PUBLICATIONS

Publications in peer-reviewed national and international journals from Ph.D thesis work

1. **Roy N**, Dihingia BR, Barah P. Integrative network-based approaches identified systems-level molecular signatures associated with gallbladder cancer pathogenesis from gallstone diseases. Journal of Biosciences. 2022 May 19;47(2):31. https://doi.org/10.1007/s12038-022-00267-6

2. **Roy N**, Kshattry M, Mandal S, Jolly MK, Bhattacharyya DK, Barah P. An integrative systems biology approach identifies molecular signatures associated with gallbladder cancer pathogenesis. Journal of Clinical Medicine. 2021 Aug 10;10(16):3520. https://doi.org/10.3390/jcm10163520

3. **Roy N**, Gaikwad M, Bhattacharrya DK, Barah P. Identification of systems-level molecular signatures from glioblastoma multiforme derived extracellular vesicles. Journal of Molecular Neuroscience. 2021 Jun;71:1156-67. https://doi.org/10.1007/s12031-020-01738-x

4. **Roy N**, Lodh R, Mandal S, Jolly MK, Sarma A, Bhattacharyya DK, Barah I. Comparative Transcriptomic Analysis Uncovers Molecular Heterogeneity in hepatobiliary cancers. (Communicated)

Appendix I

Ethical clearance certificates

BBCI Medical Ethics Committee
DR.BHUBANESHWAR BOROOAH CANCER INSTITUTE
A Grant-In-Aid Institute of Department of Atomic Energy, Govt.of India
And A Unit of Tata Memorial Centre (Mumbai)
Gopinath Nagar, Guwahati-781016

Ref. No. BBCI-TMC/Misc-01/MEC/ 254 */2021* *Date:* 28.01.2021

CLEARANCE CERTIFICATE

Title of the project	**A case-control pilot study for identification and validation of Gallbladder cancer biomarkers from North-East Indian population using transcriptomics approach**
Principal Investigator	**Dr.Pankaj Barah,** Ph.D Assistant Professor & DBT Ramalingaswami,Fellow Dept. of Molecular Biology and Biotechnology,Tezpur University
Co-investigators	**Dr. Dhruba Kumar Bhattacharyya** Professor & Dean,Dept of Computer Science and Engineering Tezpur University **Dr.Anupam Sarma** Prof & HOD, Dept of Oncopathology **Dr.A.C.Kataki** Director Dr B Borooah Cancer Institute **Dr.B.K.Choudhury** Prof & HOD, Dept of Radiology Dr B Borooah Cancer Instiute **Dr.Gaurav Das** Assoc.Prof, Dept of Surgical Oncology Dr B Borooah Cancer Instiute **Dr.Avdhesh Kumar Rai** Asst.Research Officer, Dr B Borooah Cancer Institute
Date of meeting of committee	23.01.2021
Decision of the committee	Project is approved.
Members present	Dr.N.C.Talukdar, Chairperson, Mr.N.C.Das,Legal Expert Dr.Mangala Lahkar, Basic Medical Scientist Mr.Jaideep Das, Social Scientist Dr.Mukuta Goswami,Lay person Dr.B.J.Saikia,Clinician Dr.A.K.Kalita,Clinician Dr.Anupam Sarma ,Scientific Member Dr.Ashok Kr Das, Clinician Dr.Abhijit Talukdar, Clinician Dr.M.Bhattacharyya,Member Secretary

During the review meeting held on 23.01.2021, the Principal Investigator Dr. Pankaj Barah and Co-Investigator Dr.Avdhesh Kumar Rai were requested to give a brief presentation before the members of the IEC and were questioned on different aspects of the study.Thereafter, during the deliberations and opinion forming process regarding the project, Dr.Barah and Dr.Avdhesh Kumar Rai were not present inside the room.

28.01.2021

Dr. M. Bhattacharyya
Member Secretary
Medical Ethics Committee
Dr B Borooah Cancer Institute
Guwahati-16

Member Secretary
Medical Ethics Committee
Dr B Borooah Cancer Institute
Guwahati-16

Tezpur University Ethics Committee
Tezpur: 784028 : Assam

Communication of Decision of Tezpur University Ethics Committee (TUEC)

IEC No: DoRD/TUEC/PROP/2022/06

Protocol title: Big data and artificial intelligence based integrative systems biology approaches for identifying complex pathological signatures in Gallbladder Cancer			
Principal Investigator: Dr. P. Barah			
Name & Address of Institution: Tezpur University, Tezpur, Assam 784028			
[√] New review	[ ] Revised review	[ ] Expedited review	
Date of review (D/M/Y): 29-09-2022 Date of previous review, if revised application:			
Decision of the IEC/IRB:			
[√] Recommended		[ ] Recommended with suggestions	
[ ] Revision		[ ] Rejected	
Suggestions/Reasons/Remarks: Initial approval is recommended for one year, with subsequent approval being subjected to satisfactory reports.			
Recommended for a period of: 1 year			

Please note

-Inform TUEC immediately in case of any adverse events and serious adverse events
-Inform TUEC in case of any change of study procedure, site and investigator
-This permission is only for period mentioned above. Annual report to be submitted to TUEC
-Members of TUEC have right to monitor the trial with prior intimation

Date: 21/03/2023

Signature of Chairperson (with seal)

TUEC

Chairperson
Tezpur University Ethics Committee

Appendix II

Reprint of publications

Journal of
Clinical Medicine

MDPI

Article

An Integrative Systems Biology Approach Identifies Molecular Signatures Associated with Gallbladder Cancer Pathogenesis

Nabanita Roy [1], Mrinmoy Kshattry [1], Susmita Mandal [2], Mohit Kumar Jolly [2], Dhruba Kumar Bhattacharyya [3] and Pankaj Barah [1,*]

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Abstract: Gallbladder cancer (GBC) has a lower incidence rate among the population relative to other cancer types but is a major contributor to the total number of biliary tract system cancer cases. GBC is distinguished from other malignancies by its high mortality, marked geographical variation and poor prognosis. To date no systemic targeted therapy is available for GBC. The main objective of this study is to determine the molecular signatures correlated with GBC development using integrative systems level approaches. We performed analysis of publicly available transcriptomic data to identify differentially regulated genes and pathways. Differential co-expression network analysis and transcriptional regulatory network analysis was performed to identify hub genes and hub transcription factors (TFs) associated with GBC pathogenesis and progression. Subsequently, we assessed the epithelial-mesenchymal transition (EMT) status of the hub genes using a combination of three scoring methods. The identified hub genes including, CDC6, MAPK15, CCNB2, BIRC7, L3MBTL1 were found to be regulators of cell cycle components which suggested their potential role in GBC pathogenesis and progression.

Keywords: gallbladder cancer; transcriptomics; differentially expressed genes; co-expression network; transcription factors; epithelial-mesenchymal-transition; cell cycle machinery

Citation: Roy, N.; Kshattry, M.; Mandal, S.; Jolly, M.K.; Bhattacharyya, D.K.; Barah, P. An Integrative Systems Biology Approach Identifies Molecular Signatures Associated with Gallbladder Cancer Pathogenesis. *J. Clin. Med.* **2021**, *10*, 3520. https://doi.org/10.3390/jcm10163520

Academic Editors: Stanley W. Ashley and Maria Lina Tornesello

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Accepted: 30 July 2021
Published: 10 August 2021

1. Introduction

The gallbladder is a small sac-like structure located beneath the liver that forms an integral component of the biliary tract system. Gallbladder cancer (GBC) is the sixth most frequent cancer of the gastrointestinal tract worldwide. GBC is an aggressive malignancy, with rapid progression, poor prognosis and a high mortality rate resulting in an overall 5-year survival rate of only 5% [1,2]. The incidence rate of GBC is highly marked by distinct geographic and ethnic disparities. Such regional and ethnic discrepancy in the incidence rate of GBC cases indicates the differences in GBC etiology in different populations [2,3]. According to recent GLOBOCAN report (http://globocan.iarc.fr, accessed on 1 January 2018), GBC ranks in the 20th position among the most frequent cancer types, with approximately 0.2 million cases diagnosed annually. The incidence of GBC cases is highest in the Eastern Europe, East Asian country and Latin American regions, with the incidence ratio of GBC cases being the highest in South American countries such as Chile, Bolivia and Ecuador and Asian countries, mainly including Korea, India, Japan and Pakistan [4,5].

GBC is an orphan disease and its etiology is multifactorial. The pathological spectrum of GBC mainly progresses from metaplasia to dysplasia with subsequent carcinoma-in-situ and cancer metastasis suggesting that an epithelial mesenchymal transition (EMT) event might be an important phenomenon in GBC development. The detailed molecular

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Integrative network-based approaches identified systems-level molecular signatures associated with gallbladder cancer pathogenesis from gallstone diseases

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MS received 30 September 2021; accepted 16 February 2022

Gallbladder cancer (GBC) is one of the most fatal malignancies of the biliary tract system and is ranked sixth among the neoplasms of the gastrointestinal tract. Gallstone disease (GSD) is considered the major risk factor for GBC. However, the underlying molecular mechanism of GBC pathogenesis from different stages of GSD is not yet clearly understood. We analyzed transcriptomic datasets of GBC with reference to GSD of three different follow-up periods, i.e., GBC vs. GSD3 (1–3 years), GBC vs. GSD5 (5–10 years), and GBC vs. GSD10 (more than 10 years). We identified overlapping and specific molecular signatures in GBC compared with GSD at three different follow-up periods. Using integrative network biology approaches, such as protein–protein interaction network analysis, transcriptional regulatory network analysis, and miRNA–target gene network analysis, we have identified a few hub genes. The hub genes identified from GBC vs. GSD3, GBC vs. GSD5, and GBC vs. GSD10 were directly or indirectly associated with cancer progression and initiation from GSD. Functional enrichment analysis indicated significant correlation between GSD and GBC pathogenesis. The identified hub genes can be used for future targeted validation to develop potential diagnostic, prognostic, or therapeutic biomarkers in GBC.

Keywords. Biomarker; differentially expressed genes; gallbladder cancer; gallstone disease; hub genes; network biology; transcriptomics

1. Introduction

Gallbladder cancer (GBC) is one of the most fatal malignancies of biliary tract cancers, where malignant cells form in the tissues of the gallbladder (Hundal and Shaffer 2014; Muhammad *et al.* 2018). Globally it accounts for around 80–90% of all the biliary tract cancers, and ranks sixth among gastrointestinal cancers (Hundal and Shaffer 2014; Song *et al.* 2020). As reported by the 2018 GLOBOCAN data, GBC accounts for around 1.7% of cancer-related deaths globally (Rawla *et al.* 2019). The incidence rate of GBC shows very high geographical, racial, and socioeconomic variations, suggesting the potential role of different environmental as well as genetic factors associated with the development and progression of this cancer (Hundal and Shaffer 2014; Sharma *et al.* 2017; Muhammad *et al.* 2018).

GBC does not exhibit any specific clinical symptoms. This causes difficulty in diagnosing the disease at an early stage. It is often diagnosed at an advanced stage (Letelier *et al.* 2012; Hundal and Shaffer 2014). Most of the time, GBC is incidentally diagnosed in patients undergoing cholecystectomy for the treatment of cholecystitis or cholelithiasis (Muhammad *et al.* 2018). According to different epidemiological and pathological investigations, patients with gallstones have a higher risk of GBC than healthy individuals.

This article is part of the Topical Collection: Emergent dynamics of biological networks.

Supplementary Information: The online version contains supplementary material available at https://doi.org/10.1007/s12038-022-00267-6.

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Journal of Molecular Neuroscience (2021) 71:1156–1167
https://doi.org/10.1007/s12031-020-01738-x

Identification of Systems Level Molecular Signatures from Glioblastoma Multiforme Derived Extracellular Vesicles

Nabanita Roy[1] · Mithil Gaikwad[1] · Dhruba Kr Bhattacharyya[2] · Pankaj Barah[1]

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Abstract

Glioblastoma multiforme (GBM) is one of the most lethal malignancies of the central nervous system characterized by high mortality rate. The complexity of GBM pathogenesis, progression, and prognosis is not fully understood yet. GBM-derived extracellular vesicles (EVs) carry several oncogenic elements that facilitate GBM progression. The purpose of this study was to identify systems level molecular signatures from GBM-derived EVs using integrative analysis of publicly available transcriptomic data generated from plasma and serum samples. The dataset contained 19 samples in total, of which 15 samples were from plasma (11 GBM patients and 4 healthy samples) and 4 samples were from serum (2 GBM and 2 healthy samples). We carried out statistical analysis to identify differentially expressed genes (DEGs), functional enrichment analysis of the DEGs, protein–protein interaction networks, module analysis, transcription factors and target gene regulatory networks analysis, and identification of hub genes. The differential expression of the identified hub genes were validated with the independent TCGA-GBM dataset. We have identified a few crucial genes and pathways associated with GBM prognosis and therapy resistance. The DEGs identified from plasma were associated with inflammatory processes and viral infection. On the other hand, the hub genes identified from the serum samples were significantly associated with protein ubiquitinylation processes and cytokine signaling regulation. The findings indicate that GBM-derived plasma and serum DEGs may be associated with distinct cellular processes and pathways which facilitate GBM progression. The findings will provide better understanding of the molecular mechanisms of GBM pathogenesis and progression. These results can further be utilized for developing and validating minimally invasive diagnostic and therapeutic molecular biomarkers for GBM.

Keywords Glioblastoma multiforme · Extracellular vesicles · Transcriptomic analysis · Differentially expressed genes · Protein–protein interactions · Systems biology

Abbreviations

GBM	Glioblastoma multiforme
EVs	Extracellular vesicles
DEGs	Differentially expressed genes
PPIs	Protein–protein interactions
GO	Gene ontology
TFs	Transcription factors
OS	Overall survival

Nabanita Roy and Mithil Gaikwad have contributed equally to this work.

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s12031-020-01738-x) contains supplementary material, which is available to authorized users.

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Introduction

Glioblastoma multiforme (GBM) is a lethal disease and one of the most frequent malignancies of the central nervous system in adults. GBM is associated with poor prognosis and high mortality rate with the majority of the patients dying within 1 year of diagnosis (Ohgaki and Kleihues 2007; LOBAMRDI and ASSEM 2017). The overall median survival of GBM patients is approximately 14 months even after the aggressive surgical resection followed by standard regimens of chemotherapy and radiotherapy. The recent clinical practices for molecular characterization of disease status in GBM patients are feasible with tissue specimens

Title: Integrative analysis identified common and unique molecular signatures in hepatobiliary cancers

Short/Running title: Hepatobiliary cancer biomarkers

Authors: NabanitaRoy[1#], Ria Lodh[1#], Anupam Sarma[2], Dhruba Kumar Bhattacharyya[3] and Pankaj Barah[1*]

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Keywords: Hepatobiliary cancers/ Transcriptomics/ Systems biology/ /Biological networks/Hub genes /Systems biomarker.

Abstract

Hepatobiliary cancers (HBCs) are the most aggressive and sixth most diagnosed cancers globally. Biomarkers for timely diagnosis and targeted therapy in HBCs are still limited. Considering the gap, our objective is to identify unique and overlapping molecular signatures associated with HBCs. We analyzed publicly available transcriptomic datasets on Gallbladder cancer (GBC), Hepatocellular carcinoma (HCC), and Intrahepatic cholangiocarcinoma (ICC) to identify potential biomarkers using integrative systems approaches. An effective *Common and Unique Molecular Signature Identification (CUMSI)* approach has been developed, which contains analysis of differential gene expression (DEG), gene co-expression networks (GCN), and protein-protein interactions (PPIs) networks. Functional analysis of the DEGs unique for GBC, HCC, and ICC indicated that GBC is associated with cellular processes, HCC is associated with immune signaling pathways, and ICC is associated with lipid metabolic pathways. Our findings shows that the hub genes and pathways identified for each individual cancer type of the HBS are related with the primary function of each organ and each cancer exhibit unique expression patterns despite being part of the same organ system.