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Computational Screening of Differential Gene expression on Intracranial Tumor microarray Dataset with GEO2R

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Abstract

The Gene Expression Omnibus (GEO) database is aworldwideopen source that records the next-generation sequencing, microarray data and high-throughput functional gene expression data originated from scientific investigates. GEO 2R performed in order the identify genes which are differentially expressed across experimental circumstances. In the current study, intracranial Tumor micro-array GEO datasets (GSE110052) were analysed for differentially gene expressed usingGEO2R tool. The latest report on, intracranial Tumorprovided that the last few decades the prevalence of intracranial tumour is increased at an explosive pace. The GEO2R tool predicted 250genes, on analysing the genes it was predicted that 153 genes has the capacity to cause the intracranial tumour and further evaluating 153 genes, it was concluded that 8 genes is responsible for intracranial tumour in humans. So there was an urgent need in discovery of new small molecules which can hinder the activity of the genes. The result of this *in Silico* study may provide several clues in designing of novel drugs which inhibits the function of above predicted tumour genes.

Keywords: Intracranial Tumour, GEO Datasets, Geo profile, GEO2R.

Introduction

Intracranial tumours account for 2% to 3% of all malignant neoplasms and about 85% to 90% of all primary CNS tumours, with a five-year survival rate of up to 35% for malignant tumours and about 90% for benign tumours [Neugut AI*et al.*, 2019]. Intracranial tumours are the second most prevalent malignancy in children, after leukaemia, with an incidence of up to 25% [Van Maele-Fabry G*et al.*, 2017,Ullrich NJ*et al.*, 2015]. When opposed to underdeveloped countries, where most individuals have limited access to early detection technology, the rising incidence rate in industrialised countries may be attributable to the availability of better detection and diagnosis procedures. As a result, undiagnosed and unregistered instances occur, lowering the stated incidence and prevalence [Khan I*et al.*, 2014].

Intracranial tumours are diagnosed in children between the ages of 3 and 12, and in adults between the ages of 40 and 70. Intracranial tumours can range in nature from benign to malignant to metastatic. Adults are more likely to develop metastatic cerebral malignancies [Fox BD*et al.*, 2011]. According to data from several research [Lin X *et al.*, 2015, Davis FG *et al.*, 2012, Stelzer KJ 2013], carcinomas that metastasize to intracranial include lung, breast, skin (melanoma), kidney, and colon, with lung cancer (small cell lung cancer) accounting for roughly half of all disseminated cases.

The World Health Organization (WHO) grades intracranial tumours from I to IV according on their catastrophic potential [Mabray MC*et al.*, 2015]. Low grade tumours (I & II) are acceptable for tumours with excellent and favourable prognosis, as opposed to high grade tumours (III & IV), which are more likely to be malignant and cause major problems [Guzmán-De-Villoria JA*et al.*, 2014]. Gliomas are tumours that develop from glial cells, meningiomas are tumours that develop from abnormal growth of the meninges, ependymomas are tumours that develop from cells (ependymocytes) lining the CSF filled ventricles are astrocytomas are tumours that develop from star-shaped glial cells (astrocytes) and so on.

Gliomas, a type of tumour that develops from nervous system supporting cells (glial cells/ neuroglia), account for roughly a third of all primary intracranial tumours [Ostrom QT*et al.*, 2018]. Gliomas are classified according to their histological subtypes, which range from pilocytic astrocytoma (innocent and non-offensive) to glioblastoma (serious and terminal sickness) [Ho VK *et al.*, 2014]. Gliomas are adult tumours that usually reveal themselves after the age of 45, though they can appear at any time during one's life. Men are susceptible to gliomas and other cerebral tumours, with the exception of meningiomas, which are more common in women [Allen Perkins M*et al.*,2016].

Intracranial tumours are one of the most dangerous types of cancer. Glioblastoma, the most aggressive type of intracranial cancer, kills more than two-thirds of people within two years of diagnosis [Gilbert MR*et al.*, 2016, Chinot,OL*et al.*, 2014]. In addition, among all paediatric solid tumours, intracranial malignancies are the most common and lethal [Smith MA et al., 2015]. Furthermore, the long-term implications of exposing the developing intracranial to medical operations such as surgery, radiotherapy, and/or chemotherapy are commonly harmful to children who survive and grow up with these tumours [Brinkman TM et al., 2016, Chemaitilly W et al., 2016].

Intracranial tumours have proven difficult to cure, owing to their biological peculiarities, which sometimes collude to slow treatment. For starters, because these tumours infiltrate one of the body's most vital organs, they are frequently positioned beyond the reach of even the most skilled neurosurgeon [Phoenix TN *et al.*, 2016]. These tumours are also positioned behind the blood–intracranial barrier (BBB), a system of tight connections and transport proteins that protects sensitive brain tissues from exposure to substances in the general circulation, preventing systemic chemotherapeutic exposure [Mackay

A*et al.,* 2017]. Furthermore, the intracranial tumours' distinct developmental, genetic, epigenetic, and microenvironmental properties typically render them resistant to both traditional and innovative treatments [Quail DF*et al.* 2017].These difficulties are exacerbated by the rarity of brain tumours in comparison to many other types of cancer, which limits pharmaceutical company financing and interest and attracts a tiny and dispersed research community [Nimmervoll*et al.,* 2018].

This work employed GEO 2R tool to predict the DEGs (Differential gene expressions) using statistical analysis of adj.p.value, False Discovery Rate value (FDR),log FC value and Pvalue.Contrasting the Wet lab studies, the computational study predicts which genes validateenchancingactiontowards the Tumors [Mahi NA*et al.,* 2019]. Using Bioinformatics techniques, an in silico study is being conducted to determine the genes that increase Intracranial Tumor out of 250 genes.

2. Materials and Methods

GEO profiles:

The GEO Profiles database stores gene expression profiles created from curated GEO Datasets. Each gene profile is represented as a graph that depicts the amount of expression of a single gene across all samples in a data set. The genes' experimental values were displayed in bars along the bottom of the graphs, and genes that were differentially expressed across several experimental settings were discovered by examining the experimental values. Internal and external links that connect genes with similar activity are found in GEO profiles.

GEO Datasets:

The GEO databases contain microarray blood samples, next-generation sequencing, and other types of high-throughput functional genomic data. The curation gene expression dataset, original series, and platform records are all stored in the GEO depository. GEO dataset records include other databases such as cluster tools and differential gene expression (DEG) queries. Around 90% of the information in the GEO database comes from gene expression studies, which covers a wide range of biological topics such disease development, ecology, evolution, immunology, toxicology, and metabolism.

GEO2R:

The GEO2R database evaluates two or more sets of microarray samples in a GEO Series to uncover genes that are expressed differently across research conditions.The database's predictions are presented in the form of a table and a list of genes, which are ordered in the table depending on their significant properties [Altara R*et al.*, 2018]. There are five procedures to follow while reviewing data in the GEO2R database.

1. Experiment selection from the GEO Profile(In a glioma mouse model, genome-wide study of Olig2-positive and Olig2-negative cancers).

Genes that differ in expression between Olig2-positive (oligodendrocyte-like) and Olig2-negative cancers. The current investigation examined the concept that glial phenotype influences the vascular and tumour microenvironment. The findings show that various pathways, including angiogenesis and immune response, are expressed differently in the two types of tumor. Define sample groups (GSE110052)

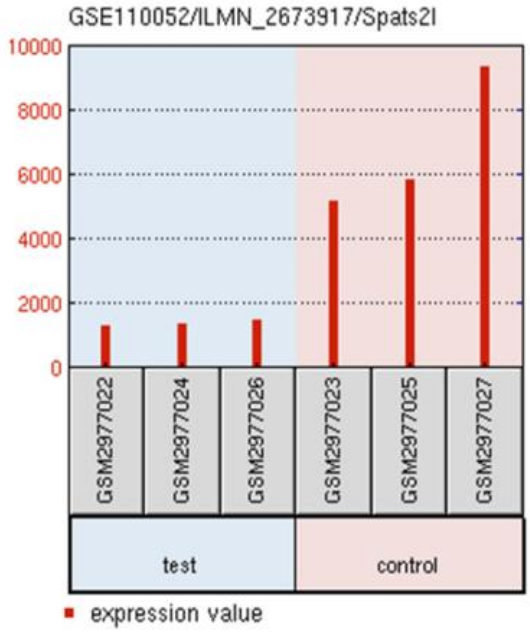
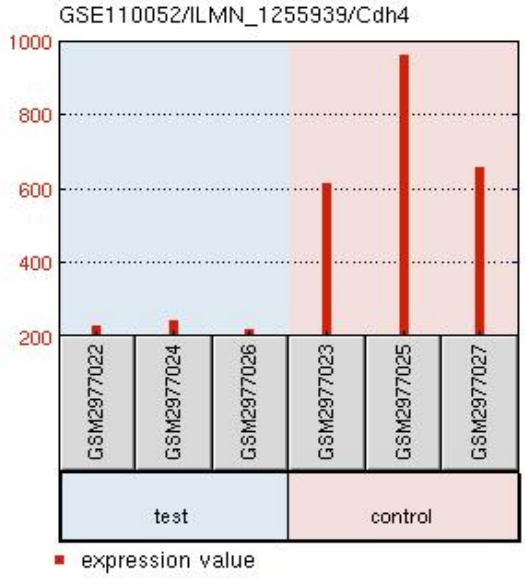
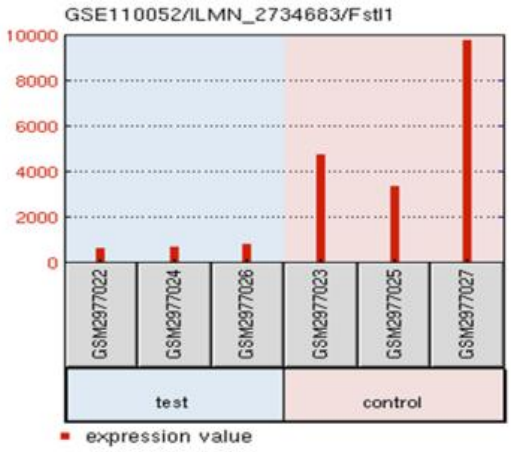
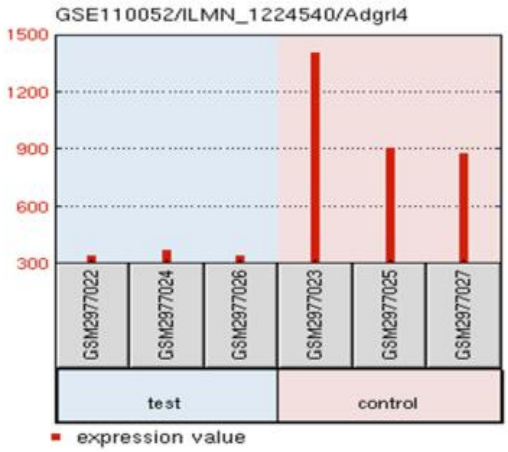
1. Use the GEO2R database to analyse the data information.
2. Assign samples to groups;
   GSM2977022, GSM2977024, GSM2977026 -Test group
   GSM2977023, GSM2977025, GSM2977027 -Control group
3. Interpret the GEO result with the profile graph.

4. Results and Discussion

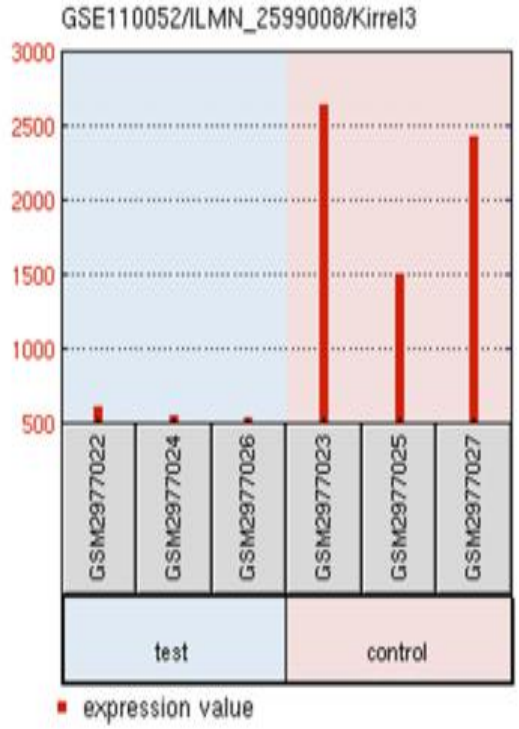
Table 1: Predicted TumorGenes using GEO2R

Gene name	Gene name	Gene name	Gene name	Gene name	Gene name
Anxa6	Hs3st3a1	Mia	Snx18	Cd40	Mest
Id1	Gna14	Bgn	Mest	Bgalt1	Pm5
Capn6	Fhdc1	Mfap2	DIx2	Gpx7	Atp8b1
Capns1	Nid2	Trp53inp1	Ppic	Shf	Anxa1
Tmem253	Gng11	Nqo2	Mnat1	Optn	Bckdk
Aard	Idgcc4	Notch4	Hmox1	Gata2	Vkonc1
Kcnc1	Ptn	Galnt2	Spats21	Cdkn1c	Dag1
Pdim7	Gch1	Pdim1	Sypl	Sic2a10	Spats21
Six1	Lyz2	Pdzm3	Id1	Gna14	Scara5
Eva1b	En2	Tn4fs1	Hs3st3a1	Mia	Gucd1
Taf10	Dix1	Gng2	Anxa6	Ramp2	PhykpI
Mfap2	Fkbp14	Mfap1	Ythdf3	Usp6nI	Prr14
Pecam1	Sic27a1	Spac	Kirrel3	Mmp14	Rhod
Cish	Gja4	Wipi1	Pdzm3	Aidh1a7	OsbpI1
Igfbp2	Wipi2	Vimp	Fam20b	F11Rik	Apabec1
Sh3rf3	Crip2	Fzd1	Lrp4	Smox	Ggta1
Emc1	Mfap2	Dhh	Chsy1	Tenm3	SmpdI3a
Sic38a3	Psg23	Igf2r	Erlec1	Susd6	PIpp1
Ezr	Cdh4	Car12	Rnaset2b	Prrc1	Sic25a10
Mfxd4	Rbpms	Sgk3	Dclre1b	Lyz1	Cdh2
Mnd1	AdgrI4	Fsti1	Icam1	CoI4a2	Lrrk1
Parva	Bcap31	Lpar6	PIcd1	Rras	OPtn
Sic29a1	PleKhf2	Fam180a	Fkbp9	Nudt7	Pdpn
Zfand6	Icam2	Suv420h1	Bnip2	Ppic	Bc028528
Timm10b	Hpcal1	Tulp3	Ifngr1	Usp6ni	Nectin2	Bmpr1a

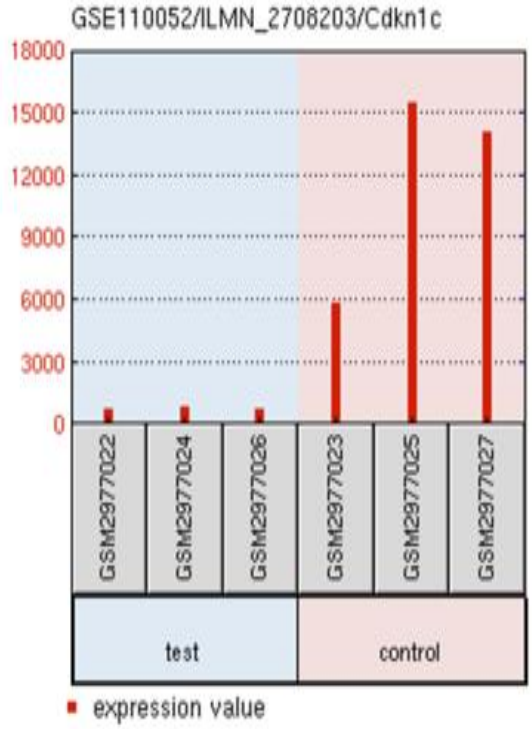
Table 2: Description of gene and its Profile Graph

Gene Expression	Gene Expression
Spats21 	Cdh4 
Fsti1 	AdgrI4 

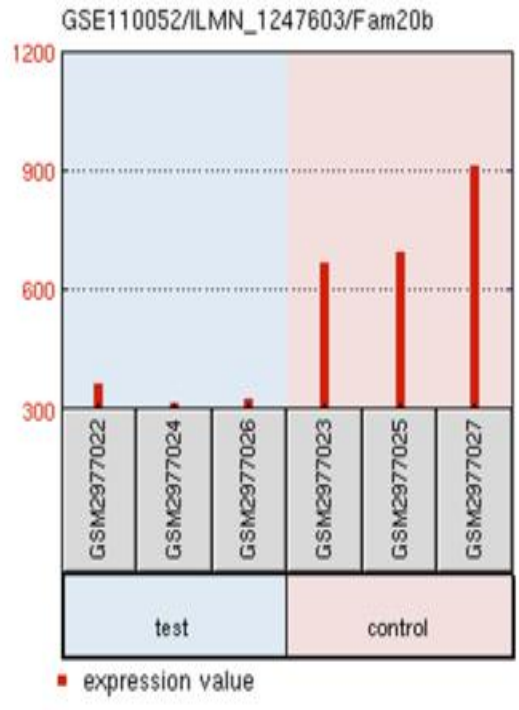
Kirrel3



Cdkn1c



Fam20b



OsbpI1

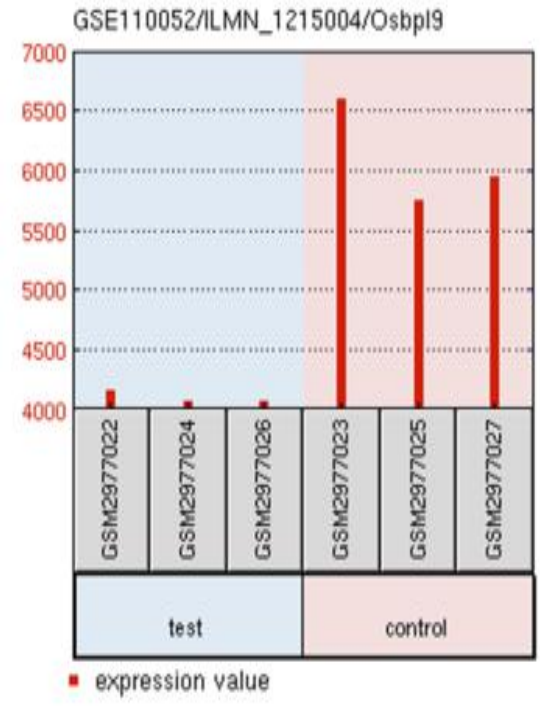


Table 3 : Gene and Its Function

Gene ID	Gene name	Function
FAM20B	Glycosaminoglycan Xylosylkinase	The alcohol group serves as an acceptor for phosphotransferase activity. It's thought to play a role in the biosynthesis of proteoglycans. Located in the nucleoplasm and Golgi apparatus.
OSBP19	Oxysterol-Binding Protein 19	Oxysterol binding protein is an intracellular protein that transports sterols from lysosomes to the nucleus, where the sterols down-regulate the LDL receptor, HMG-CoA reductase, and HMG synthetase genes.
SPAT	Subtilin transport ATP-binding protein	Probably involved in the lantibioticsubtilin export pathway.
SPA21	Spermatogenesis Associated 21	Identify the Calcium ion binding activity.
KIRREL3	kin of irregular chiasm-like protein 3	These proteins are found in the foetal and adult brains, as well as kidney glomeruli podocytes.
CDH4	Cadherin 4	This gene belongs to the cadherin superfamily and is a conventional cadherin.
FSTI1	Follistatin like 1	This gene produces a protein that looks like follistatin, which is an activin-binding protein.
CDKH1C	cyclin dependent kinase inhibitor 1C	In osteosarcoma, high CDK4 expression is linked to tumor growth and metastasis.

The GEO2R application estimated DEG profile graphs for Olig2-positive and Olig2-negative tumors in a glioma mouse model using patient data (GSM2977022, GSM2977023, GSM2977024, GSM2977025, GSM2977026, and GSM2977027). The aforementioned 8 genes (FAM20B, OSBP19, SPAT, SPA21, KIRREL3, CDH4, FSTI1, CDKH1C) are certainly responsible for intracranial tumors, according to the results of the GEO2R tool.

4. Conclusion

The GEO2R programme was used to analyse the intracranial tumour micro-array GEO datasets (GSE110052) for differential gene expression. The GEO2R programme projected that eight genes out of 250 would have the potential to cause intracranial tumours in people. The findings of this study offer fresh insights into the genes that cause intracranial tumours and may pave the way for the development of new intracranial tumour medicines targeting the eight anticipated genes.

5. Conflict of interest:

The authors declare they have no competing interests.

6. Acknowledgments

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