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LEVERAGING IN SILICO NETWORK BIOLOGY APPROACHES TO ESTABLISH THERAPEUTICS AGAINST BRAIN ABSCESS CAUSATIVE AGENTS.

Ambika Singh

Msc microbiology student

Amity Institute of Biotechnology, Amity university Uttar Pradesh, Lucknow, India

1. **.Abstract:**

Brain abscess / intracranial abscess is a central nervous system disease caused by the infection from bacterial viral ,fungal etc. sources leading to a pus filled capsule inside the brain. It is a complicated and life threatening disease since currently there are no widely accepted neurosurgical management guidelines. Brain abscess has a high morbidity and mortality rate thus, the disease is currently a major public health problem.

Majority of the pathogens are bacterial in nature eg -streptococcus , staphylococcus etc. In this study ,we have established some therapeutics against brain abscess using in silico network biology approaches. The selection of therapeutics and antibiotics depends on the microorganisms isolated from blood or CSF and their ability to cross the natural barriers of brain (BBB).

The construction of network consisting genes associated with brain abscess were collected from different databases like malacard,genecard, and thorough literature study using cytoscape. The network consists of nodes representing genes and interactions between them. We identified two hub genes (STAT3 and IL6)from the network having highest degree and satisfying various parameters like MCC,MNC,stress etc. .We analyzed the role of target gene in brain abscess.

A virtual library consisting of various antimicrobial compounds as ligands was made .Molecular Docking using auto dock vina1.5.6 version was done and through this study we found out promising therapeutics against brain abscess .In conclusion we found out the role of STAT3 and IL6 gene in brain abscess and established therapeutics against the causative agents .

The docking simulations revealed several promising candidates with high binding affinity and favorable interaction patterns with the target proteins implicated in brain abscess pathophysiology. Furthermore, structural analysis of the ligand-receptor complexes provided insights into the molecular mechanisms of action and potential modes of inhibition for the identified compounds.

Our findings highlight the potential of computational docking techniques in accelerating the discovery and development of novel therapeutics for brain abscess treatment. Future experimental validation of the identified lead compounds is warranted to confirm their efficacy, selectivity, and safety profiles in preclinical and clinical settings. Overall, this computational study contributes to the ongoing efforts to combat brain

abscesses and improve patient outcomes through the rational design of targeted pharmacological interventions.

Keywords : BBB, network construction , virtual library, docking, stat3 gene .

2. Introduction

2.1 Overview of brain abscess

Brain abscess (also known as intracranial abscess)is a central nervous system disease caused by the infection from bacterial,viral,fungal etc sources leading to a pus filled capsule inside the brain. It is a complicated and life threatening disease since currently there are no widely accepted neurosurgical management guidelines. **(miranda, 2013)** Brain abscess has high morbidity ,mortality rate thus, the disease is a threatening public health problem. Recent studies ,researches shows that brain abscesses are more predominant in males than in females with a male-to-female ratio varying between 2:1 and 3:1 and can occur at any age, but mostly occur between the third and fifth decades of life. **(Muzumdar, 2011)** Brain abscess is a type of infectious disease, therefore it is expected to be more common in a setting with poor sanitation and medical facilities (developing countries).

Brain abscesses occurs when pathogens grow inside the parenchyma of brain. Abscess occurs most commonly in the frontal lobe in the brain but the location can depend on the type of infection . It has been observed that Abscess occur more on the left side of brain than on the right. Initial infection of parenchyma is known as cerebritis.

Brain abscess can be divided into four stages- **early cerebritis stage, late cerebritis stage ,early capsule formation stage and late capsule formation stage**. Cerebritis is further divided into early and late phases and duration is commonly 10-14 days depending on the virulence of the pathogen causing the infection. During this stage there is a increase in the permeability of blood vessels without angiogenesis. During early cerebritis (2-3 days),edema, vascular congestion, coagulative necrosis etc occurs. After 7-8 days after the infection liquefactive necrosis occurs in various parts of the brain. Late cerebritis progresses and leads to form a cerebral abscess, where a pus filled thick capsule is formed.

Brain abscesses can be spread in various ways for example from nearby structures, such as sinusitis, dental infections, or ear infections, can spread directly into the brain tissue. Pathogens are mostly polymicrobial in nature .

Bloodstream /hematogenous spread : Bacteria or other infectious agents can enter the bloodstream from other parts of the body, such as the lungs or heart, and then travel to the brain, where they can lodge and cause an abscess. E.g.-staphylococcus and streptococcus.

Trauma or brain surgery: Traumatic injuries to the head that penetrate the skull can introduce bacteria directly into the brain tissue, leading to the formation of an abscess. Majority of the pathogens are skin colonizing bacteria for example staphylococcus aureus ,staphylococcus epidermidis,gram negative bacilli.

Contiguous spread: Infections from adjacent structures, such as the skull or spinal cord, can spread to the brain tissue, resulting in the formation of an abscess. Inside the brain the most common locations of abscesses were the frontal (37%) and parietal lobes (27%). The majority of frontal abscesses were caused by contiguous spread.

Brain abscess in immunocompromised patients or with acquired immunodeficiency syndrome (AIDS) is higher, probably due to the disrupted natural barriers of brain(BBB)leading to a growing number of opportunistic infections. The bacteria's are responsible for >95% of brain abscesses in immunocompromised patients. Treatment of infections in the central nervous system (CNS) is life threatening and complicated due to the blood-cerebrospinal fluid (CSF)-barrier (B-CSF-B) and the blood-brainbarrier (BBB). They prevent the entry of any antibiotics across the BBB.

The parenchyma of brain is protected from any exposure to drugs by BBB. Both the BBB and B-CSFB are very important in the entry and distribution of antibiotics inside the brain. The BBB is important in delivery of drugs to the brain parenchyma in areas of the brain with cerebritis and abscess **(raza, 2005**).

2.2 Common symptoms and signs of brain abscess:

symptoms vary depending on the size and location and number of the abscess in the brain:

- Headache (69% to 70%) the most common medical symptom.
- Pain is usually common to the side of the abscess, and it can occur slowly or suddenly. The pain is most severe in intensity and not relieved by over-thecounter pain medications.
- Fever (45% to 53%)
- Seizures (25% to 35%) can be the first manifestation of brain abscess. Grand mal seizures are particularly common in frontal abscesses. Seizures are one of the most important neurological complications of bacterial brain abscesses.
- Nausea and vomiting (40%) are mostly seen with raised intracranial pressure due to large size of abscesses and can even cause brain shift.

2.3**Common pathogens/causative agents causing the infection:**

Majority of the pathogens are aerobic in nature than anaerobes. Streptococci are most often identified among aerobic pathogens. Bacteroidesfragilis and Peptostreptococcus species are the most common anaerobic organisms isolated from the abscesses. Organisms vary significantly with the origin of abscess **(maher, 2018).** The most common pathogens in communityacquired brain abscess(outside of hospital) are microorganisms present in the oral cavity for example Streptococcus anginosus group, Fusobacterium spp., and Aggregatibacter spp., which are often related with dental and chronic ear infections., Mycobacterium tuberculosis in endemic areas, and Nocardia spp., fungi, and parasites in the severely immune-compromised patients. **(JD, 2018)**

- Staphylococcus aureus and epidermidis: after brain surgery
- Gram-negative species are more common in infants
- Listeria in pregnant women and older patients
- Group B Streptococcus (GBS) and E. coli in neonates
- Fusobacteriumnucleatum

2.4 Current Treatment and therapeutics available for brain abscess

Diagnosis of abscess starts with brain MRI including DWI/ADC and T1 weighted imaging with and without gadolinium for patients being suspected of having brain abscess. MRI is more sensitive than computated tomography (CT)to the early changes of cerebritis and will demonstrate the signal changes more easily expected for an area of inflammation. If MRI is not available, CT scan is done (**ming-jung, 2010)**. Management and treatment of brain abscess requires both medical and surgical methods. Surgical treatment includes - aspiration or excision of lesions larger than 2.5 cm in diameter, depending on brain location **(m, 2018)**Duration of treatment depends upon the size , location, number of abscesses, the pathogen involved in the infection . In majority of the cases, 8-12 weeks therapy is required. Usually, both medical and surgical treatments are considered for the treatment .CT and MRI is used to diagnose brain abscess for localizing the abscess and number of abscess .If the abscess is2 to 2.5 cm in diameter then surgery is required as soon as possible to prevent brain shift and rupture of abscess(ventriculitis).

The selection of therapeutics and antibiotics depends on the microorganisms isolated from blood or CSF. Several antimicrobials are unable to cross the blood-brain barrier and are not useful in treating brain abscess for example first-generation cephalosporins, Aminoglycosides, and tetracyclines.etc (**miranda, 2013**).Brain abscess is a type of infectious disease, therefore it is expected to be more common in a setting with poor sanitation and medical facilities . Brain abscess is a complicated disease to manage with neurosurgical drainage and high-dose antibiotics due to the regional differences in pathogens and antimicrobial susceptibility as well as risk of drug toxicity during the prolonged treatment. **(nathoo, 2011**) Brain abscess also carries a high risk of death. The most common abscess locations are the frontal (37%) and parietal lobes (27%). In 21% of cases, multiple (>1) abscesses are observed. The majority of frontal abscesses are caused by contiguous spread. In most of the cases by the time diagnosis is made cerebritis has progressed to cerebral abscess but if detection of cerebritis is done early enough, treatment with antibiotics can successfully treat cerebritis in the early stage. Broadspectrum intravenous antibiotics are also needed and can later be changed to agents tailored to the specific organisms.

2.5 The appropriate duration of antibiotic treatment :

The majority (89%) of the patients are treated surgically. The patients who are treated with antibiotics often have multiple abscesses, poorly accessible abscesses, such as in the cerebellum, or a poor premorbid conditions. Seventy six % of patients requiring surgical treatment had needle aspiration performed, while 24% of those requiring surgical treatment underwent a craniotomy with excision of the absces . **(Lumbiganon P, 2018)**

For the past 20 years high dose intravenous penicillin G and chloramphenicol have been used to treat brain abscess in this setting with satisfactory outcomes.The most Important side effect of chloramphenicol is its toxic hematologic effect including a common and predictable, but reversible, erythroid suppression of the bone marrow. However, serious irreversible aplastic anemia, leading in many cases to fatal pancytopenia, has been described in patients who received chloramphenicol . Third generation cephalosporins, either cefotaxime or ceftriaxone have good central nervous system penetration and excellent in vitro activity against many pathogens isolated from bacterial brain abscess. Metronidazole is highly active against anaerobic bacteria, including
Bacteroidesfragilis, the most resistant anaerobe. Therefore, metronidazole is usually combined with third generation cephalosporins or penicillin G for the treatment of cyanotic brain abscess .

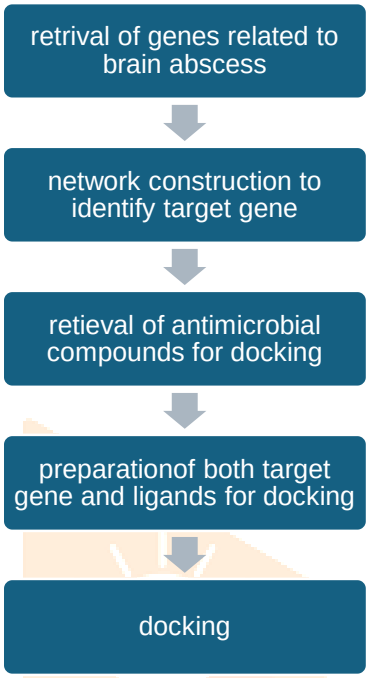
The type of antibiotic treatment is mainly dependent on microbial findings with most patients receiving 4–8 weeks of intravenous antibiotics, frequently followed by a course of oral antibiotics. The preferred treatment regimen involved a beta-lactam antibiotic (high-dose penicillin, cephalosporin, or carbapenem) combined with metronidazole or other agents targeting anaerobic bacteria. Specifically, high-dose penicillin, cefuroxime, or ceftriaxone in combination with metronidazole were typically used for abscesses related to ear, nose, and throat (ENT) infections. In recent years, meropenem combined with metronidazole has become more common for culturenegative infections. The selection and duration of antibiotic therapy varied, often adjusted based on microbial findings, patient tolerance, and physician preference. An increasing number of patients received meropenem, both empirically before culture results were available and after microbial diagnosis.

2.6 In silico approaches to establish therapeutics

Conventional drug discovery and development are inherently risky and time-consuming processes, involving target identification and validation, lead compound discovery and optimization, and extensive preclinical and clinical trials. In recent years, in silico approaches have shown promise in reducing both the time and cost associated with the drug discovery process. **(torres, 2019)**The availability of crystal structures for various disease-related proteins enables genome structure-based methods, such as molecular docking and virtual library screening, to identify potential ligands (hits) from extensive compound databases. These hits can then be experimentally validated or used to explore structureactivity relationships for optimization. The primary objective of drug discovery is to identify small molecules capable of modulating the function of target proteins, thereby influencing the disease phenotype. (**MM, 2022**)

Computer-aided drug design (CADD) utilizes computational models and simulations in the discovery and design of new drugs. This approach helps identify potential drug candidates, predict their interactions with biological targets like proteins or enzymes, and optimize their properties for effectiveness and safety**. (yu, 2017)**

3. Materials and method :



MALACARD: MalaCards is a comprehensive database that provides a wealth of information about human diseases and their related conditions. **(espe, 2018)** It was used to collect genes related to brain abscess.**URl:.https://www.malacards.org**

Gene card: Gene Cards is a comprehensive database that provides a wealth of information about human genes, their functions, and their associated diseases. It was also used to collect genes related to brain abscess . **URl : https://www.genecards.org**

PDB: Protein data bank is a freely accessible database for the three dimensional structural data of large biological molecules. The (PDB) is a comprehensive and widely used resource in the field of structural biology.PDB was used to get three dimensional structure of our target genes..**URl:https://www.rcsb.org**

PubChem : PubChem is a comprehensive database of chemical compounds, their properties, and their biological activities. Developed and maintained by the National Center for Biotechnology Information (NCBI). The database was used to collect antimicrobial compounds.
URl:https://pubchem.ncbi.nlm.nih.gov

ZINC database - The ZINC Database is a comprehensive resource for virtual screening and drug discovery in the field of computational chemistry and pharmaceutical research. ZINC contains a large and diverse library of chemical compounds, including small molecules, fragments, building blocks, and drug-like compounds. **(irwin, 2005)** These compounds are sourced from various suppliers, including commercial vendors, chemical catalogs, and virtual libraries generated through computational methods. **URl :https://zinc.docking.org**

NPASS:

The NPass (Natural Product Activity and Species Source) database is a valuable resource in the field of natural products research. It serves as a repository of information about natural products, their biological activities,

and the species from which they are derived. NPASS was used to collect antimicrobial compounds needed for docking.

URl:https://bidd.group/NPASS/

Open Babel:

Open Babel is open-source software designed for molecular modeling, cheminformatics, and computational chemistry tasks. Open Babel supports the conversion of chemical files between different formats, making it easier to work with diverse chemical databases and software packages. It can read and write over 100 different chemical file formats. It was used to convert ligands format required for docking .

URl :https://www.cheminfo.org

- **FOR TARGET IDENTIFICATION**

DISCOVERY AND RETRIEVAL OF GENES:

A drug receptor in our body is a biological entity, usually a protein, that can change the disease phenotypes . Therefore, the identification of main drug receptors is the first and most important step in drug discovery. To identify instances of "Gene/Protein AND Target "different databases were used. To get genes related to brain abscess a thorough literature study, databases like MALACARD, GENECARD, OMIM (NCBI) were used. All the genes associated with brain abscess were compiled together into a table and duplicates were removed from the list of genes. The total genes we got were 2612 in number.

NETWORK CONSTRUCTION:

To form network of genes cytoscape software is used. Cytoscape is a tool for viewing and analyzing very large networks. The network contains nodes and edges .The nodes are used to represent genes/proteins and edges represent the interactions between the nodes. The network was formed at different confidence levels and analyzed for example at 0.40, 0.90, 0.70 etc. Using cytohubba a plug-in in cytoscape, different parameters like MCC, MNC, DEGREE,STRESS etc was analyzed for top 20 genes at 0.95 confidence level.

IDENTIFICATION OF HUB GENES :

For getting the hub gene/target gene a list was made of all the parameters and most repeating gene was listed out and their degree was checked in the whole network at 0.95 confidence level .Target gene STAT3 is the most repeating gene satisfying the majority of parameters and having most degree in the whole network at 0.95 confidence level.

- **Ligand identification :**

After thorough literature study a list of antimicrobial compounds from different chemical databases like PUBCHEM,LOTUS,COCONUT,DRUG BANK was made and all the compounds(ligands) structure were downloaded in sdf format.

- **DOCKING:**

Docking involves various steps before actual docking .it includes different steps like

- protein preparation
- ligand preparation

- grid generation
- actual docking

❖ **protein/gene preparation:**

The target gene /protein is downloaded from protein data bank (PDB)in pdb format, using discovery studios software protein preparation is done .Protein preparation is done to improve polarity of structure, addition of charges,AD4 atoms in order to minimize electron density. Lastly the protein is converted into pdbqt format from pdb which is required for docking using autodock vina .

Steps for protein preparation

- Download the 3D structure of genes/proteins from Protein Data Bank in pdb format and open in discovery studios.•
- Delete Heta Atoms ,water molecules and ligand from the receptor and save the receptor in pdb format.
- Open the receptor using autodock and add polar hydrogen's for equal polarity.
- Compute gasterior and add kollman charges for balance and assign AD4 atoms and write the receptor in pdbqt format.

❖ **Ligand preparation :**

A ligand is a molecule that binds to a receptor with specificity, typically forming a complex with the receptor and modulating its activity. Ligands bind to receptors through non-covalent interactions such as hydrogen bonding, electrostatic interactions, van der Waals forces, and hydrophobic interactions.

All the antimicrobial compounds and phytochemicals are downloaded in SDF format and for docking they should be converted into pdbqt format.

❖ **Steps for ligands preparation :**

- Ligands or phytocompounds are downloaded from any chemical database for eg -ZINC, COCONUT,NPASS,pubchem etc in SDF format .
- All the ligands are then opened in discovery studios and saved as pdb format.
- Using openbable all the ligands are converted from pdb format to pdbqt format.
- For large number of ligands command prompt is used for conversion giving some commands to the command prompt.
- All the pdbqt format files of ligands/ phytochemicals are saved in notepad for further steps of docking.

❖ **Grid generation :**

During the grid generation in our receptor STAT3 nine residues were found which helped in grid generation.

AutoDock uses a grid-based approach to explore the binding site of the receptor. The binding site is defined as a three-dimensional grid of points within the receptor's active site where the ligand (small molecule) can potentially bind.

Grid generation is necessary for finding out the active sites in the receptor needed for docking. The grid box size was selected to be sufficiently large to encompass the ligand while ensuring adequate conformational sampling within the available search space.

❖ **Preparation of configuration file (config.txt):**

The "configuration.txt" file in AutoDockVina is a text file used to specify the parameters and settings for a molecular docking simulation. This file contains various parameters that control the behavior of AutoDockVina during the docking simulation.
Some of the key parameters include:

Ligand: Specifies the input file containing the ligand molecule in PDBQT format.

Receptor: Specifies the input file containing the receptor molecule (protein) in PDBQT format.

Out: Specifies the output file where the docking results (poses) will be written in PDBQT format.

Exhaustiveness: Controls the exhaustiveness of the global search algorithm. Higher values increase the accuracy of the docking predictions but also increase computation time.center_x, center_y, center_z, size_x, size_y, size_z: Define the coordinates and dimensions of the search space (binding site) within the receptor where the ligand will be docked.

Num_modes: Specifies the number of output poses (conformations) to generate for each docking run.

Energy_range: Specifies the energy range for reporting output poses. Only poses with energies within this range are output.

Max_evals: Specifies the maximum number of allowed energy evaluations during the docking simulation.

These parameters can be adjusted based on the specific requirements of the docking File configuration includes protein and ligand file inputs (*.pdbqt), the values of centre

And size of of a grid box (centre_x, centre_y, centre_z; and size_x, size_y, size_z), and Docking parameters.

❖ **Docking**: docking between antimicrobial compounds and target gene .

Steps for docking

A folder is made containing the following:

- Vina three files
- Ligand pdbqt file
- Receptor pdbqt file
- Perl script file
- Config.txt

Perl was given commands to run docking process and results were analysed.

4. Results and discussion

❖ **Network construction analysis:**

Figure 1 shows the network constructed at 0.95 confidence level using the genes associated with brain abscess which were collected from different databases.

Figure 1. Picture of network at 0.95 confidence level

The results after network construction at different confidence levels using cytohubba for the identification of target gene are given in table 1.nodes represent genes and edges represent interactions between genes.

table 1 . Results of network construction between nodes and edges

Confidence level	Edges	Nodes
0.40	86159	2385
0.70	23289	2385
0.90	8769	2385
0.95	5495	2385

❖ **Analysis of different parameters**

Using cytohubba a plug-in in cytoscape, different parameters like MCC, MNC, DEGREE, and STRESS etc was analyzed for top 20 genes at 0.95 confidence level.

table2. Results of top 20 genes at different parameters

Parameter	Nodes	Edges
MCC	20	98
MNC	20	64
DMNC	20	70
DEGREE	20	63
EPC	20	79
BOTTLENECK	20	61
ECCENTRICITY	20	18
CLOSENESS	20	85
RADIALITY	20	85
BETWEENESS	20	56
STRESS	20	56

Stat3 was identified as the target gene satisfying the majority of parameters like degree, closeness, bottleneck and having the highest degree of 11 at 0.95 confidence level network .

About STAT3:

The STAT3 gene, also known as Signal Transducer and Activator of Transcription 3, is a gene that encodes a protein which is involved in transmitting signals from the cell surface to the nucleus. This protein plays a crucial role in various cellular processes, including cell growth, differentiation, survival, and immune responses. STAT3 is known to play a role in regulating the immune response, including the inflammatory response.

STAT3 is involved in tissue repair and regeneration. In the context of brain abscesses, STAT3 activation in certain cell types may contribute to the process of tissue healing and recovery following the resolution of infection. STAT3 activation in various cell types within the brain, including neurons and glial cells, may affect their responses to infection and their ability to survive under inflammatory conditions. The overall progression and outcome of brain abscesses could be influenced by various factors. Stat3, a well-known transcription factor, is activated in the brain in response to signals such as ciliary neurotrophic factor (CNTF) and leptin. Stat3 is essential for the neurotrophic effects of CNTF and leukemia inhibitory factor (LIF) on developing sensory neurons intro, and a similar survival requirement is observed in vivo, where few neurons survive without .Stat3 is crucial for the survival of injured motoneurons

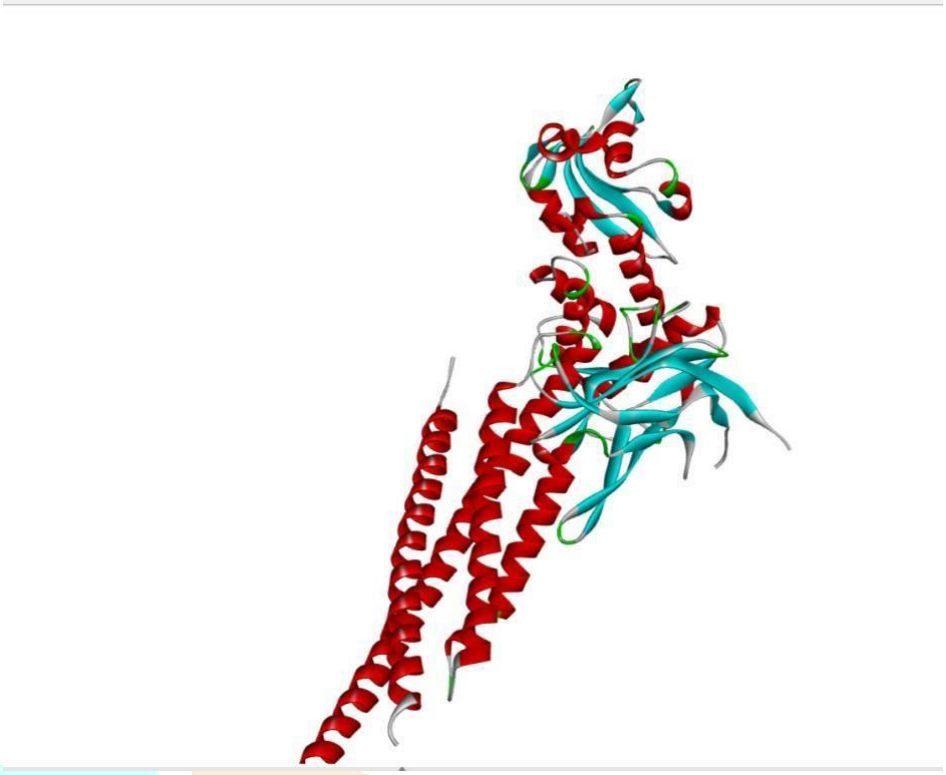


Figure 2. picture of stat3 gene in discovery studios after gene preparation

Table 3 shows the computed gasteiger charges of stat 3 gene and added kollman charges during protein preparation.

Table 3 showing results of stat3 gene after preparation

Receptor	Gasteiger charges	Kollman charges
Stat3 (6njs receptor)	3.0062	8.325

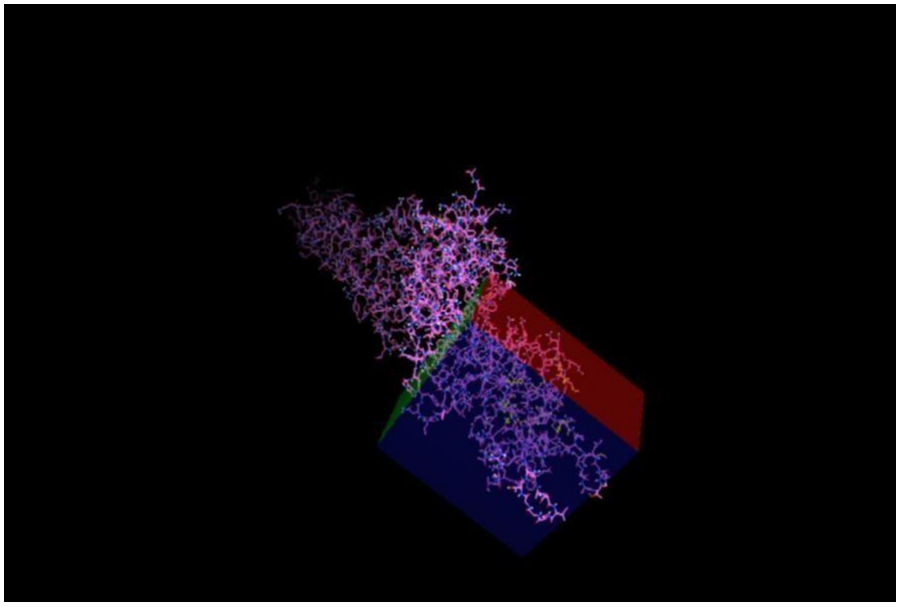


Figure 3. Picture showing grid box of stat3 gene

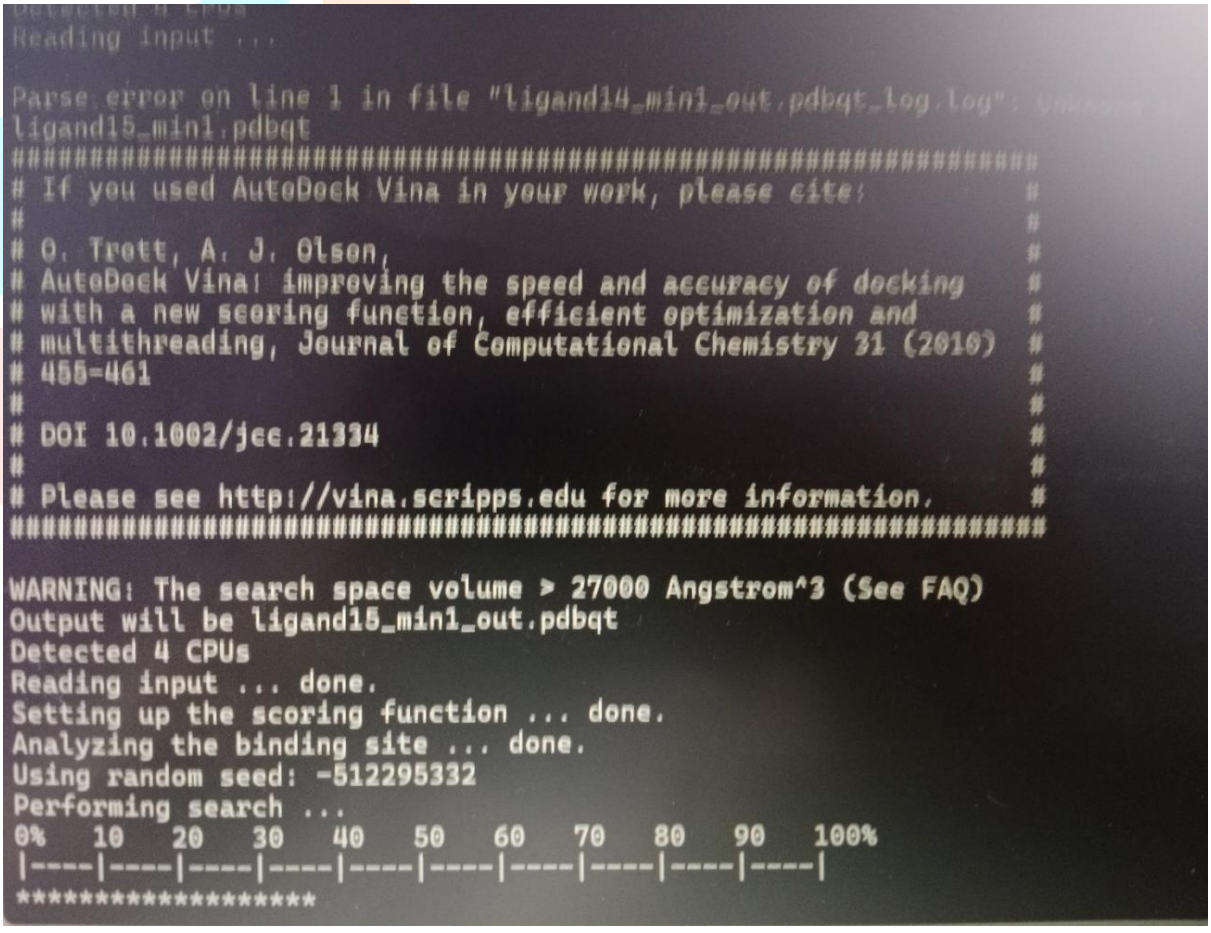


Figure 4. Picture showing docking process using perl

Docking results:

Docking was done using auto dock vina for Stat3 gene as target and ligands and results were analyzed using the binding energy (affinity) reference:

table 4 For receptor STAT 3 these were the results after docking with different ligands

Ligand	affinity
Ligand. Allantoin	-2.9
Ligand pyrazinamide	-3.1
Ligand triclosan	-3.0
Ligand D –cycloserine	-2.8
Ligand thymol	-2.8
Ligand benzoyl peroxide	-2.6
Ligand triclocarbon	-3.1
Ligand cutronellal	-2.4
Ligand phenyl 4-aminosalicylate	-3.2
Ligand cyanoacetohydrazide	-2.4
Ligand carvacrol	-2.9
Ligand ethambutol	-2.1
Ligand alpha TERPINEOL	-3.1
Ligand 4 isopropyl 3methyl phenol	-2.9
Ligand sparfloxacin	-4.0
Ligand enrofloxacin	-3.8
Ligand pretomanid	-3.5
Ligand ketoconazope	-3.6
Ligand 15 alpha hydroxyestradeol	-3.9
Ligand etheonamide	-2.9
Ligand methyl 2-(4-hydroxy-1-methyl-3methylidene-2-oxopiperidin-4yl)butanoate	-4.0
Ligand andrographolide	-3.6
Ligand bedaquiline	-4.3
Ligand clofoctol	-4.5

Based on the results the ligand clofoctol has the highest negative binding energy (-4.5) therefore the best ligand to be docked with STAT3 receptor . Clofoctol is an antibacterial agent used to treat respiratory tract infections. It belongs to the class of medicines known as quinolone antibiotics. Clofoctol works by inhibiting the growth of bacteria, thereby helping the body to fight off the infection.

The aim of the research work was to identify potential drug targets and therapeutics against brain abscess by analyzing the expression of genes and utilizing network biology appraoches.construction of network using cytoscape and andanalysing the network using cytohubba plug in .stat3 and Il6 were the genes which emerged as important target genes related to cerebral abscess having highest number of interactions in the network.further study of hub genes and thier interaction with the potential phytochemicals could lead to potentail lead therapeutics against brain abscess.

5. Conclusion:

In conclusion based on the results of this research work , brain abscess is a rare but serious condition characterized by a localized collection of pus in the brain tissue. It can be caused by bacterial, fungal, or parasitic infections, or as a complication of infections elsewhere in the body, such as in the lungs or heart. Symptoms may include headache, fever, nausea, vomiting, neurological deficits, and altered mental status. The aim of this research work was to identify the target genes/protein related to the brain abscess and establish therapeutics against the causative agents using in silico approach. The research work included various online databases and tools for data mining for example PDB, pubchem,npass,zinc,malacard,genecard etc.After a lot of filtration and selection the target genes were selected for further analysis.

The network construction to find out the target gene was done using cytoscape which got us two target genes stat3 and IL6.For functional enrichment of proteins discovery studios and auto dock vina was used. The phytochemicals were collected from different databases like npass,pubchem, and prepared using openbabel,autodock tools etc. Docking was done using autodockvina between hub gene and ligands. This study throws light on the role of stat3 and IL6 gene in brain abscess disease .

Overall this study used in silico network biology method to identify the target genes related to brain abscess and helped in establishing therapeutics against bacterial causative agents. The study gives important information related to brain abscess ,and may aid in the development of more therapeutics against different types of causative agents of brain abscess.

6. Acknowledgement:

With all due respect and sincerity, I, Ambika Singh would like to express my gratitude to my institution, Amity university, Uttar Pradesh, Lucknow campus for providing me with such a good opportunity that tests our abilities and encourages us to strive for knowledge. It is a golden opportunity indeed.

I would like to take this opportunity to acknowledge the people who have helped me to complete my research work. I feel fortunate to have done my work in such a friendly environment. I would like to thank **Ruby Singh Senger and Anurag sir** of Gevanam genomics for guiding me with constant help and supervision throughout the entire period. It has been a great honor to work under your supervision during the past four months. All the tasks could be readily and easily performed with their beneficial support.

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