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INSPIRED CELL SOLUTIONS

Up to 40% off all catalog RNAi and CRISPR libraries until December 31st

Get reliable screening data fast with CRISPRko, CRISPRa, and RNAi Libraries

We know your time in the lab is more precious than ever. Let us help you make the most of it. Our CRISPRko, CRISPRa, and RNAi libraries are all designed with your requirements in mind, such as:

- Algorithm designed sequences for functionality and specificity
- Chemical modifications to improve performance and limit cytotoxicity
- 96- and 384-well plate formats
- Pooled lentiviral libraries provided as high-titer ready-to-use lentiviral particles

Find out more and view **screening libraries**

Flexible library options:

Choose from predesigned gene family libraries and whole genome collections. Not finding what you need? Turn your gene list into a Cherry-pick custom library

Reliable editing and knockdown:

Use pooled synthetic reagents with multiple guides or siRNAs per well targeting the same gene to get maximum effects while minimizing resources

Minimize off-target effects:

Industry leading RNAi knockdown data using ON-TARGETplus siRNA, proven and patented to prevent off-target effects arising from both strands

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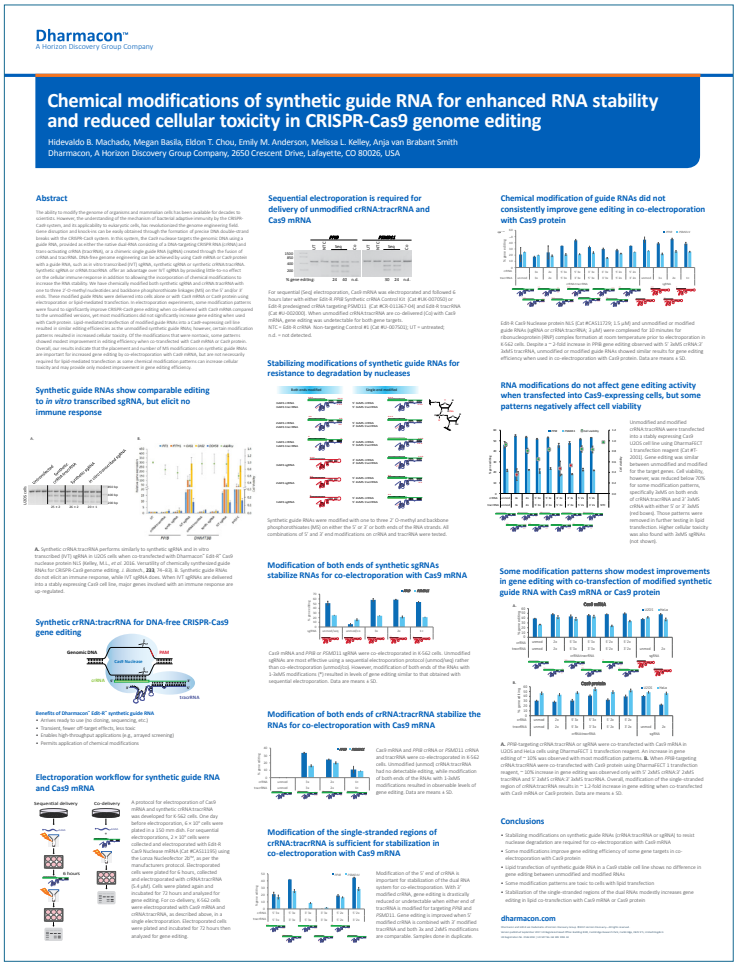

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Chemical modifications of synthetic guide RNA for enhanced RNA stability and reduced cellular toxicity in CRISPR-Cas9 genome editing

Hidevaldo B. Machado, Megan Basila, Eldon T. Chou, Emily M. Anderson, Melissa L. Kelley, Anja van Brabant Smith
Dharmacon, A Horizon Discovery Group Company, 2650 Crescent Drive, Lafayette, CO 80026, USA

Abstract

Sequential electroporation is required for delivery of unmodified crRNA:tracrRNA and Cas9 mRNA

Chemical modification of guide RNAs did not consistently improve gene editing in co-electroporation with Cas9 protein

Synthetic guide RNAs show comparable editing to *in vitro* transcribed sgRNA, but elicit no immune response

Stabilizing modifications of synthetic guide RNAs for resistance to degradation by nucleases

RNA modifications do not affect gene editing activity when transfected into Cas9-expressing cells, but some patterns negatively affect cell viability

Synthetic crRNA:tracrRNA for DNA-free CRISPR-Cas9 gene editing

Modification of both ends of synthetic sgRNAs stabilize RNAs for co-electroporation with Cas9 mRNA

Some modification patterns show modest improvements in gene editing with co-transfection of modified synthetic guide RNA with Cas9 mRNA or Cas9 protein

Benefits of Dharmacon™ Edit-R™ synthetic guide RNA

- Arrives ready to use (no cloning, sequencing, etc.)
- Transient, fewer off-target effects, less toxic
- Enables high-throughput applications (e.g., arrayed screening)
- Permits application of chemical modifications

Modification of both ends of crRNA:tracrRNA stabilize the RNAs for co-electroporation with Cas9 mRNA

Electroporation workflow for synthetic guide RNA and Cas9 mRNA

Modification of the single-stranded regions of crRNA:tracrRNA is sufficient for stabilization in co-electroporation with Cas9 mRNA

Conclusions

- Stabilizing modifications on synthetic guide RNAs (crRNA:tracrRNA or sgRNA) to resist nuclease degradation are required for co-electroporation with Cas9 mRNA
- Some modifications improve gene editing efficiency of some gene targets in co-electroporation with Cas9 protein
- Lipid transfection of synthetic guide RNA in a Cas9-stable cell line shows no difference in gene editing between unmodified and modified RNAs
- Some modification patterns are toxic to cells with lipid transfection
- Stabilization of the single-stranded regions of the dual RNAs modestly increases gene editing in lipid co-transfection with Cas9 mRNA or Cas9 protein

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t +44 (0)1223 976 160 (UK) **or** +1 800 235 9880 (USA); +1 303 604 9499 (USA)
f +44 (0)1223 655 581
e info@horizondiscovery.com
w horizondiscovery.com/contact-us
Horizon Discovery, 8100 Cambridge Research Park, Waterbeach, Cambridge, CB25 9TL, United Kingdom

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