Editorial: Non-Coding RNAs in Gastrointestinal and Gynecological Cancers: New Insights Into the Mechanisms of Cancer Therapeutic Resistance

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Editorial on the Research Topic

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BACKGROUND

Chemoresistance is mediated by a variety of molecular mechanisms, including inhibition of drug influx, increased drug efflux, evasion of cell apoptosis, enhanced repair of DNA damage, induction of epithelial-mesenchymal transition (EMT), activation of cancer stem-like features, induction of autophagy, alterations in cancer metabolism, mutations of drug targets, and dynamic interactions between tumor cells and their surrounding microenvironment (Holohan et al., 2013). Tumor cells can become resistant to chemotherapeutic agents through a combination of different mechanisms (Vasan et al., 2019). Non-coding RNAs (ncRNAs), such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), have been implicated in chemoresistance (Wang et al., 2019).

In this research topic, 21 papers (including thirteen reviews and eight original research articles) that have shed light on the therapeutic resistance mechanisms controlled by non-coding RNAs in human gastrointestinal and gynecological cancers were chosen. The latest findings presented in this Research Topic add to our understanding of the mechanisms by which non-coding RNAs govern cancer cell resistance to chemotherapy, and may also point to meaningful molecular targets that could be utilized to eliminate chemoresistance and increase the survival of cancer patients.

MIRNA AND CHEMORESISTANCE

Tumor cells frequently have a high rate of glucose metabolism, and aerobic glycolysis has been linked to chemoresistance in tumors (Marcucci and Rumio, 2021). Hexokinase 2 (HK2), an
CIRCRNA AND CANCER PROGRESSION

Li et al. report that circDNMT1, a circular RNA overexpressed in gastric cancer, can sponge miR-576-3p and subsequently elevate the levels of hypoxia-inducible factor-1 alpha (HIF-1α) in gastric cancer cells. By regulating the miR-576-3p/HIF-1α axis, circDNMT1 promotes gastric cancer cell proliferation, migration, invasion, and glycolysis.

COMPUTATIONAL STUDIES OF NCRNAS

An original article by Wang et al. highlighted the importance of an immune-related lncRNA signature in predicting the prognosis of patients with colon cancer. Ding et al. confirmed that the expression of RP4-616B8.5, RP11-389G6.3, and CTD-2377D24.6 was increased in endometrial cancer tissues and that this 3-lncRNA signature was closely associated with histological subtype and advanced clinical stage in endometrial cancer patients. Their results indicate that this new lncRNA model might be useful for predicting the prognosis of patients with endometrial cancer.

REVIEWS

13 review articles focus on the recent advances in the ncRNA research field and summarize the function and mechanisms of miRNAs, circRNAs, and lncRNAs in the pathogenesis of gastrointestinal and gynecological cancers. Zhao et al. outline the important impacts of miR-30d-5p on many types of malignancies, indicating that miR-30d-5p has broad potential as a diagnostic and therapeutic target for tumors. Ma et al. discuss the potential use of circRNAs as biomarkers or therapeutic agents for gynecological cancers. Wang et al. summarize the mechanisms underlying the involvement of circRNAs in modulating gastrointestinal cancer chemoresistance. Furthermore, Ghafoori-Fard et al. summarize the tumor suppressor role for a circRNA circITCH in various cancers. All these studies improve our understanding of the underlying mechanisms of ncRNAs and may aid in the development of new therapies for gastrointestinal and gynecological cancers.

SUMMARY

Taken together, the discovery of novel non-coding RNAs involved in the regulation of glycolysis or drug efflux has revealed fresh insights into the molecular basis of chemoresistance in gynecological cancers. aberrant regulation of the miRNA-miRNA pathway, or the lncRNA/circRNA-miRNA-mRNA ceRNA network, contributes to chemoresistance in gastrointestinal and gynecological cancer cells. Notably, lncRNAs can interact with RNA-binding proteins and some RNA-binding proteins have critical roles in circRNA biogenesis. Further research on the interplay between ncRNAs and their molecular partners might provide opportunities for more...
effective strategies to prevent or overcome chemoresistance in gastrointestinal and gynecological cancer patients.

**AUTHOR CONTRIBUTIONS**

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication.

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