# Infinite reliability for functional genomics.

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Dharmacon™ Reagents

# Introduction

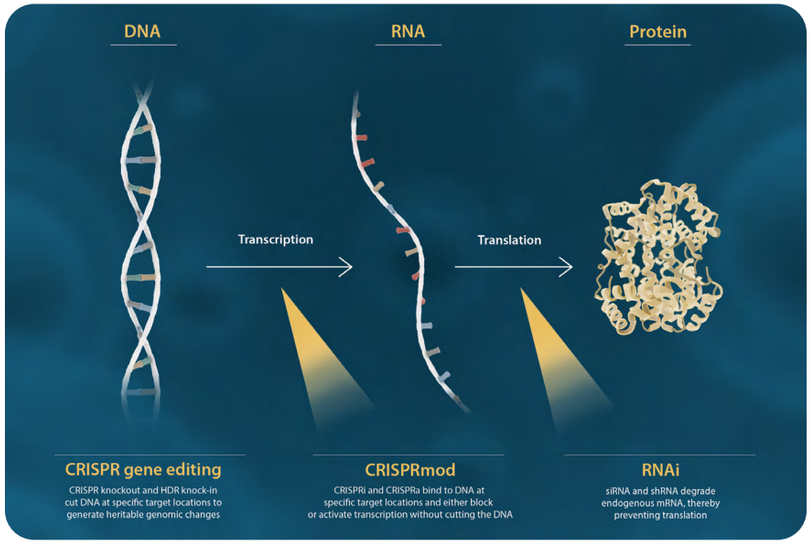
Dharmacon™ Reagents encompass the broadest range of experimental tools for reliable and accurate manipulation of functional gene expression. Our gene editing and CRISPR modulation portfolios were developed, manufactured and supported by the same groups that brought you Dharmacon™ siRNA and custom oligonucleotide solutions.

**Flexible format options to suit your experimental design**

**Scalable workflows to fit your project scope**

**Proven reagents to deliver accurate results**

**One destination, many paths...**




*Loss- or gain-of-function can be achieved in many ways. We support functional genomics research with unique reagents that target gene expression at the transcription or translational levels.*

| | CRISPR editing | CRISPRmod | RNAi |
|---|---|---|---|
| Level of operation | Transcription | Transcription | Translation |
| Down regulation | CRISPRko | CRISPRi | siRNA, shRNA, miRNA |
| Up regulation | Gene insertion via HDR knock-in | CRISPRa | cDNA/ORF |
| Benefits | Specific and efficient programmable gene editing | CRISPR-level specificity without cutting DNA | Simplest knockdown/ overexpression workflows |
| Ideal applications | Cell line engineering; making permanent changes to the genome | Exploring essential gene knockdown, endogenous gene activation | Transient knockdown assays (siRNA), inducible knockdown for essential genes (shRNA), rescue experiments (cDNA/ORF) |

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# Translational gene modulation

## Trusted Dharmacon solutions

Well-known techniques that affect gene expression at the translational level, such as RNA interference and gene overexpression.


### RNA interference

#### Synthetic siRNA for fast and straightforward transient loss-of-function studies

| | Ideal for |
|---|---|
| ON-TARGETplus siRNA | Minimizing off-target effects |
| siGENOME siRNA | Efficient gene silencing at a lower cost |
| Accell self-delivering siRNA | Difficult-to-transfect cells |

See our siRNA product selection guide or applications page to learn more.

#### Lentiviral shRNA for generating stable knockdown cell lines in longer term studies

| | Ideal for |
|---|---|
| SMARTvector lentiviral shRNA | Flexibility in promoter/reporter options |
| SMARTvector inducible lentiviral shRNA | Controlling the timing of gene silencing |

See our shRNA product selection guide or applications page to learn more.

#### miRNA solutions for microRNA pathway studies

| | Ideal for |
|---|---|
| miRIDIAN microRNA Mimic | Upregulating microRNA activity |
| miRIDIAN microRNA hairpin inhibitors | Suppressing endogenous microRNA activity |
| shMIMIC lentiviral microRNA | Flexibility in promoter/reporter options |
| shMIMIC inducible lentiviral microRNA | Fine-tuning microRNA expression |

See our miRNA applications page to learn more.

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# Translational gene modulation


## Gene overexpression

### cDNA and ORFs covering a wide variety of species for straightforward gain-of-function studies

Both cDNAs and open reading frames (ORFs) can be used to overexpress genes-of-interest. cDNA is ideal for overexpressing a gene within the context of native regulation, while ORFs have both 5′ and 3′ UTRs removed providing a shortcut to protein expression. We provide cDNA and ORF collections for human, mouse, yeast, C. elegans, zebrafish, Xenopus, and E. coli. Select from individual clones, lentiviral ORFs, or genome-scale libraries.

**Scale up your experiment**

Order pre-designed gene family sets

More

**Scale up your experiment**

Build and order a custom siRNA, shRNA, cDNA, or ORF library with the Dharmacon cherry-pick library tool.

More

| | cDNA | |
|---|---|---|
| | Mammalian Gene Collection (MGC) | CCSB Human ORFeome |
| Species | Human, Mouse, Rat | Human |
| Fully sequenced | ✓ | |
| Expression-ready | Subsets only | |
| Easy-to-transfer | | ✓ |
| Ready-to-use | | |
| Genome-scale | ✓ | ✓ |
| Formats | glycerol, arrayed, gene families | glycerol, arrayed, gene families |

| | ORF | | | |
|---|---|---|---|---|
| | Human ORFeome V8.1 | ORFeome Collaboration | CCSB-Broad Lentiviral Expression ORF Library | Precision LentiORF |
| Species | Human | Human, Mouse | Human | Human |
| Fully sequenced | ✓ | ✓ | ✓ | ✓ |
| Expression-ready | | | ✓ | ✓ |
| Easy-to-transfer | ✓ | ✓ | | |
| Ready-to-use | | | ✓ | ✓ |
| Genome-scale | ✓ | ✓ | ✓ | ✓ |
| Formats | glycerol, arrayed, gene families | glycerol, arrayed | glycerol, arrayed, gene families | glycerol, arrayed, gene families, starter kits and high-titer lentivirus |

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# Transcriptional gene modulation (CRISPRmod)

## CRISPR without the cut

Dharmacon CRISPR modulation (CRISPRmod) uses CRISPR-based systems with deactivated nucleases to modulate gene expression at the transcriptional level without cutting DNA. CRISPRmod is available for both loss- (CRISPRi) and gain-of-function (CRISPRa). Both systems require a gene-specific guide RNA and a specialized deactivated Cas9 (dCas9) nuclease.


### CRISPR interference

CRISPR interference (CRISPRi) is used to down-regulate gene expression at the transcriptional level and is an option for studying essential genes or orthogonal validation of RNAi results.


### CRISPR activation

CRISPR activation (CRISPRa) is used to up-regulate endogenous gene expression at the transcriptional level and is ideal for studying gene function within its native context.

| CRISPRi guide RNA |
| --- |
| Algorithm-designed lentiviral and synthetic guide RNA target immediately downstream of the gene's transcriptional start site, blocking transcription. |

[CRISPRi dCas9-SALL1-SDS3*]
Deactivated Cas9 for CRISPRi is available as:

- Lentiviral particles for creating your own dCas9-CRISPRi stable cell lines
- mRNA for DNA-free workflows

[CRISPRi all-in-one lentiviral sgRNA]
Single reagent – CRISPR sgRNA + dCas9- SALL1-SDS3 in one vector for easy transcriptional repression.

See our CRISPRi applications page to learn more.

| CRISPRa guide RNA |
| --- |
| Algorithm-designed lentiviral and synthetic guide RNA target the gene's promoter region, activating transcription. |

[CRISPRa dCas9-VPR]
Deactivated Cas9 for CRISPRa is available as:

- "CRISPRa ready" dCas9-VPR expressing stable cell lines
- Lentiviral particles for creating your own dCas9-CRISPRa stable cell lines
- mRNA for DNA free workflows

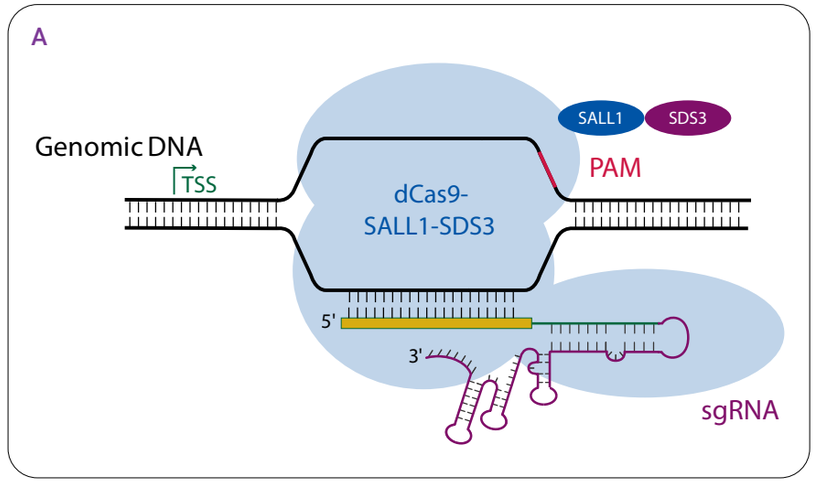
[CRISPRa all-in-one lentiviral sgRNA]
Single reagent – CRISPR sgRNA + dCas9-VPR in one vector for easy gene activation.

See our CRISPRa application page to learn more.

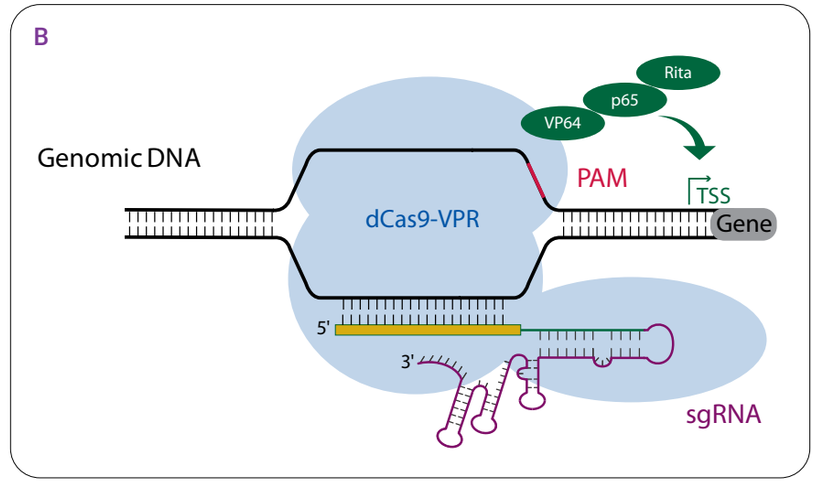
* Patent Pending

# Transcriptional gene modulation

## CRISPRi system




## CRISPRa system




Schematic diagrams showing a) CRISPRi machinery binding downstream of target gene TSS to block transcription, and b) CRISPRa machinery binding upstream of TSS to activate transcription.

**Scale up your experiment**

Order pre-designed gene family sets

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**Scale up your experiment**

Build and order a custom CRISPRmod library with the Dharmacon cherry-pick library tool

More

# Gene editing

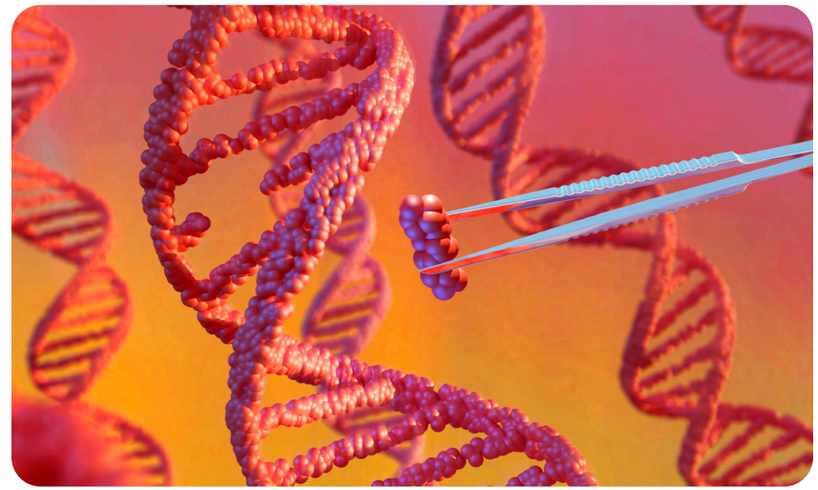
## Genome engineering made simple

CRISPR-Cas9-based gene editing allows researchers to permanently knockout gene function, introduce (knock-in) a gene selection marker, or change individual bases in the genome, thereby creating a novel edited cell line.

Gene Knockout

### Edit-R™ gene knockout

Dharmacon Edit-R CRISPR-Cas9 system is used to reliably knockout gene function with flexible format options to fit your workflow.



#### CRISPR guide RNA

Algorithm designed to maximize both the likelihood of generating a functional knockout, while retaining high targeting specificity – available in synthetic and lentiviral formats.

#### Cas9 nuclease is available as:

- "Knockout ready" Cas9 expressing stable cell lines
- Lentiviral particles for creating your own Cas9 stable cell lines (inducible options available)
- Purified Cas9 protein or mRNA for DNA-free workflows

#### All-in-one lentiviral sgRNA

Combines all required components for gene knockout (gene-specific guide RNA + Cas9 nuclease) into a single, ready-to-use reagent.

# Gene editing




## Dharmacon HDR knock-in

Precisely edit a single DNA base or insert an entire gene. Use CRISPR-Cas9 to cut the DNA at a specific location, while introducing a donor template with sequence similarity near the cut site.

See our HDR knock-in applications pages to learn more about using HDR with oligos or plasmids

## Dharmacon design tools for knock-in applications

### Custom CRISPR guide RNA design

The site-specific editing algorithm analyzes both the expected editing functionality of the guide RNA and its proximity to the ideal cut site. The tool returns a distance-weighted functionality rank, and checks for off-targets with a specificity check.

### HDR donor design & synthesis

Design and order ssDNA donors (for short, SNP alterations) and plasmid donor assembly kits (for longer donors, e.g., entire genes or fluorescent reporter tags) by inputting the guide RNA sequence used to edit the target DNA site and required donor sequence.

**Improve your gene editing workflow**

View our free video series

More

**Working in an uncommon species or with an alternative nuclease?**

Use the Dharmacon CRISPR design tool

More

**Scale up your experiment**

Order pre-designed gene family sets

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**Scale up your experiment**

Build and order a custom gene editing library with the Dharmacon cherry-pick library tool

More

# Dharmacon custom oligo synthesis

## Numerous modifications, greater yield, rapid delivery

Our custom synthesis lab has nearly 30 years of experience supplying highly consistent Dharmacon RNA oligos for research and pre-clinical use. Our patented 2′-ACE chemistry has a proven record of stability and flexibility in modifications, providing greater yield at longer lengths (up to 120 nt) resulting in higher value than any other supplier.

### Custom RNA synthesis

Create and order RNA molecules with a wide variety of chemical modifications, or learn about our capabilities for long RNA oligos, dye labelling, and custom amidites.

### Custom CRISPR guide RNA design & synthesis

Design and order custom CRISPR guide RNA for alternative species or nucleases, or for site specific editing.

### Preclinical & midscale synthesis

Our preclinical/OEM manufacturing service provides cost-effective and timely oligonucleotide materials for novel research (*in vitro*) through preclinical use (*in vivo*).

### siRNA synthesis

No predesigned product to fit your needs? Use our online design tools and extensive synthesis options to create a custom siRNA specific for our application. Numerous combinations of modifications, sizes, and purification options are available for convenient online ordering.

### microRNA synthesis

Modify an existing microRNA mimic or inhibitor, target a novel microRNA, or request an miRIDIAN microRNA inhibitor or mimic for special applications. Multiple scales and processing options are available, as well as a wide variety of 5′ and 3′ modifications.

# Dharmacon custom oligo synthesis

## Flexibility to meet your needs

### Need a straightforward method for reducing human, mouse or rat gene function?

Get started with predesigned siRNA, shRNA, or CRISPR guide RNA for guaranteed results. Or skip the editing altogether with premade stable knockout Hap1 cell lines.

### Working in an uncommon species?

Use our custom siDesign or CRISPR design tool to find and order the best sequences for your experiment.

### Have your own sequence?

Upload them directly to our CRISPR design tool, custom siRNA tool, or custom microRNA tool for rapid quote and ordering.

### Need a long or uniquely modified oligo? Or interested in plating custom products?

Use our ssRNA ordering tool or contact us to get started.

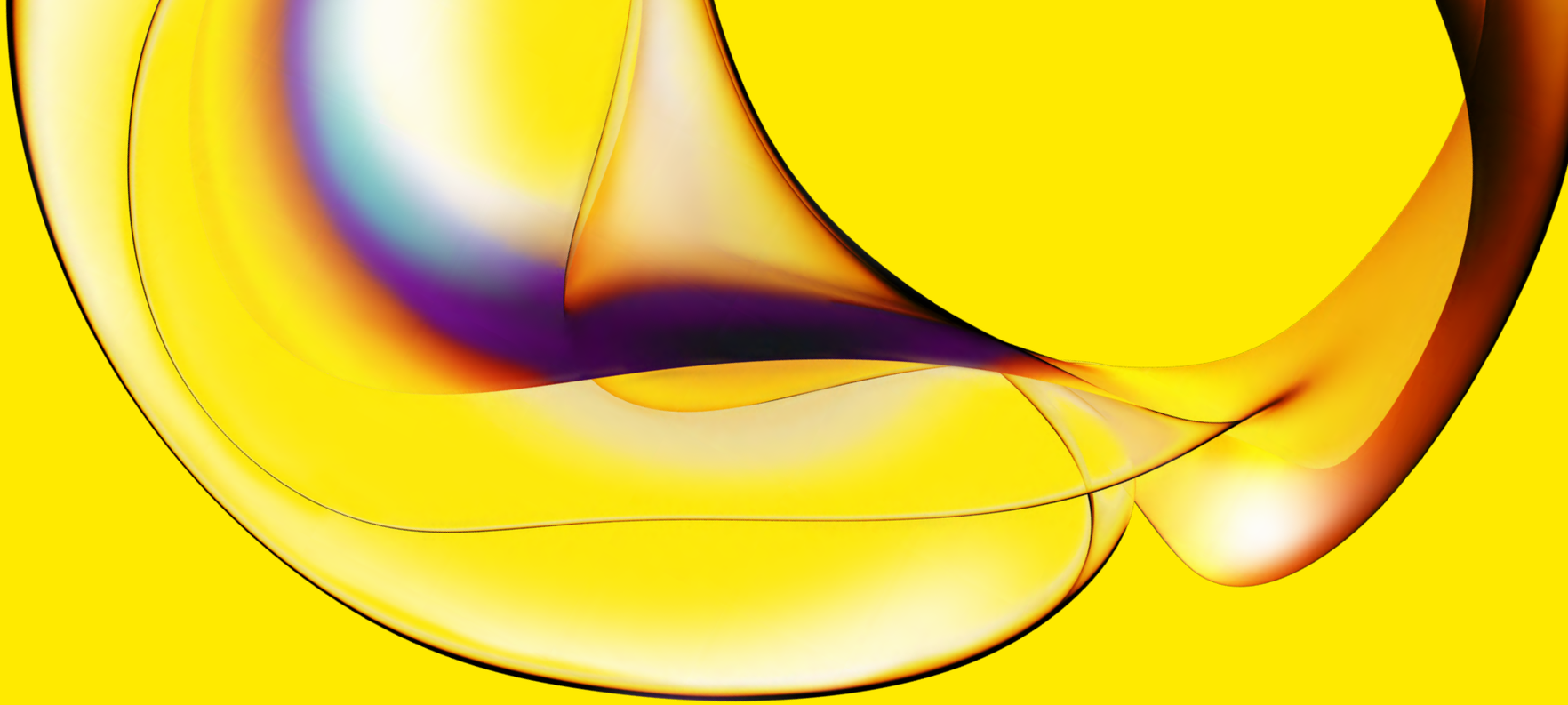
## Scalability to fit any sized project

### Interested in probing a group of genes?

Use our Cherry-pick custom library design tool to build your own mini-screening library.

### Planning to scale-up to a larger functional genomic screen?

See our predesigned gene family, pathway or whole genome libraries or contact us to discuss outsourcing your project with our expert screening team.



**www.revvity.com**

**Revvity**
940 Winter Street, Waltham, MA 02451 USA
(800) 762-4000 | www.revvity.com

**For a complete listing of our global offices, visit www.revvity.com**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