

CRISPRInc: New IncRNA-specific SgRNA design method proposed

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Overview of CRISPRInc web version. (A) Services and downloads available on the website. (B) Examples of the website usage. (C) sgRNA design results based on CRISPRko mechanism. (D) sgRNA design results based on CRISPRi mechanism. (E) Statistics of sgRNA target results for lncRNA from Homo sapiens, Mus musculus and Danio rerio. Credit: *Briefings in Bioinformatics* (2024). DOI: 10.1093/bib/bbae066

Long non-coding RNAs (lncRNAs) are non-protein-coding transcripts. Currently, CRISPR/Cas9 is a promising RNA-guided genome editing technology consisting of a Cas9 nuclease and a single-guide RNA (sgRNA). Considering the significant differences between lncRNAs and protein-coding genes, it is necessary to investigate sgRNA design method optimized for lncRNAs.

Researchers from the Xishuangbanna Tropical Botanical Garden (XTBG) of the Chinese Academy of Sciences (CAS) studied the application of CRISPR/Cas9 technology in gene editing, especially for sgRNA design against long noncoding RNA (lncRNA).

They first evaluated the performance of a series of known sgRNA design tools on coding and noncoding <u>datasets</u> and analyzed the different performances in terms of sgRNA specificity to lncRNA, including nucleic acid sequence, genomic location, and editing mechanism preference. Results were <u>published</u> in *Briefings in Bioinformatics*.

The researchers also introduced a support vector machine-based machine learning algorithm, CRISPRInc, which aims to simulate the CRISPR knockout (CRISPRko) and CRISPR inhibition (CRISPRi) mechanisms to predict the targeting activity of the target. CRISPRInc combines paired sgRNA design and off-target analysis to achieve one-stop design of CRISPR/Cas9 sgRNA for noncoding genes.



By comparing the performance of CRISPRInc with several existing methods on multiple datasets, the researchers conclude that CRISPRInc performs much better than existing methods for lncRNA-specific sgRNA design for both CRISPRko and CRISPRi mechanisms.

"We have proposed a new machine learning method, CRISPRInc, for the design of lncRNA-specific sgRNA in the CRISPR/Cas9 system. The performance comparison shows that CRISPRInc is far superior to existing methods for lncRNA-specific sgRNA design in both CRISPRko and CRISPRi mechanisms," said Liu Changning of XTBG.

To facilitate the use of CRISPRInc, the researchers developed a <u>web</u> <u>server</u> and made it available for download on GitHub. For the convenience of users, they integrate services such as paired sgRNA design and off-target risk analysis into the implementation of the CRISPRInc tool, and provide a variety of information such as on-target validity, off-target risk and genomic location to help further select sgRNAs.

More information: Zitian Yang et al, CRISPRInc: a machine learning method for lncRNA-specific single-guide RNA design of CRISPR/Cas9 system, *Briefings in Bioinformatics* (2024). DOI: 10.1093/bib/bbae066

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