Molecular-targeted drugs

Development of molecular-targeted therapeutic drugs for cancer

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Abstract

Bladder cancer causes an estimated 150,000 deaths per year worldwide. Although 15% of the recurrent bladder cancer becomes an invasive type, currently used targeted therapy for malignant bladder cancer is still not efficient. We focused on the miR-130 family (miR-130b, miR-301a, and miR-301b) that was significantly upregulated in bladder cancer specimens than that of the normal urothelial specimens. We found that miR-130 family has a crucial role in malignant progression of bladder cancer, and miR-130 family-targeted LNA oligonucleotides were found to suppress tumor growth in an in vivo xenograft model. We also found that miR-130 family was also highly expressed in non-small cell lung cancer (NSCLC) and act as an oncomiR, promoting metastasis and invasion activities in NSCLC cells.

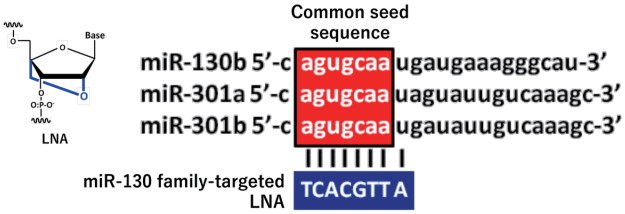
Background & Results

MicroRNAs (miRNAs) are small noncoding RNA molecules 20–25 nucleotides in length. These molecules regulate gene expression through translational repression or degradation of mRNA by binding to the 3′ -untranslated region (3′ -UTR) of target mRNAs. Each miRNA typically targets approximately 200 genes. Because 30–60% of human genes can be regulated by miRNAs, these molecules have the potential to modulate various cellular processes, such as cell growth, migration, invasion, apoptosis, and angiogenesis. Our study showed that the miR-130 family, including miR-130b, miR-301a, and miR-301b, is highly expressed in bladder cancer specimens and functions as an oncogenic miRNA (oncomiR) family by promoting the migration and invasion of bladder cancer cells. Moreover, miR-130 family-targeted LNA oligonucleotides were found to suppress tumor growth in an in vivo xenograft model. Furthermore, miR-130 family was found to act as an oncomiR, promoting metastasis and invasion activities in NSCLC cells.

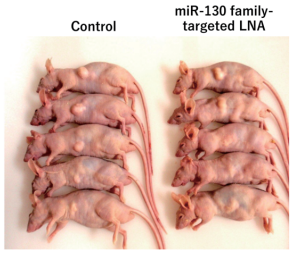
Significance of the research and Future perspective

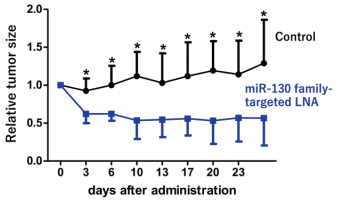
Our findings indicated that miR-130 family functioned as an oncogenic miRNA in NSCLC and bladder cancer and could therefore facilitate the development of molecular-targeted therapeutic drugs for these cancers.

Construction of LNA targeting common seed sequence in miR-130 family



miR-130 family-targeted LNA suppresses tumor growth in vivo





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Treatise
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URL

Keyword locked nucleic acid (LNA), miRNA, bladder cancer, non-small cell lung cancer