Evaluation of Long Non Coding RNA (CCAT1) as a Prognostic Biomarker in Acute Myeloid Leukemia

A Thesis

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DEDICATION

TO MY FAMILY

SPECIAL DEDICATION FOR ALL MY

FAMILY ESPECIALLY

MY FATHER AND MY MOTHER

ALSO MY HUSBAND

FOR THEIR CONTINUED SUPPORT AND

ENCOURAGEMENT THROUGHOUT MY

WORK

LIST OF ABBREVIATIONS

Ago2	Argonaute protein 2
ALL	Acute lymphoblastic leukemia
AML	Acute myeloid leukemia
APL	Acute pomyelocytic leukemia
Ara-C	Cytosine arabinoside
AS	Antisense
AT1R	Angiotensin II type 1 receptor
ATRA	All-trans-retinoic acid
AUC	Area under the curve
BANCR	BRAF-activated non-protein coding RNA
BLACAT1	Bladder cancer-associated transcript 1
CBC	Complete blood picture
CCA	Cholangiocarcinoma
CCAT1	Colon cancer-associated transcript-1
CCATs	Colon cancer associated transcripts
cDNA	Complementary DNA
CEBPA	CCAAT enhancer-binding protein-α
ChIRP-Seq	Chromatin Isolation by RNA purification
CI	Confidence interval
CLIP	Crosslinking immunoprecipitation
CLL	Chronic lymphocytic leukemia
CML	Chronic myeloid leukemia
CN-AML	Cytogenetically normal acute myeloid leukemia
CNV	Copy number variation
CRC	Colorectal cancers
CRISPRs	Clustered regularly interspaced short palindromic repeats
dsRBD	double-stranded RNA binding
EC	Esophageal cancer
EGOT	Eosinophil granule ontogeny transcript
EMPs	Early myeloid progenitors
FAB:	French-American-British
FRET	Fluorescence resonance energy transfer
G2DHE	GATA2 distal hematopoietic enhancer
GBC	Gallbladder cancer:
GC	Gastric cancer
GCF	First-degree relatives of patients with gastric cancer
HCC	Hepatocellular carcinoma
HGNC	The HUGO Gene Nomenclature Committee
HK	Housekeeper gene
HMGA2	High mobility group AT-hook 2

HS	highly significant
HSCs	Hematopoietic stem cells
IQR	Interquartile range
IT	Intronic
ITDs	Internal tandem duplications
LINC	Long intergenic non-coding
LNA	Locked nucleic acids
LncRNAs	Long non-coding RNAs
LPS	Lipo poly saccharide
LSC	leukemic stem cell
M0	Minimally differentiated Acute Myeloblastic leukemia
M1	Myeloblastic leukemia
M2	Myelocytic leukemia
M3	Promyelocytic leukemia
M4	Myelomonocytic leukemia
M5:	Acute monocytic leukemia
M6	Acute erythroid leukemia
M7	Acute megakaryoblastic leukemia
MBC	metastatic breast cancer
MGB	Minor groove –binding
miRNAs	Micro RNAs
MRD	Minimal/measurable residual disease in AML
MTX	Methotrexate
NEAT1	Nuclear paraspeckle assembly transcript 1
NF-κB	Nuclear factor-κB
NPM1	Nucleophosmin 1
NSCLC	Non-small cell lung carcinoma
NUD	Nonulcer dyspepsia
OS	Overall survival
p-ALL	pediatric Acute Lymphocytic Leukemia
PAZ	Piwi/Argonaute/Zwilli domain
PBS	Phosphate-buffered saline
PDCD4	programmed cell death 4
PLTs:	Platelets
poly IC	polyriboinosinic–polyribocytidylic acid
premiRNA	Precursor miRNA
pri-miRNA	primary miRNA
PSPs	paraspeckle proteins
PTEN	phosphatase and tensin homolog
RFS	Shorter relapse-free survival
RISC	RNA-induced silencing complex
RNaseP	Ribonuclease P

ROC Curve	Receiver operator characteristic curve
RTqPCR	Real-time quantitative PCR
SCT	Rtem cell transplant
SnoRNA	Small nucleolar RNA
SnoRNP	Small nucleolar RNA protein
SNP	Single-nucleotide polymorphism
SPEM	Spasmolytic polypeptide- expressing metaplasia
STAT5	Signal transducer and activator of transcription 5
SZ	Schizophrenia
T2D	Type 2 diabetes
TC	Tongue cancer
TKDs	Tyrosine kinase domains
TNF-α	Tumor Necrosis Factor-α
TPM1	Tropomyosin1
WHO	World Health Organization

CONTENTS

ABSTRACT

Colon cancer-associated transcript-1 (CCAT1) is along noncoding RNA that maps to chromosome 8q24.21,it was first discovered to be upregulated in colorectal cancer . Recent studies have observed the CCAT1 overexpression in primary human solid cancers as in AML. Moreover, it repressed monocytic differentiation and promote cell growth of HL-60. The present study aims to investigate the correlation of CCAT1 expression with clinic-pathological features and the clinical prognosis of the patients with AML. To find out the association between CCAT1 expression and expression of miRNA-155 as a targeting gene for CCAT and to improve our understanding of the roles and the clinic implications of CCAT1 in the development and progression of AML. This study obtained by measuring the expression of CCAT1 and miR-155a of 50 AML patients. The results of the present work showed that CCAT1 and miR-155a were increased by 3.0 and 5.6 folds respectively in AML compared to normal controls and also upregulation of both biomarkers was significantly associated with high risk AML . It could be concluded that CCAT1 and miR-155a can be considered as a diagnostic and prognostic biomarker in AML.

Key words

Leukemia, Acute myeloid leukemia, Long Non Coding RNA and MicroRNA-155a

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