

Chemically Synthesized Guide RNAs

Introduction

Agilent's Chemically Synthesized Guide RNAs are the industry standard for quality nucleic acids. Using a patented, proprietary chemistry¹ makes the synthesis of long RNA oligonucleotides as robust and efficient as DNA synthesis. This chemistry is used to synthesize and deliver high quality CRISPR guides, and our processing provides guides with fewer contaminants. Agilent researchers have developed chemical modifications which improve the efficiency, stability and specificity of guide RNAs in a variety of cell types^{2,3}. These modifications are patent pending and are available in a variety of options.

Key features

- Custom sequences up to 120nt
- Quantities from 100 µg to 100 mg (3-3000 nmol)
- Purification by HPLC provides high quality guides
- Chemical modifications at no extra charge (M or MS at 5' and 3' ends)
- Additional modifications and longer lengths available upon request

Background

Stability and activity are greatly enhanced by Agilent developed chemical modifications

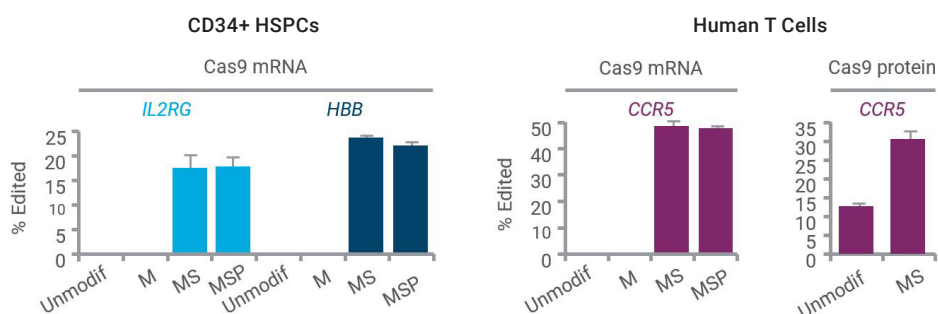


Figure 1. Chemically modified sgRNAs facilitate high frequencies of indels and homologous recombination in cells.² 2'-O-methyl 3'-phosphorothioate (MS), 2'-O-methyl (M)

Agilent sgRNA meets the most stringent quality standards

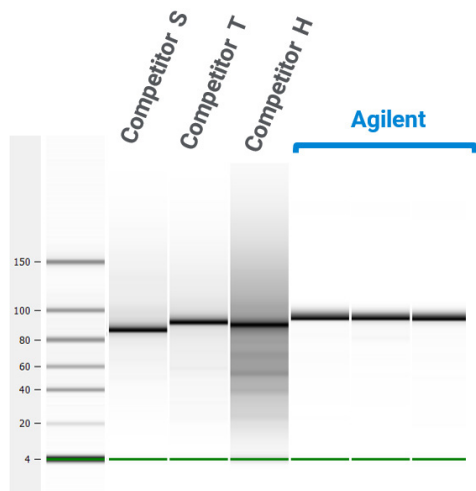


Figure 2. sgRNA samples of varying lengths analyzed on Agilent Bioanalyzer using a Small RNA Assay kit, following the kit protocol.

Agilent chemistry enables synthesis of long RNA oligos

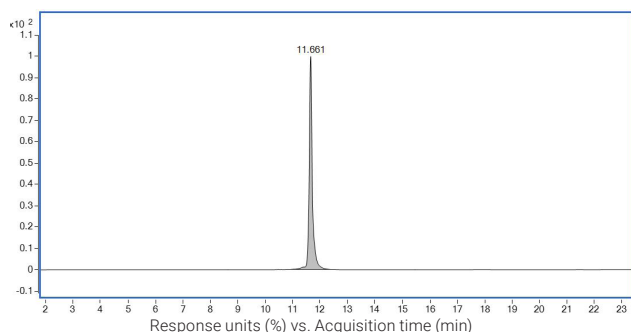


Figure 3A. HPLC chromatogram (diode array detector, 260 nm) of purified stability-modified 100mer sgRNA on Agilent 1290 Infinity II chromatography system. Similar results have been obtained with oligos up to 144 nucleotides. Custom sequences up to 162mer are available by request.

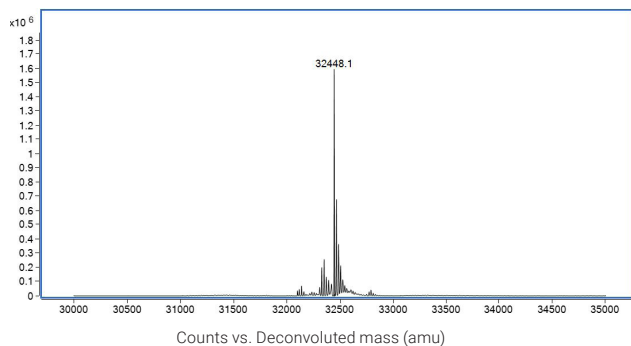


Figure 3B. Deconvoluted mass spectrum of purified stability-modified 100mer sgRNA on Agilent 6545 QTOF mass spectrometer. Expected mass, 32446.9 amu; observed mass, 32248.1 amu. Similar results have been obtained with oligos up to 144nt. Custom sequences up to 162mer are available by request.

References

Publications

1. Dellinger, D.J., *et al.* Streamlined Process for the Chemical Synthesis of RNA Using 2'-O-Thionocarbamate-Protected Nucleoside Phosphoramidites in the Solid Phase, *J. Am. Chem. Soc.* 133, 11540–11556 (2011); DOI: [10.1021/ja201561z](https://doi.org/10.1021/ja201561z)
2. Hendel, A., *et al.* Chemically modified guide RNAs enhance CRISPR-Cas genome editing in human primary cells. *Nature Biotechnology*, Vol. 33 No. 9 (2015); DOI: [10.1038/nbt.3290](https://doi.org/10.1038/nbt.3290)
3. Ryan, D.E., *et al.* Improving CRISPR–Cas specificity with chemical modifications in single-guide RNAs. *Nucleic Acids Research*, Vol. 46, No. 2 (2018); DOI: [10.1093/nar/gkx1199](https://doi.org/10.1093/nar/gkx1199)

Agilent patent application (United States)

- US20160289675, US20180051281 - Guide RNA with chemical modifications, Ryan, *et al.*
- US20170355985 - High specificity genome editing using chemically modified guide RNAs, Dellinger, *et al.*

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| Order Information | Product Name |
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