



Commentary

Future perspectives of Sleeping Beauty transposon system in cancer research


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With the unsolved challenges to explore potential predictors of metastasis in colorectal cancer patients, Nicoloso and colleagues endeavored in this issue to combine a transposon-based forward genetic screen with the forced Single Cell Suspension assay (fSCS) to discover specific regulators of metastatic colorectal cancer [1]. They found that the fSCS was a simple and scalable *in vitro* assay to select cells with pro-metastatic traits. Meanwhile, the Sleeping Beauty transposon integration was proven to generate fSCS-resistant colorectal cancer cells. Also, its insertion in the 3'UTR of *BTBD7* disrupted miR-23b::*BTBD7* interaction and contributed to metastasis. In addition, both miR-23b and Btbd7 protein show promising potential for prognostic biomarkers in colorectal cancer patients.

Colorectal cancer remains to be the second and third most prevalent cancers in 2019 among males and females, respectively [2]. Despite of the developments in diagnostic technologies and treatments, cancer metastasis is still a severe threat to patients' survival. Searching for prognostic biomarkers and therapeutic targets will help developing efficient therapies and good outcomes of colorectal cancer patients.

Recently, liquid biopsy technique is increasingly adopted for evaluating diagnostic or prognostic biomarkers in various kinds of cancers. Sources for biomarker development can include circulating tumor cells (CTCs), circulating tumor DNA (ctDNA), circulating cell-free RNA (cfRNA), circulating extracellular vesicles (EVs), tumor-educated platelets (TEPs), proteins or metabolites in patients' peripheral blood. All these have the potential to provide information about traits of the primary tumor or metastases [3]. Besides, sensitivity and specificity of a single analyte should be verified by multiple preclinical studies before moving into clinical application of liquid biopsy assay. However, chemicals, radiation or viruses are used frequently in science with the intention to test the function of the potential biomarker associated with cancer metastasis. Biomarkers found under such conditions have a high potential to fail. The Sleeping Beauty transposon system

demonstrates to be a more stable and better method for laboratory applications [4].

The Sleeping Beauty transposon system consists of the Sleeping Beauty transposase and a transposon which was found in the genome of salmonid fish in 1997 [5]. The Sleeping Beauty elements act to insert specific sequences of DNA into the genome of humans resulting in truncating the encoded proteins (inserting in a gene) or increasing the gene products (inserting near a gene) [6]. Therefore, advantages of Sleeping Beauty integration over other genetic tools rely on its location in the host genome which has no serious biases for any chromosomes [7]. For decades, researchers have already applied Sleeping Beauty the genetic system to identify altered genes in varieties of cancers [8,9]. While in colorectal cancer, the Sleeping Beauty method was only applied in a mice model to explore cancer-related genes by Starr and co-workers [10]. In this study, Nicoloso and colleagues utilized this tool and explored miR-23b and Btbd7 as novel prognostic predictors of colorectal cancer metastasis both *in vitro* and *in vivo* [1]. These findings will be more accurate and more credible than studies employing other tools such as viruses in need of huge amounts of sequencing. As a result, utilization of liquid biopsy following the Sleeping Beauty genetic screen data could show good potential in medicine.

Nevertheless, in this context, other six genes were transformed due to the Sleeping Beauty insertion. So whether the miR-23b::*BTBD7* interaction is essential in the process of metastasis in colorectal cancer remains uncertain. More evidences should be acquired to confirm the full potency of miR-23b and Btbd7 as well as of the Sleeping Beauty transposon system as liquid biopsy in the clinical management of patients with colorectal cancer.

Funding

This research was supported by the National Key Research and Development Program of China (No. 2016YFC0905900), National Natural Science Foundation of China (No. 81872365), and Postgraduate Research and Practice Innovation Program of Jiangsu Province (KYCX18_1490).

Declaration of Competing Interest

None.

DOI of original article: <https://doi.org/10.1016/j.ebiom.2019.06.044>.

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<https://doi.org/10.1016/j.ebiom.2019.07.038>

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