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Long Noncoding RNAs: Emerging Biomarkers of Therapy Resistance and Tumor Progression

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Long noncoding RNAs (lncRNAs) have a sequence greater than 200 nucleotides long and are increasingly appreciated for their role in multiple biological processes including differentiation, cellular proliferation metastasis, apoptosis, and therapeutic resistance.[1,2] On the mechanistic scale, noncoding RNAs and circular (circ) RNAs act as either oncogenes or tumor suppressor genes by contributing to the development and progression of solid tumors by affecting the function of endogenous targets like miRNAs and transcription factors. For miRNA, evidence suggests that lncRNAs may act as competing endogenous RNA through which miRNAs are deprived of regulating the downstream target.[3,4] In addition, lncRNAs are shown to alter the transcription factor accessibility through chromatin modification and thereby regulating the expression of downstream effectors.[5] Because of this, it is necessary to uncover the regulatory aspects of lncRNAs and circRNAs to undertake better therapeutic measures.

Therapy resistance has been the major clinical obstacle in the treatment of cancer. LncRNAs received increasing attention due to their complex regulatory network and are viewed as an attractive biomarker for chemotherapy, radiotherapy, and immunotherapy resistance. The chemotherapy resistance is generally attributed to lncRNA functions such as altering drug efflux, affecting the expression of proto-oncogenes and tumor suppressor genes.[6] Similarly, the radiotherapy resistance is reported to be mediated by lncRNAs through regulating the cellular processes such ad DNA damage and repair, autophagy, and cell cycle.[7]

Cancer stem cells are known to participate in metastasis, recurrence, and drug resistance.[8] Studies have demonstrated that lncRNAs regulate the tumor progression through controlling the tumor stem cell activity. For instance, lncRNA IPW is shown to potentiate the DCIS progression to invasive ductal carcinoma (IDC) by ID2 though miR29c.[3] It is therefore essential to decode the functional module of how lncRNA affects the stem cell component for improved translational impact.

Another important dimension of noncoding RNA research that is gaining momentum is its role as a biomarker for tumor progression and treatment resistance. The profiling of lncRNAs in liquid biopsy samples can potentially provide valuable insights on early diagnosis and to stratify patients as potential responders or nonresponders to the competent therapy.[9]

Taken together, noncoding RNA research is opening the flood gates to explore the vast regulatory and functional aspects of lncRNA-mediated gene regulation for distinct translational applications.

I thank the editorial team in facilitating the release of this special issue "LncRNAs and CircRNAs: biomarkers of therapeutic resistance tumor progression." The articles in this special collection are intended to provide valuable insights on the role of lncRNAs in the broad area of cancer progression and therapeutic resistance. We hope that it may enrich our understanding and facilitate the application of this knowledge in clinical setting.

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