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Editorial

Significance of Long Noncoding RNAs in Regenerative Medicine

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ABSTRACT

Long noncoding RNAs (lncRNAs) are a heterogeneous class of RNAs with generally longer than 200 nucleotides. It has been proposed that LncRNAs as a piece of paracrine action would control cellular pluripotency, differentiation, maintenance and regulate tissue development, organogenesis and regeneration. Next generation sequencing (RNA-seq) has produced huge data about lncRNAs expression profile in different cell types and condition, but understanding the roles and functions of these novel lncRNAs is poorly understood.

Keywords: LncRNAs function, Stem cell therapy, RNA sequencing, Bioinformatics, Exosome

Stem cells are considered as the promising candidates to regenerate damaged tissues. A number of clinical trials have encouraged the researchers and clinicians to use stem cells especially mesenchymal stem cells (MSCs) due to its several unique properties. These cells, in addition to multilinage differentiation potential and high proliferation capacity, exert paracrine effects via the release of exosomes and microvesicles which are known as the main mediators of cell to cell communication (Figure 1). The concept that lncRNAs might be paracrine or even endocrine effectors, is based on the evidence that they can transport via extracellular vesicles (EVs), i.e. exosomes and microvesicles (MVs) between cells, either within a surrounding tissue or remotely by entering into blood (1, 2). It has been shown that the EVs may contain mRNA, noncoding RNA (microRNA, LncRNA, and etc) and sometimes even DNA, in addition to lipids and proteins; secreting from the stem cells and having the capacity to alter the phenotype and cell fate of neighboring cells to restore injury tissues/organs (2, 3). Recently, Wang et al. have investigated the expression profiles of lncRNAs during the chondrogenic differentiation of hBM-MSCs. By bioinformatic analyses, they found that 3638 lncRNAs differentially expressed in differentiated and undifferentiated state. With further analyses to find biological function of lncRNAs and their involvement in the mechanism of differentiation, it has been determined that two ZBED3-AS1 and CTA-941F9.9 lncRNAs are most likely playing important roles in chondrogenic differentiation process (4). Several other reports focused on the findings about the regulatory roles of lncRNAs in self-renewal and differentiation into any lineage, and explained the underlying molecular mechanisms (5, 6). Sheik Mohamed et al. have shown that conserved lncRNAs regulated transcriptionally by Oct4 and Nanog, thereby modulating pluripotency in mESCs (7). Additionally, Zhang et al. have highlighted the pivotal role of lncRNA DANCR in chondrogenic differentiation of human synovium-derived stem cell (SMSCs) (8). Moreover, lncRNA H19 promotes osteoblast differentiation of hMSCs Via TGF-β1/Smad3/HDAC signaling pathway by deriving miR-675 and may serve as a potential target for enhancing bone formation *in vivo* (9). Interestingly,

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in another study, it has been determined that the H19 long noncoding RNA promotes skeletal muscle differentiation and regeneration through encoding miR-675-3p and miR-675-5p (10). Experiments of gain and loss of function of H19 showed that this LncRNA plays a central role in the exosome-mediated phenotype of endothelial cells (11). Although lncRNAs have been recognized in recent years as a key player in the self-renewal, differentiation, and paracrine action of stem cells and many other types of cells, however, their roles and functions have yet remained fully being determined. Furthermore, it is still difficult to large-scale determination of their functions from just lab experiments. Therefore, several studies have developed a computational pipeline to large-scale prediction of the functions for lncRNA (12-14).

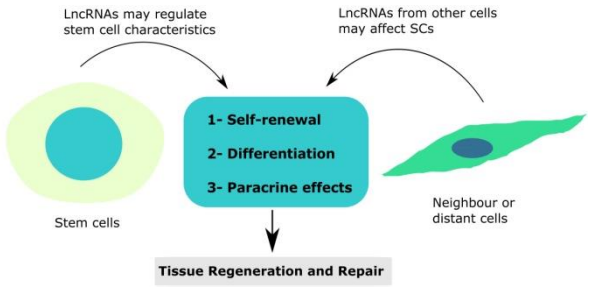

Figure 1. LncRNAs: a novel tool for regenerative therapy. Stem cell can secrete exosome and microviscicle containing lncRNAs which are responsible to control self-renewal and differentiation behavior along with their specific paracrine effect on neighboring cells and vice versa.

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