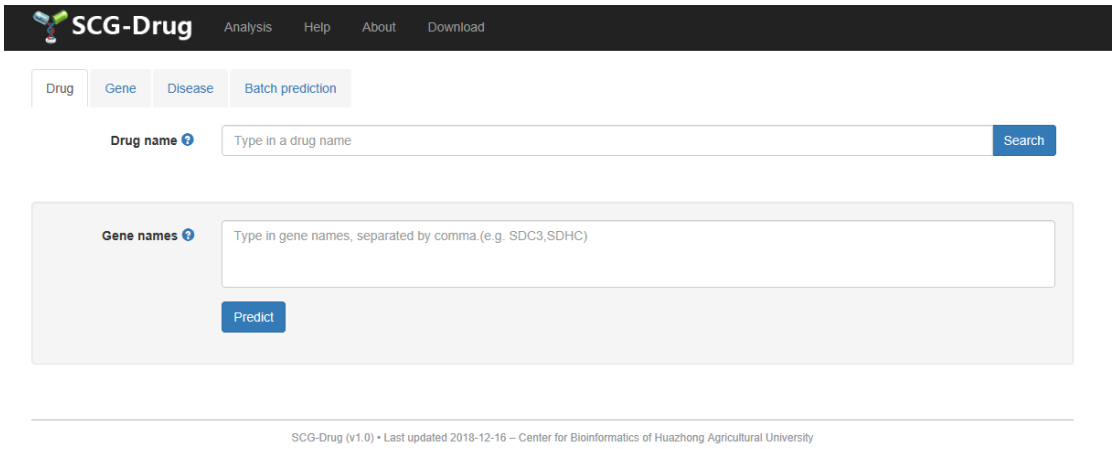
Currently, SCG-Drug contains 5,759 agents, 703 diseases and 19,238 genes derived from various databases. By retrieving SCG-Drug, researchers can detect the complex relationships between agents, genes, and diseases, which are definitely helpful to evaluate the agent activity and druggability.

Analysis

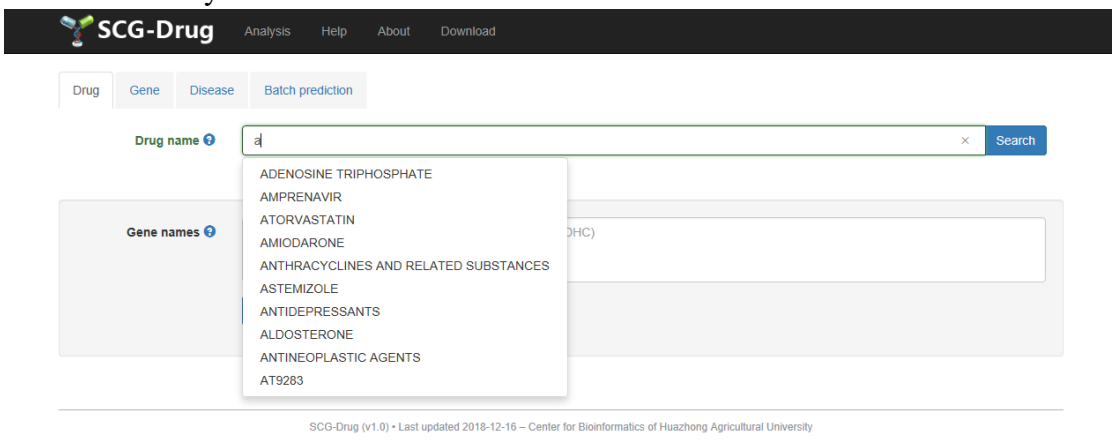
The SCG-Drug web interfaces allow users to explore medicinal information related to a given drug or gene through three interfaces: “Drug”, “Gene”, “Disease” and “Batch prediction”. By inputting the target information of any agents into SCG-Drug, one can use the established machine-learning models to predict the potential activities of the agents. In addition, all of the information for documented drugs (with normalized indications) and targets/genes (with normalized disease annotations) can be downloaded from the server. The data and the machine-learning models will be updated regularly.

Drug

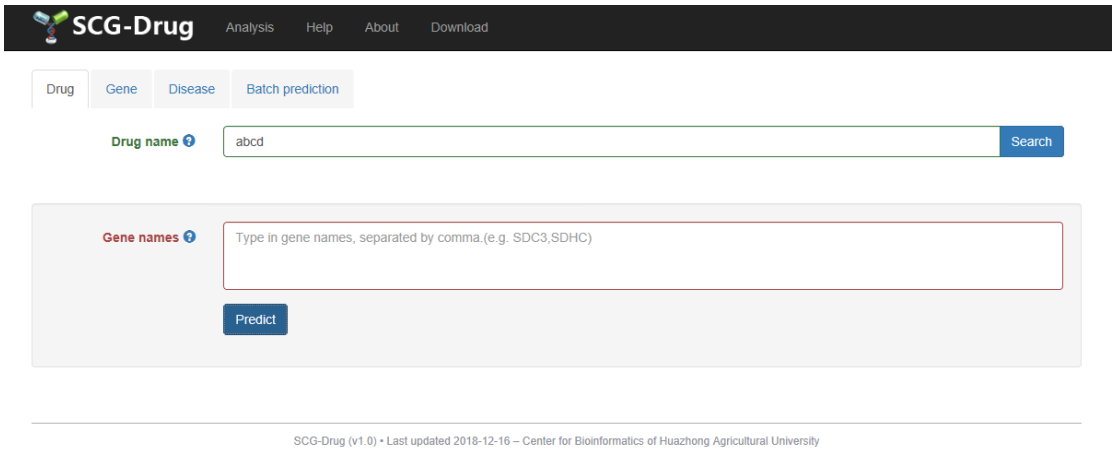
The “Drug” interface allows users to submit a single drug to retrieve target genes and potential activities of the query drug.



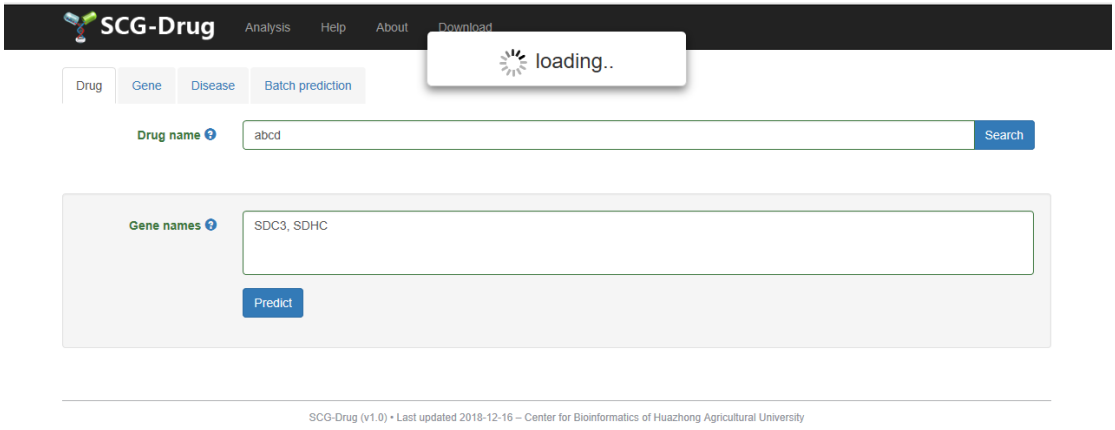
When you submit a single drug in the dropdowns, the drug will be searched in the database directly.



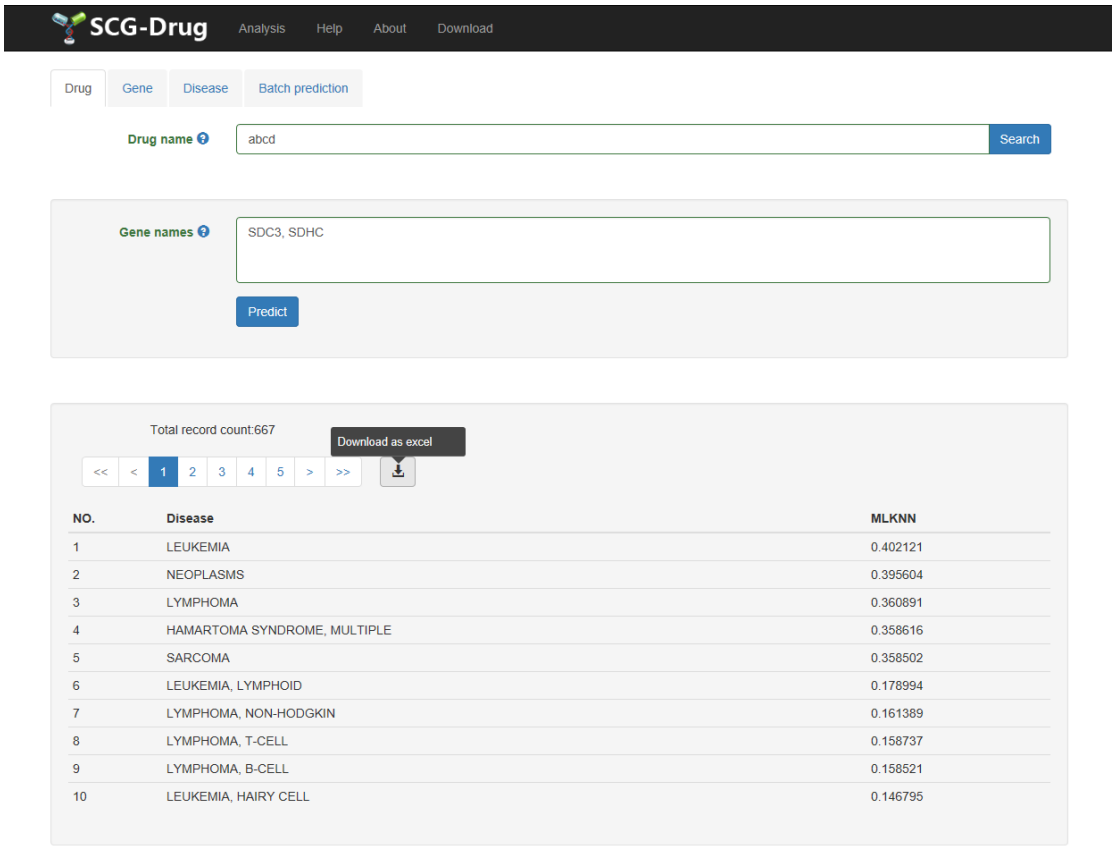
If it is unable to find any matches for the search term, the user will be asked to input the corresponding target genes of the drug.



Then, the system will call the prediction module automatically.

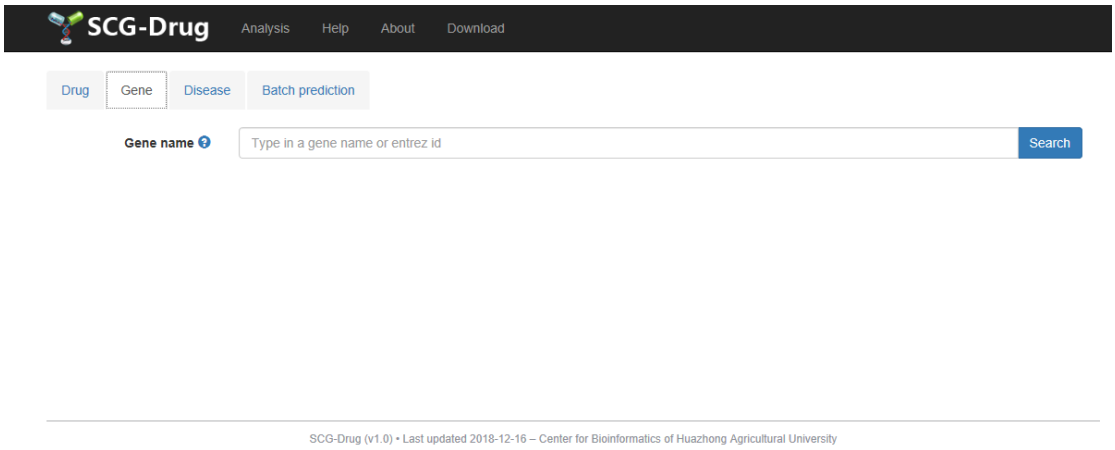


The predicted results will be present on the website and sorted by prediction score of MLKNN. And it can be downloaded as excel file.

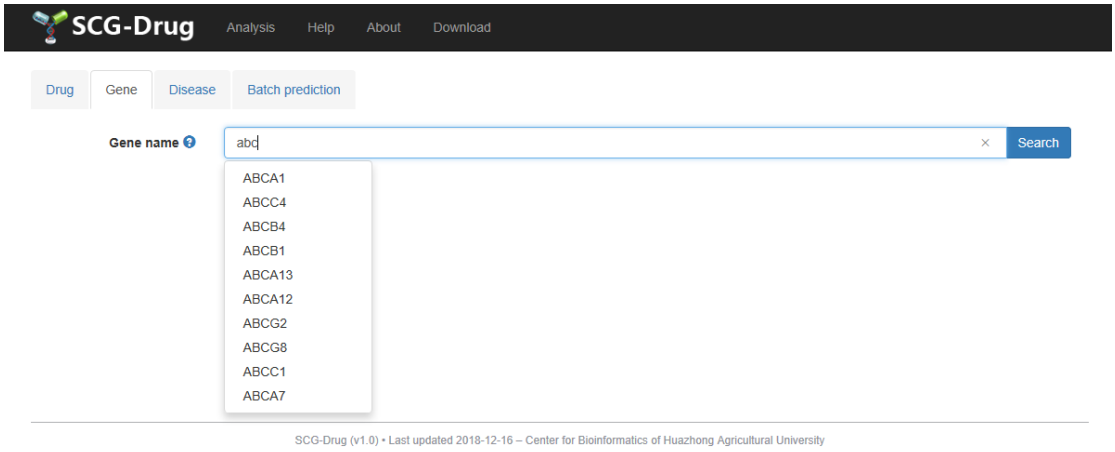


Gene

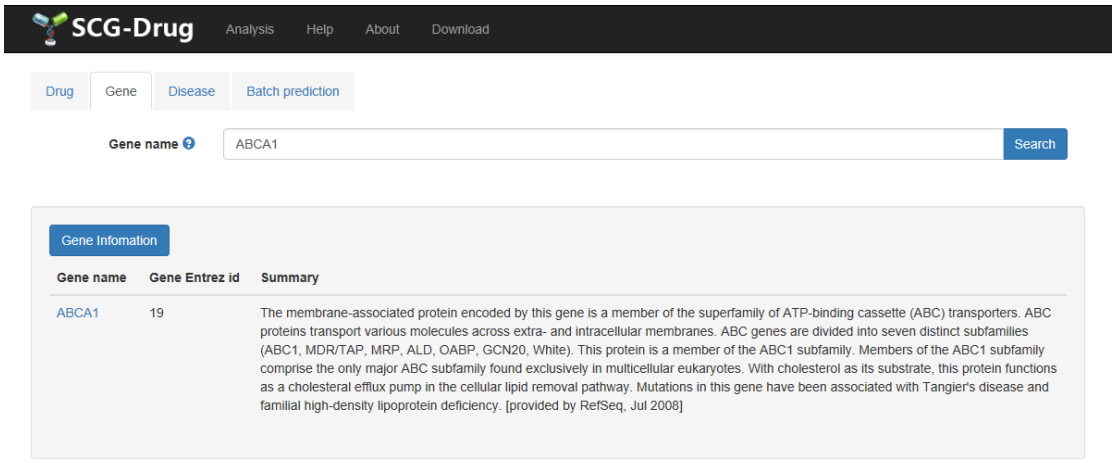
The “Gene” interface allows users to explore gene-related diseases and drugs only by submitting a gene name or an Entrez ID, which have been documented in the server. In addition, users can download overall information.



When you submit a single gene in the dropdowns, the drug will be searched in the database directly.



The searched result of gene will be present on the website.



The related disease will be present separately on the website and sorted by the druggability score. Meanwhile the related drugs will also be presented on the website on another page and sorted by the source of database. And they can be downloaded as excel file.

Related diseases | Related drugs

Total record count:97

<< < 1 2 3 4 5 > >>

NO.	Disease Name	Disease Description	Source	Score
1	GUILLAIN-BARRE SYNDROME	An acute inflammatory autoimmune neuritis caused by T cell- mediated cellular immune response directed towards peripheral myelin. Demyelination occurs in peripheral nerves and nerve roots. The process is often preceded by a viral or bacterial infection, surgery, immunization, lymphoma, or exposure to toxins. Common clinical manifestations include progressive weakness, loss of sensation, and loss of deep tendon reflexes. Weakness of respiratory muscles and autonomic dysfunction may occur. (From Adams et al., Principles of Neurology, 6th ed, pp1312-1314)	Clinvar; GAD; OMIM; Orphanet; HGMD; GWASdb; DisGeNET	33
2	WISKOTT-ALDRICH SYNDROME	A rare, X-linked immunodeficiency syndrome characterized by ECZEMA; LYMPHOPENIA; and, recurrent pyogenic infection. It is seen exclusively in young boys. Typically, IMMUNOGLOBULIN M levels are low and IMMUNOGLOBULIN A and IMMUNOGLOBULIN E levels are elevated. Lymphoreticular malignancies are common.	HGMD; DisGeNET	7
3	RETINAL DISEASES	NA	GAD; DisGeNET	3
4	RADIATION INJURIES	Harmful effects of non-experimental exposure to ionizing or non-ionizing radiation in VERTEBRATES.	GAD; DisGeNET	3
5	SUPRANUCLEAR PALSY, PROGRESSIVE	A degenerative disease of the central nervous system characterized by balance difficulties; OCULAR MOTILITY DISORDERS (supranuclear ophthalmoplegia); DYSARTHRIA; swallowing difficulties; and axial DYSTONIA. Onset is usually in the fifth decade and disease progression occurs over several years. Pathologic findings include neurofibrillary degeneration and neuronal loss in the dorsal MESENCEPHALON; SUBTHALAMIC NUCLEUS; RED NUCLEUS; pallidum; dentate nucleus; and vestibular nuclei. (From Adams et al., Principles of Neurology, 6th ed, pp1076-7)	GAD; DisGeNET	3
6	BEHCET SYNDROME	Rare chronic inflammatory disease involving the small blood vessels. It is of unknown etiology and characterized by mucocutaneous ulceration in the mouth and genital region and uveitis with hypopyon. The neuro-ocular form may cause blindness and death. SYNOVITIS; THROMBOPHLEBITIS; gastrointestinal ulcerations; RETINAL VASCULITIS; and OPTIC ATROPHY may occur as well.	GAD; DisGeNET	3
7	GLOMERULONEPHRITIS	Inflammation of the renal glomeruli (KIDNEY GLOMERULUS) that can be classified by the type of glomerular injuries including antibody deposition, complement activation, cellular proliferation, and glomerulosclerosis. These structural and functional abnormalities usually lead to HEMATURIA; PROTEINURIA; HYPERTENSION; and RENAL INSUFFICIENCY.	GAD; DisGeNET	3
8	SMALL CELL LUNG CARCINOMA	A form of highly malignant lung cancer that is composed of small ovoid cells (SMALL CELL CARCINOMA).	GAD; DisGeNET	3
9	PULMONARY DISEASE, CHRONIC OBSTRUCTIVE	A disease of chronic diffuse irreversible airflow obstruction. Subcategories of COPD include CHRONIC BRONCHITIS and PULMONARY EMPHYSEMA.	GAD; DisGeNET	3
10	DIABETES COMPLICATIONS	Conditions or pathological processes associated with the disease of diabetes mellitus. Due to the impaired control of BLOOD GLUCOSE level in diabetic patients, pathological processes develop in numerous tissues and organs including the EYE, the KIDNEY, the BLOOD VESSELS, and the NERVE TISSUE.	GAD; DisGeNET	3

Related diseases | Related drugs

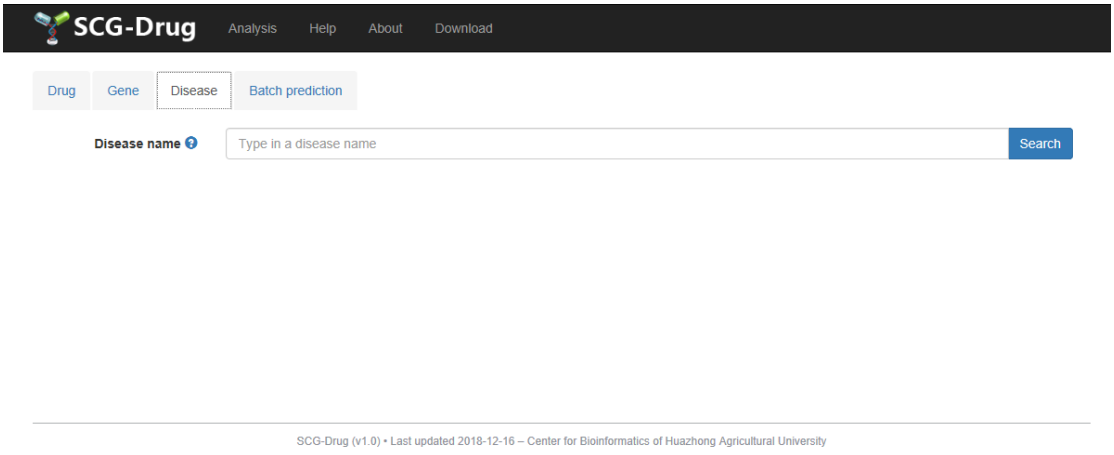
Total record count:4

<< < 1 > >>

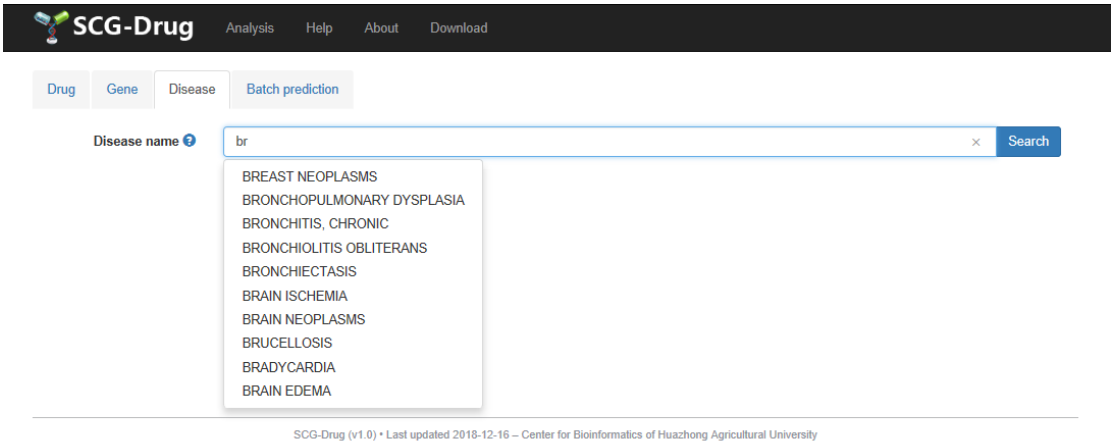
NO.	Drug name	Drug Description	Source
1	HMG COA REDUCTASE INHIBITORS	NA	DGIdb
2	ADENOSINE TRIPHOSPHATE	DB00171:An adenine nucleotide containing three phosphate groups esterified to the sugar moiety. In addition to its crucial roles in metabolism adenosine triphosphate is a neurotransmitter. [PubChem] & TTDS00350:Dietary shortage	Drugbank; DGIdb
3	PROBUCOL	DB01599:A drug used to lower LDL and HDL cholesterol yet has little effect on serum-triglyceride or VLDL cholesterol. (From Martindale, The Extra Pharmacopoeia, 30th ed, p993). & TTDS00278:Coronary artery disease	Drugbank; DGIdb
4	GLYBURIDE	DB01016:Glyburide is an oral antihyperglycemic agent used for the treatment of non-insulin-dependent diabetes mellitus (NIDDM). It belongs to the sulfonylurea class of insulin secretagogues, which act by stimulating β cells of the pancreas to release insulin. Sulfonylureas increase both basal insulin secretion and meal-stimulated insulin release. Medications in this class differ in their dose, rate of absorption, duration of action, route of elimination and binding site on their target pancreatic β cell receptor. Sulfonylureas also increase peripheral glucose utilization, decrease hepatic gluconeogenesis and may increase the number and sensitivity of insulin receptors. Sulfonylureas are associated with weight gain, though less so than insulin. Due to their mechanism of action, sulfonylureas may cause hypoglycemia and require consistent food intake to decrease this risk. The risk of hypoglycemia is increased in elderly, debilitated and malnourished individuals. Glyburide has been shown to decrease fasting plasma glucose, postprandial blood glucose and glycosolated hemoglobin (HbA1c) levels (reflective of the last 8-10 weeks of glucose control). Glyburide appears to be completely metabolized, likely in the liver. Although its metabolites exert a small hypoglycemic effect, their contribution to glyburide's hypoglycemic effect is thought to be clinically unimportant. Glyburide metabolites are excreted in urine and feces in approximately equal proportions. The half-life of glyburide appears to be unaffected in those with a creatinine clearance of greater than 29 ml/min/1.73m².	Drugbank; DGIdb

Disease

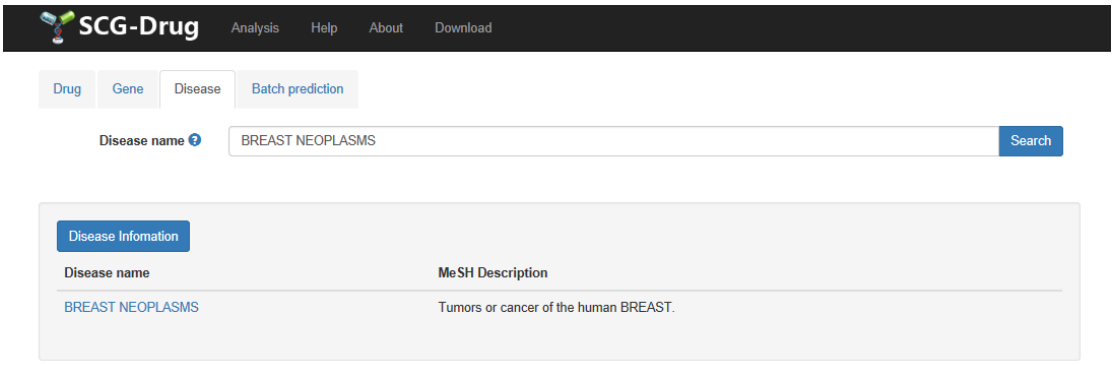
The “Disease” interface allows users to obtain relevant disease genes with druggability score, and database source by querying standardized disease descriptions of MeSH.



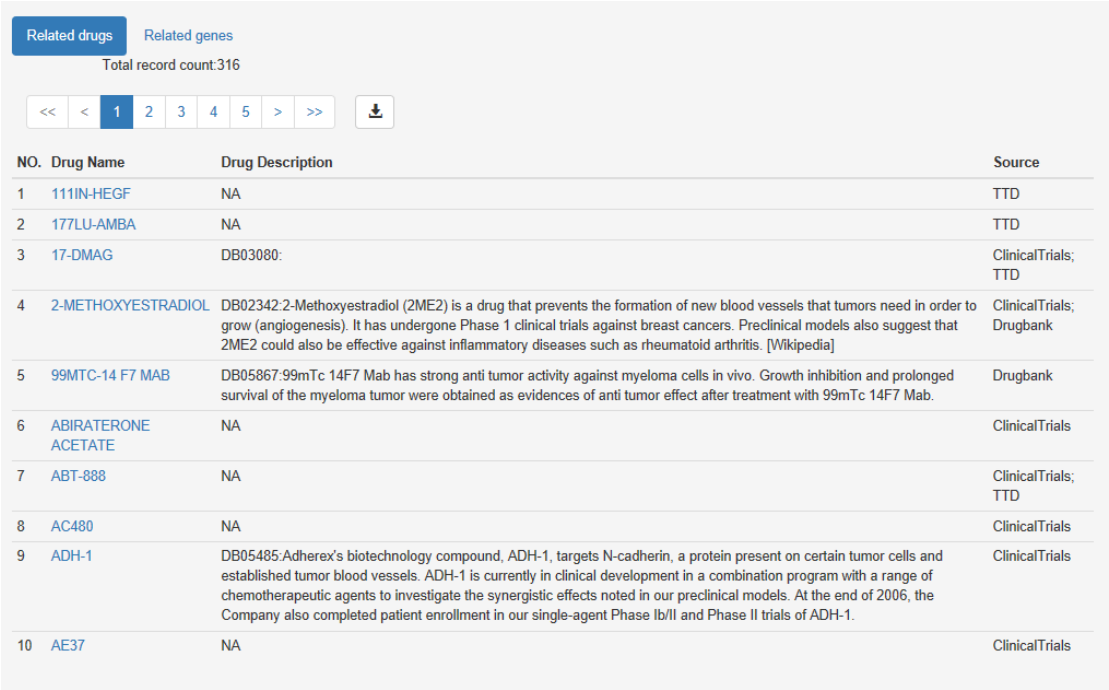
When you submit a single disease name in the dropdowns, the drug will be searched in the database directly.



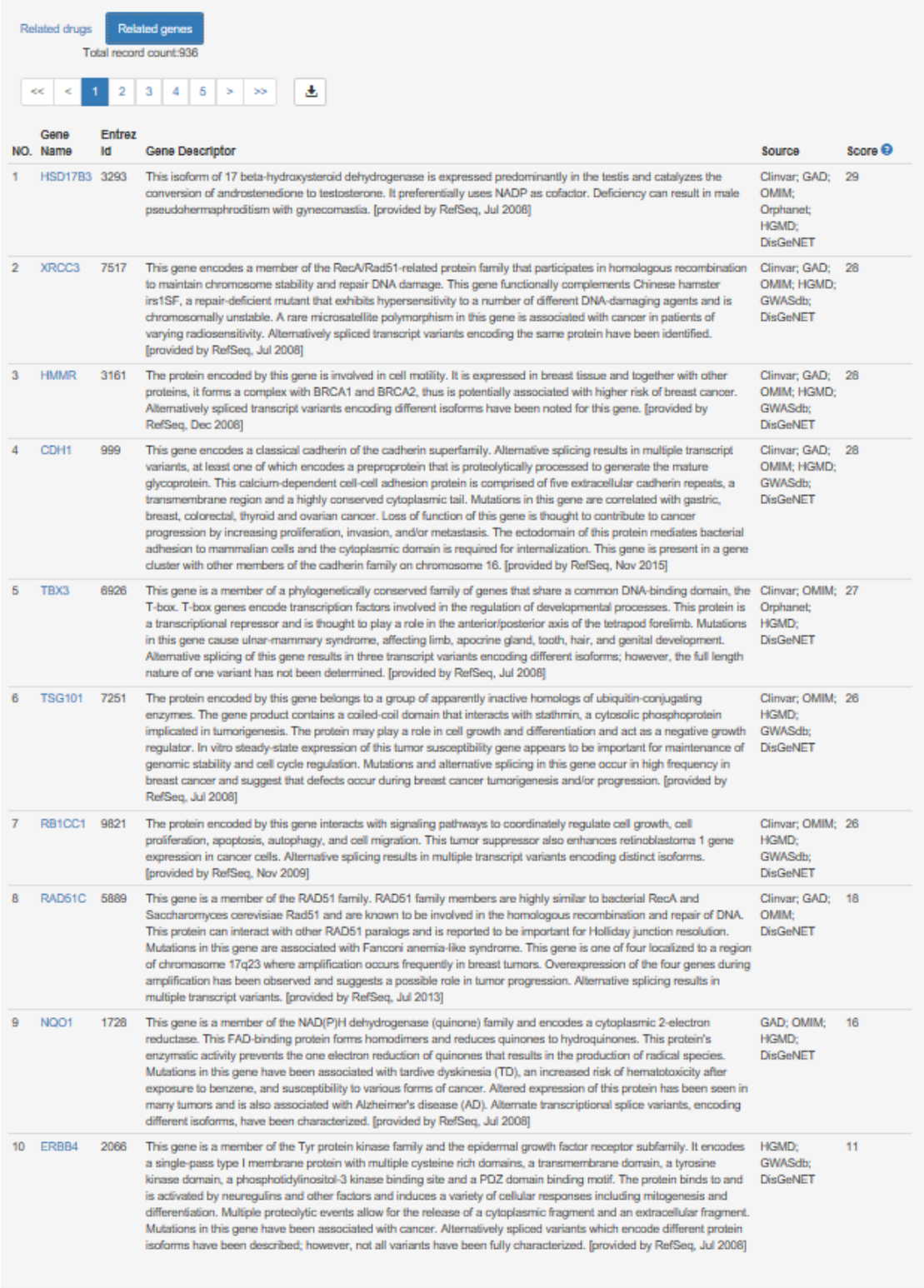
The searched result of gene will be present on the website.



The related drugs will be present separately on the website and sorted by the druggability score. Meanwhile the related genes will also be presented on the website on another page and sorted by the source of database. And they can be downloaded as excel file.



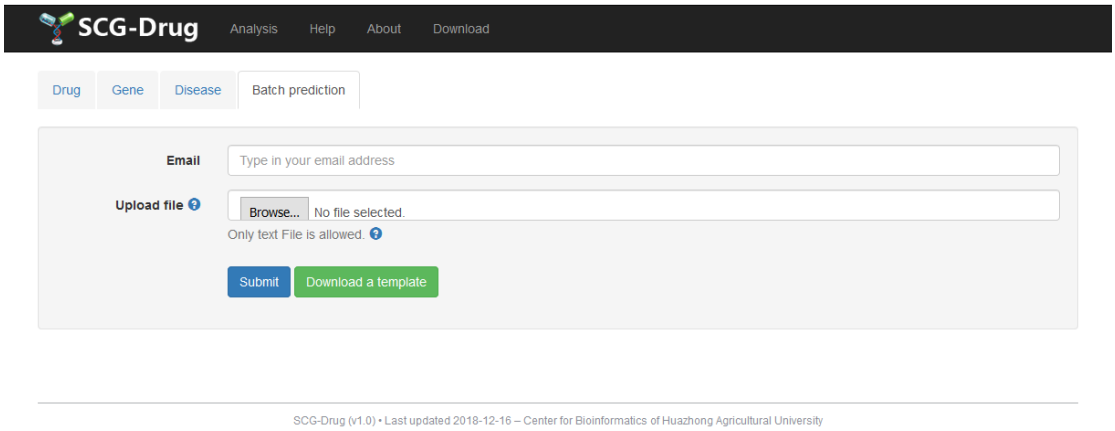
NO.	Drug Name	Drug Description	Source
1	111IN-HEGF	NA	TTD
2	177LU-AMBA	NA	TTD
3	17-DMAG	DB03080:	ClinicalTrials; TTD
4	2-METHOXYESTRADIOL	DB02342:2-Methoxyestradiol (2ME2) is a drug that prevents the formation of new blood vessels that tumors need in order to grow (angiogenesis). It has undergone Phase 1 clinical trials against breast cancers. Preclinical models also suggest that 2ME2 could also be effective against inflammatory diseases such as rheumatoid arthritis. [Wikipedia]	ClinicalTrials; Drugbank
5	99MTC-14 F7 MAB	DB05867:99mTc 14F7 Mab has strong anti tumor activity against myeloma cells in vivo. Growth inhibition and prolonged survival of the myeloma tumor were obtained as evidences of anti tumor effect after treatment with 99mTc 14F7 Mab.	Drugbank
6	ABIRATERONE ACETATE	NA	ClinicalTrials
7	ABT-888	NA	ClinicalTrials; TTD
8	AC480	NA	ClinicalTrials
9	ADH-1	DB05485:Adherex's biotechnology compound, ADH-1, targets N-cadherin, a protein present on certain tumor cells and established tumor blood vessels. ADH-1 is currently in clinical development in a combination program with a range of chemotherapeutic agents to investigate the synergistic effects noted in our preclinical models. At the end of 2006, the Company also completed patient enrollment in our single-agent Phase Ib/II and Phase II trials of ADH-1.	ClinicalTrials
10	AE37	NA	ClinicalTrials



Batch prediction

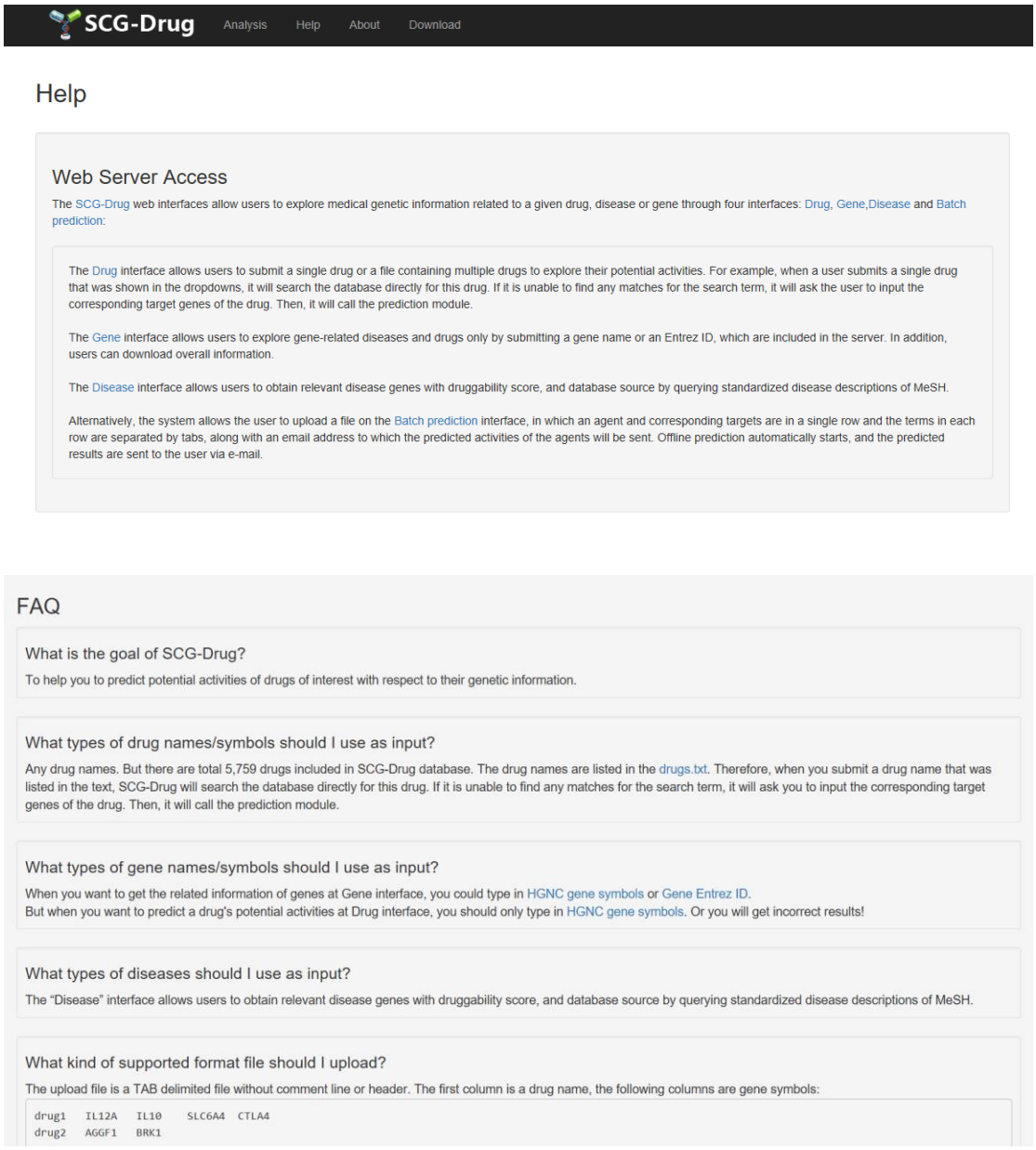
The system allows the user to upload a file on the “Batch prediction” interface, in which an agent and corresponding targets are in a single row and the terms in each row are separated by tabs, along with an email address to which the predicted activities of

the agents will be sent. Offline prediction automatically starts, and the predicted results will be sent to the user via e-mail.



Help

The “Help” interface presents users useful information about the website Server Access and several Frequently Ask Questions (FAQ).



Download

Users can obtain the information for documented drugs (with normalized indications) and targets/genes (with normalized disease descriptions) from “Download” page.