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Commentary

Identification and validation of N7-methylguanosine-associated gene NCBP1 as prognostic and prognostic immune-associated biomarkers in breast cancer patients

Yusi Yang[1], Lin Zheng[2], Jianrong Li[3], Baiqi Wen[3,*]

[1]Department of Cardiology, Third Hospital of Shanxi Medical University, Shanxi Bethune Hospital, Shanxi Academy of Medical Sciences Tongji Shanxi Hospital, Taiyuan, 030032, China

[2]Department of Vascular Surgery, Second Hospital of Shanxi Medical University, Taiyuan 030001, China

[3]Gastroenterology, Shanxi Province Cancer Hospital/ Shanxi Hospital Affiliated to Cancer Hospital, Chinese Academy of Medical Sciences/ Cancer Hospital Affiliated to Shanxi Medical University, Taiyuan, China

*Author for correspondence:
Email: baiwenqi1998@163.com

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Epigenetics is the study of heritable modifications to gene expression, such as DNA methylation, histone modifications, and RNA modifications, that do not alter the nucleotide sequence of the corresponding gene. Recently, RNA modification has emerged as a novel research focus. We have detected over 170 different RNA modifications [1], such as N6-methyladenosine (m6A), N7-methylguanosine (m7G), 5-methylcytosine (m5C), N1-methyladenosine (m1A), N3-methylcytosine (m3C), and pseudouridine (ψ) [2]. These modifications are important for biological processes like RNA metabolism and post-transcriptional regulation. m7G has emerged as a new RNA modification research hotspot due to the swift advancement of sequencing technologies. It is common to find positively charged m7G alterations in prokaryotes, eukaryotes, and archaea [3]. The majority of RNA metabolism processes, such as pre-mRNA splicing, stabilization of mRNA structure, transcription, translation, and nuclear export [4-7] are impacted by M7G modifications, which are frequently found in mRNA, tRNA, rRNA, miRNA, and the 5′ cap end of eukaryotic mRNA [8,9].

The first confirmation of m7G inside mammalian mRNA was made in 2019 by Zhang et al. They also invented a novel epigenetic sequencing method called m7G-seq, which allowed researchers to map out the distribution sites of m7G modifications [10]. These discoveries paved the way for further studies on m7G subsequent modification. Both the maintenance of the human body's regular physiological processes and the development of cancer are significantly influenced by m7G alteration and associated regulatory variables. Thus far, methyltransferases and translation factors such as METTL1/WDR4, RNMT/RAM, NCBP1, and WBSCR22/TRMT112 have been identified as m7G regulators in mammals.

Higher eukaryotes have a nuclear cap binding complex. The complex, which is made up of nuclear cap binding proteins NCBP1 and NCBP3, could bind to the elements of the mRNA processing machinery and increase the production of poly (A) RNA [11]. When newly transcribed mRNA is bound to its m7G′-cap structure, it orchestrates subsequent RNA biosynthesis procedures, including the transfer of nucleoplasm and the cytoplasmic recruitment of translation components [12,13]. There is a connection between immune cell infiltration in osteosarcoma and adrenal cancer and NCBP1 expression. Diffuse large B-cell lymphoma and lung adenocarcinoma have been shown to express NCBP1 aberrantly [14,15]. To verify that the high level of NCBP1 could influence the overall survival in BC patients, using breast cancer cells as the *in vitro* model, the authors provided evidence that NCBP1 can considerably enhance the transfer and proliferation of breast cancer cells.

In order to clarify the role of NCBP1 in the migration and invasion of cancer cells in triple

negative breast cancer, this study found that NCBP1 expression was significantly increased in human breast cancer, the survival time of patients with high expression of NCBP1 was significantly shortened, and NCBP1 also affected the abundance of immune cell infiltration in the tumor. NCBP1 knockout was performed using triple negative breast cancer cells and the invasion, migration and proliferation of cancer cells were significantly reduced.

A number of previous studies have proved that m7G mechanism affects the migration and proliferation of cancer cells, but no one has clarified whether m7G mechanism plays a role in breast cancer cells or which genes in m7G are crucial targets. Therefore, we determined the expression of key regulatory factors in the m7G mechanism through difference analysis. Survival analysis was used to determine the survival of patients with different m7G expressions, further identify the key targets affecting patients with breast cancer and use *in vitro* knock-out verification to determine whether the core gene of m7G NCBP1, acts significantly on breast cancer. There are a number of previous studies that have proven that the m7G mechanism affects the migration and proliferation of cancer cells.

Altogether, Li et al. [16] identify a hub gene of m7G in patients with BC, NCBP1, involved in the proliferation and migration of BC, and this finding provides a new insight into molecular mechanisms for BC. In addition, this study demonstrated that, for the first time, NCBP1 could influence BC by m7G, extending our knowledge of the regulation of NCBP1.

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