Dedicated to my beloved parents

I hereby declare that the thesis "Integrative systems biology approaches to identify molecular signatures in gallbladder carcinoma" being submitted to the Department of Molecular Biology and Biotechnology, Tezpur University, Tezpur, Assam in partial fulfillment for the award of the degree of Doctor of Philosophy in Molecular Biology and Biotechnology, has previously not formed the basis for the award of any degree, diploma, associateship, fellowship or any other similar title or recognition.

Date: 25.04, 2024. Place: Tezpur

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# **TEZPUR UNIVERSITY**

# **CERTIFICATE OF SUPERVISOR**

This is to certify that the thesis entitled "Integrative systems biology approaches to identify molecular signatures in gallbladder carcinoma" submitted to the School of Sciences, Tezpur University in requirement of partial fulfillment for the award of the degree of Doctor of Philosophy in Molecular Biology and Biotechnology is a record of research work carried out by Ms. Nabanita Roy under my supervision and guidance. All help received by her from various sources has been duly acknowledged. No part of this thesis has been submitted elsewhere for award of any other degree.

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#### Abbreviations **Full form** 76GS: 76 gene signatures AAR: Age-adjusted rates AJCC: American Joint Committee on Cancer ASR: Age-standardized rates Dr. B. Borooah Cancer Institute **BBCI: BLAST:** Basic local alignment search tool **BP**: **Biological processes** BTS: Biliary tract system Cell adhesion molecules CAMs: cDNA: Complementary DNA Competitive endogenous RNA ceRNA **CHOL:** Cholangiocarcinoma **CIS-BP:** Regulatory Sequence Analysis Tool Colorectal adenocarcinoma **COAD:** CPC2: Coding potential calculator 2 **DEGs:** Differentially expressed genes **DE-IncRNA:** Differentially expressed lncRNA **DEmRNA:** Differentially expressed mRNA Differentially expressed novel lncRNA **DE-nlncRNA:** ECM: Extracellular matrix EMT: Epithelial-mesenchymal transition ENA: European nucleotide archive **EPC:** Edge percolated centrality **ETENBR:** End-to-end and Beyond RNA-Seq analysis pipeline **ETENLNC:** End-to-end Novel LncRNA analysis pipeline **FASTP:** Fast preprocessing **FASTQC:** FAST Quality Check GB: Gallbladder **GBC:** Gallbladder cancer **GBC+GS**: Gallbladder cancer with gallstones

### LIST OF ABBREVIATIONS

GCN:	Gene coexpression network
GEO:	Gene expression omnibus
GLM:	Generalized linear model
GLOBOCAN:	Global cancer observatory
GS:	Gallstones
GSD:	Gallstone disease
GSD10:	GSD with a follow-up period of more than 10 years
GSD3:	GSD with a follow-up period of 1-3 years
GSD5:	GSD with a follow-up period of 3-5 years
HBCs:	Hepatobiliary cancers
HCC:	Hepatocellular carcinoma
HISAT2:	Hierarchical indexing for spliced alignment of transcripts
HSV1:	Herpes simplex virus 1
ICC:	Intra hepatic cholangiocarcinoma
KEGG:	Kyoto Encyclopedia of Genes and Genomes
KLF:	Kruppel-like factors
KS:	Kolmogorov Smirnov test
LIHC:	Liver hepatocellular carcinoma
LncRNA:	Long noncoding RNA
Log2FC:	Log2 Fold Change
LoH:	Loss of heterozygosity
MCC:	Maximum clique centrality
MCODE:	Molecular Detection Complex
MF:	Molecular functions
miRNA:	microRNA
MLR:	Multinomial logistic regression
MNC:	Maximum neighbourhood component
MRE:	miRNA response element
mRNAs:	Messenger RNAs
MSI:	Microsatellite instability
MsigDB:	Molecular Signature Hallmark Database
NATs:	Natural antisense transcript
NCBI:	National Center for Biotechnology Information

NCCN:	The National Comprehensive Cancer Network
ncRNAs:	Noncoding RNAs
NE:	North-East
NF-kB:	Nuclear factor-kappa B
NGS:	Next generation sequencing
ORF:	Open reading frame
PAAD:	Pancreatic adenocarcinoma
Padj:	P-adjusted value
pcRNAs:	Protein-coding RNAs
PDJ:	Pancreaticobiliary duct junction
PPI:	Protein-Protein Interactions
PROMPTs:	Promoter upstream transcripts
PWM:	Position weight matrix
qRT-PCR:	Quantitative Real-Time PCR
RIN:	RNA integrity number
RSAT:	Regulatory Sequence Analysis Tool
SSSSH:	Swagat Super Specialty Surgical Hospital
STAD:	Stomach adenocarcinoma
TCGA:	The Cancer Genome Atlas
TERC:	Telomerase RNA component
TFs:	Transcription factors
TF-TG:	Transcription factor-Target gene
TF-IncRNA:	Transcription factor-Target lncRNA
TGF-β:	Transforming growth factor-beta
TNF-alpha:	Tumor necrosis factor-alpha
TNM:	Tumor Node Metastasis
TOM:	Topological Overlap Matrix
TRN:	Transcriptional Regulatory network
TSG:	Tumor suppressor gene
USG:	Ultrasonography
WGCNA:	Weighted Gene Co-expression Network Analysis
XMEs:	Xenobiotic metabolism enzymes