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総 説

RNA工学を用いた医薬品への挑戦～siRNAを中心として～

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Development of siRNA drug by RNAi technology

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Summary

Small interfering RNAs (siRNAs) are expected to have medical application in human therapy as drugs with a high specificity for their molecular target mRNAs and functioning in the cell cytoplasm. This RNA interference (RNAi) therapy that permits a highly specific inhibition of the selected gene expression provides an excellent way to reduce adverse events very often associated with cancer chemotherapy.

In this study, we investigated the anti-cancer effects of RecQL1-siRNA in various tumor-bearing mouse models to assess the potential of RecQL1-siRNA as an anti-cancer agent and to search for the most effective administration. To this end, a few plausible drug delivery systems were tested that protect siRNA from hydrolysis by nucleases, direct siRNA to specific tissues and organs, and facilitate entry into cells. To find the best feasible therapy, several tumor-bearing nude mouse models were tested by local or systemic administration by intravenous injection. Although siRNA has many excellent profiles as a drug candidate, the highest hurdle to its therapeutic application is finding a way to deliver siRNA molecules safely and specifically to target organs and cells. Our fundamental study should help overcome the hurdles confronting the medical application of siRNA.

Key words

Human cancer, DNA repair, RecQL1 helicase, siRNA, Mitotic catastrophe, Liver cancer