# invitrogen



Discover the only complete genome editing solution designed to expedite your research. Our easy-to-use, optimized, and validated solutions span the entire cell engineering workflow, making genome editing accessible to anyone at any level. We're continually expanding our suite of genome editing products to span the entire cell engineering workflow, from reagents for cell culture, transfection, and sample preparation to kits for genome modification and detection and analysis of known genetic variants. We offer our state-of-the-art online Invitrogen<sup>™</sup> CRISPR Search and Design Tool along with Invitrogen<sup>™</sup> CRISPR-Cas9 editing products in four formats: an all-in-one expression vector, Cas9 mRNA, Cas9 protein, and CRISPR library services. These gene editing solutions are paired with optimal cell culture reagents, delivery methods, and analysis tools, based on your application and cell type.

#### The perfect pairing

We've paired the CRISPR-Cas9 format and delivery methods\* to help ensure the highest efficiencies.



GaneArt CRISPR protein



Invitrogen<sup>™</sup> Lipofectamine<sup>™</sup> CRISPRMAX<sup>™</sup> Transfection Reagent

\*For the most efficient transfection of primary cells, stem cells, and difficultto-transfect cells, use the Invitrogen<sup>™</sup> Neon<sup>™</sup> Transfection System.

Not sure which CRISPR-Cas9 format to use? Go to **thermofisher.com/genomeeditselect** to view our new selection guide.





## Complete suite of CRISPR-Cas9 genome editing tools

#### Choose the optimized and validated toolset that's right for you, and bypass the trial and error.

	CRISPR protein	CRISPR mRNA	CRISPR plasmid	CRISPR libraries	
Product name	GeneArt Platinum Cas9 Nuclease	GeneArt CRISPR Nuclease mRNA	GeneArt CRISPR Nuclease Vector	GeneArt CRISPR Arrayed Libraries	
gRNA design	Use the GeneArt CRISPR Search and Design Tool for optimal design and minimal off-target effects. Go to thermofisher.com/crisprdesign				
gRNA synthesis	GeneArt Precision gRNA Synthesis Kit	GeneArt Precision gRNA Synthesis Kit	DNA oligo cloned into plasmid		
Reporter-based enrichment	Sold separately as the GeneArt Genomic Cleavage Selection Kit	Sold separately as the GeneArt Genomic Cleavage Selection Kit	✓ Included; all-in-one expression plasmid		
No promoter constraint	$\checkmark$	$\checkmark$	CMV promoter		
Ready-to-use	$\checkmark$	$\checkmark$	Requires cloning step	Ready-to-use lentiviral particles	
No random integration concern	$\checkmark$	$\checkmark$	Concern; plasmid stays within the cell longer	Stable expression of CRISPR-Cas9 system	
Controlled dosage	$\checkmark$	$\checkmark$			
Fast turnover	$\checkmark$	$\checkmark$			
Microinjection-ready	$\checkmark$	$\checkmark$	Larger payload size		
Multiplexing and screening capable	$\checkmark$	$\checkmark$	Larger payload size	High-throughput screening	
Ready-to-act, stable RNP complex	$\checkmark$				
Modification options	Knockout and knock-in	Knockout and knock-in	Knockout and knock-in	Loss-of-function screening	
Delivery method	Lipofectamine CRISPRMAX reagent	Lipofectamine MessengerMAX reagent	Lipofectamine 3000 reagent		

CRISPR-Cas9 genome editing-leading in engineering, inspiring design, and empowering discovery.



### CRISPR protein-the most talked-about genome editing tool

#### Maximum efficiency, minimal off-target cleavage

Invitrogen<sup>™</sup> GeneArt<sup>™</sup> Platinum<sup>™</sup> Cas9 Nuclease is wild type Cas9 in protein format. Cas9 protein and guide RNA (gRNA) form a very stable ribonucleoprotein protein (RNP) complex that provides the next level of cleavage efficiency over CRISPR-Cas9 vector and mRNA systems. The Cas9 RNP complex can act immediately after it enters the cell, since transcription and translation are not required. It is rapidly cleared from the cell, minimizing the chance for off-target cleavage events, compared to vector-based systems (Figure 1). The Cas9 protein is microinjection-ready with 3 nuclear localization signals (NLS). Design to analysis is possible in just 4 days. For a complete set of data that illustrate cutting efficiencies by cell line and delivery method, download our latest publication, "Rapid and highly efficient mammalian cell engineering via Cas9 protein transfection", at thermofisher.com/crisprprotein. Examples of the use of Cas9 are shown in Figure 2.



Figure 2. Genome editing of human stem cells with the GeneArt Cas9/gRNA RNP. Gibco<sup>™</sup> human iPSCs and H9 ESCs were transfected in triplicate with GeneArt Cas9/gRNA ribonucleoprotein (RNP) complex, and target sites were analyzed for cleavage using the Invitrogen<sup>™</sup> GeneArt<sup>™</sup> Genomic Cleavage Detection Kit 48–72 hours posttransfection. (See "Detection and analysis reagents".)





### CRISPR mRNA

#### Versatile and simple-to-use Cas9 mRNA format

Invitrogen<sup>™</sup> GeneArt<sup>™</sup> CRISPR Nuclease mRNA is wild type, capped, and polyadenylated Cas9 mRNA. This format is ready to transfect along with gRNA (Figure 3), and allows multiplex genome editing, where multiple target gene sequences can be edited simultaneously in a single transfection reaction with the addition of multiple gRNAs.



### CRISPR plasmid

#### All-in-one expression vector system

Invitrogen<sup>™</sup> GeneArt<sup>™</sup> CRISPR Nuclease Vector Kits offer an all-in-one expression vector consisting of both a Cas9 nuclease expression cassette and gRNA cloning cassette, for simple and efficient cloning of a double-stranded DNA oligo encoding a target-specific crRNA.

### **CRISPR** libraries

CRISPR libraries are emerging as the next-generation tool for high-throughput functional genomics screening. We recently introduced the first-ever Invitrogen<sup>™</sup> GeneArt<sup>™</sup> Arrayed CRISPR Libraries for screening applications.

These libraries come in an arrayed format, which is compatible with existing screening platforms (96- and 384well formats are available).

# B % of cleaved band 0 0 78.3 65.7

**Figure 3. Cas9 nuclease mRNA functions robustly in iPSCs when used under the right conditions.** CRISPR mRNA was transfected along with *in vitro* transcribed (IVT) gRNA using Lipofectamine MessengerMAX Transfection Reagent. Editing efficiency on the *HPRT* locus was determined by a cleavage assay using the GeneArt Genomic Cleavage Detection Kit 72 hours posttransfection. (A) iPSCs grown in feeder-free conditions. (B) iPSCs grown on feeder cells and made feeder free prior to transfection.

#### Search, design, and order

So simple, so easy-check it out for yourself.

The GeneArt CRISPR Search and Design Tool provides instant access to over 600,000 predesigned CRISPR gRNAs targeting human and mouse genes. Or you can analyze your



#### Invitrogen<sup>™</sup> GeneArt<sup>™</sup> Precision gRNA Synthesis Kit —a complete system for rapid synthesis of gRNA Get transfection-ready gRNA in

as little as 4 hours.



sequence of interest for *de novo* gRNA designs using our proprietary algorithms for minimal off-target effects. Once you've selected the optimal gRNA designs, you may purchase your gRNAs and other recommended products directly from the web tool; it's that easy.

### Detection and analysis reagents

# Essential tools for monitoring the efficiency of your genome editing experiments

#### GeneArt Genomic Cleavage Selection Kit

A quick method for screening the functionality of nuclease cleavage with enriching capabilities.

- Screen—for functionality of engineered nucleases as early as 24 hours posttransfection using fluorescence standard microscopy
- Enrich—for modified cells using fluorescence-activated cell sorting (FACS) or Invitrogen<sup>™</sup> Dynabeads<sup>™</sup> CD4 Magnetic Beads

#### GeneArt Genomic Cleavage Detection Kit

A quick, simple, and reliable method for detecting and quantifying locus-specific double-strand breaks (Figure 4).

- Easy—with direct PCR amplification, there's no need for genomic DNA isolation
- Rapid-5-hour total processing time
- Quantitative—gel band density is directly correlated to target indel introduction



# CRISPR engineered cell lines and engineering services

# Designer cell lines to accelerate your research

We now offer both off-the-shelf engineered cell lines and custom design and engineering services to deliver the cell lines you need with high-quality and dedicated service.

#### Engineered cell models

Discover the world's largest collection of ready-to-go CRISPR engineered cell lines. Accelerate your research and search for your engineered cell line at **thermofisher.com/** engineeredcells

#### Cell line engineering services

We collaborate with you as partners to accelerate your discovery. Our premier design and engineering concierge will help you from start to finish. Get started with your custom engineered cell line at **thermofisher.com/genomeedit** 

Figure 4. Comparison of the GeneArt Genomic Cleavage Detection Kit with a competitor kit. (A) With the competitor's kit, the expected 620 bp product is not observed on the gel; 10  $\mu$ L of the 50  $\mu$ L PCR was loaded on the gel. (B) The GeneArt Genomic Cleavage Detection Kit results show a visible and specific product at the expected 620 bp mark; 3  $\mu$ L of the 50  $\mu$ L PCR was loaded on the gel. Data courtesy of BioMarin Pharmaceuticals Inc.

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#### **Ordering information**

Product		Quantity	Cat. No.
CRISPR protein	GeneArt Platinum Cas9 Nuclease	25 µg	B25640
	GeneArt Platinum Cas9 Nuclease	75 µg	B25641
CRISPR mRNA	GeneArt CRISPR Nuclease mRNA	15 µg	A29378
	GeneArt Strings U6 DNA	>200 ng	Contact geneartsupport@lifetech.com
	GeneArt Strings T7 DNA	>200 ng	Contact geneartsupport@lifetech.com
	Custom in vitro transcribed gRNA	250 nmol	Contact geneartsupport@lifetech.com
CRISPR plasmid	GeneArt CRISPR Nuclease Vector: OFP Reporter	10 reactions	A21174
	GeneArt CRISPR Nuclease Vector: OFP Reporter with Competent Cells (Combo)	10 reactions	A21178
	GeneArt CRISPR Nuclease Vector: CD4 Enrichment	10 reactions	A21175
	GeneArt CRISPR Nuclease Vector: CD4 Enrichment with Competent Cells (Combo)	10 reactions	A21177
CRISPR-Cas9 gRNA	GeneArt Precision gRNA Synthesis Kit	25 reactions	A29377
CRISPR libraries	Visit thermofisher.com/crisprlibraries for details.		
CRISPR engineered cell lines	Visit <b>thermofisher.com/engineeredcells</b> to search our collection of over 14,000 pre-engineered cell lines.		
Detection and analysis reagents	GeneArt Genomic Cleavage Detection Kit	20 reactions	A24372
	GeneArt Genomic Cleavage Selection Kit	10 reactions	A27663

Get everything you need to design, deliver, and engineer—all in one place. Learn more at **thermofisher.com/genomeedit** 



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