

# Tips and tricks for CRISPR-Cas9 success

The discovery of CRISPR-Cas9 gene editing technology completely transformed life science research in 2012 by introducing a precise and efficient “cut-and-paste” tool for inserting or removing portions of DNA.

## CRISPR-Cas9 best practices

Set yourself up for success with these expert tips for each stage of the CRISPR-Cas9 workflow.



### Use optimal gRNA design

Design and test 3 guide RNAs (gRNAs) for every target to help maximize editing efficiency for a greatly increased chances of success.



### Select most efficient delivery method for your cells

Based on your specific cell types, select the best delivery method: lipid-mediated transfection, electroporation, or viral transduction.



### Confirm and validate editing efficiency

Confirm cleavage efficiency with a genomic cleavage detection (GCD) assay or validate edits using other sequencing methods such as next-generation sequencing and Sanger sequencing.

### Pro tip



#### Try this

Achieve higher editing efficiency and fewer off-target effects by circumventing transcription and translation. Instead of using Cas9-expressing plasmids, opt for direct transfection of purified Cas9 protein and synthetic gRNA delivery.

## Troubleshooting common CRISPR-Cas9 challenges

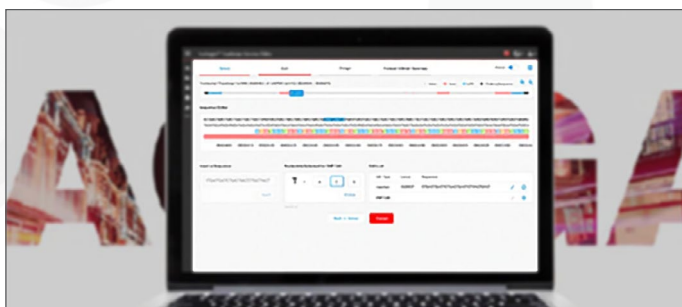
Having trouble? You're not alone—here are a few of the most common hurdles researchers face when using CRISPR and how to handle them.



### Low editing efficiency



Opt for purified Cas9 protein, like [Invitrogen™ TrueCut™ Cas9 Protein v2](#), that's engineered for the highest editing efficiency (>90%).



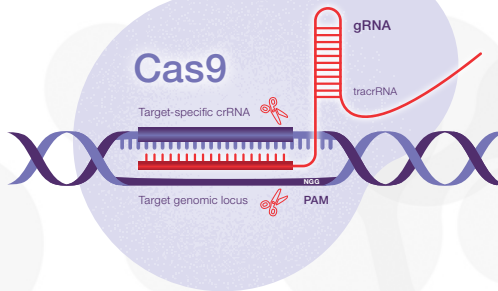
Design and test 3 gRNAs for every target to help maximize editing efficiency. Leverage software tools, like the [Invitrogen™ TrueDesign™ Genome Editor](#), to design the most optimal gRNA for your intended gene target and cell types.

Use an optimized delivery system, like the [Invitrogen™ Lipofectamine™ CRISPRMAX™ Transfection Reagent](#), to efficiently deliver your editing tool (Cas9 and gRNA) to your cells.



### Off-target effects

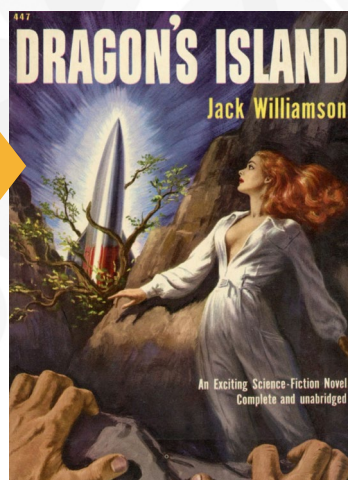
Minimize off-target effects by carefully designing your CRISPR gRNA and avoid homology with other regions in the genome.



Use a synthetic gRNA and a high-fidelity Cas9 protein like [Invitrogen™ TrueCut™ HiFi Cas9 Protein](#) to further reduce off-target effects.

## Did you know?

It was science fiction writer Jack Williamson who first popularized the term “genetic engineering” in his 1951 novel, *Dragon's Island*, two years before Watson, Crick, and Franklin revealed the double helix structure of DNA and more than 70 years before CRISPR made precise gene editing possible in 2012.



### Additional CRISPR tools and resources

To access additional resources like our comprehensive genome editing resource guide, validated protocols, and technical support, visit [thermofisher.com/crispr101](https://thermofisher.com/crispr101)

For more quick guides with tips and tricks to popular protocols, subscribe to [Connect to Science](#).

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