



## How gene synthesis and protein services can help get your therapeutic to market faster

In therapeutic research areas such as chimeric antigen receptors (CARs) for T cell therapy, therapeutic monoclonal antibody production, or SARS-CoV-2 DNA or protein vaccines, the fast and reliable production of DNA is critical.

When DNA sequences are required for the purpose of protein production, low yield poses a significant challenge for biotech companies seeking to accelerate their path to the clinic—that's in addition to the hurdles that accompany the potential need to obtain template DNA from harmful or infectious agents. Factors that can contribute to low protein yield include sequence complexity and length, very high or low GC content, direct or indirect repeats, and long polypurine or polypyrimidine runs.

A traditional PCR-based approach to generating DNA requires many hands-on steps that can be time consuming, and requires downstream cloning and plasmid preparation.

Even with an optimized sequence in hand, the classic cloning workflow poses further challenges to the therapeutic development workflow, with its many steps from PCR amplification to plasmid preparation (Figure 1).

### Benefits of using synthetic DNA

Custom gene synthesis circumvents the limitations of PCR-based workflows. With this technique, synthetic biology has made it possible to reliably, safely, and cost-effectively obtain customized DNA constructs with 100% verified sequence accuracy.

A typical gene synthesis workflow begins online, with the design of a DNA construct using online tools or software. The resulting sequence is then broken up into smaller overlapping pieces (typically 200–1,500 bp) that are easier to synthesize from oligonucleotides. The pieces are then assembled and cloned into a vector (basic delivery of gene or expression vector) and the sequence verified.

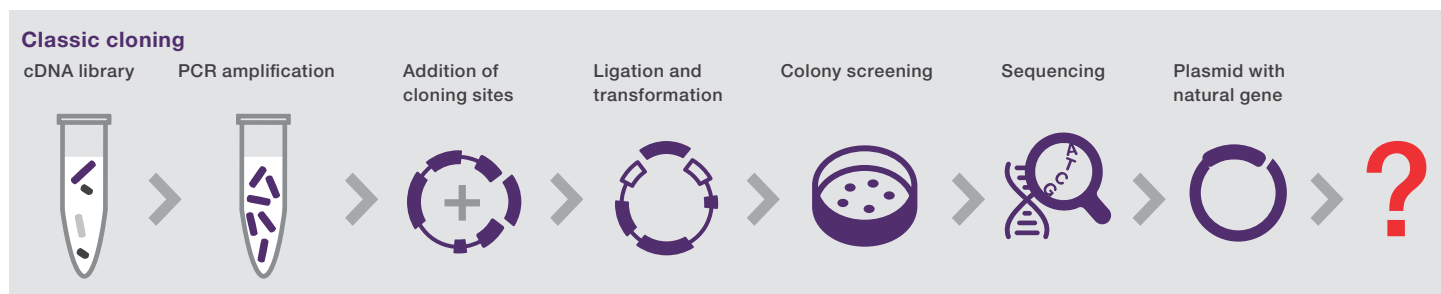


Figure 1. Traditional PCR and cloning workflow.

Advantages of custom gene synthesis for the therapeutic development workflow include:

- **Eliminates steps, saving valuable time**—the corresponding natural DNA is not required; start with just an electronic sequence
- **Higher downstream protein yield**—the computer-based design process allows for precise sequence design and optimization via an algorithm, which ultimately results in higher expression levels and easier purification of the final product, compared to classic cloning (see gene optimization)
- **Vector flexibility**—choose to receive your genes in your own custom vector, or select from a library of expression vectors

These advantages, along with the convenience of customizable gene synthesis services, can afford biotech companies a significant edge and accelerate getting a novel therapeutic to market.

## Count on connections to help you realize the benefits of gene optimization

Invitrogen™ GeneArt™ Gene Synthesis services were designed to tackle sequences both simple and complex. Our peer-reviewed GeneOptimizer algorithm utilizes a multifactorial approach (up to 20 parameters) beyond just traditional codon optimization, to significantly improve protein expression when it comes wild-type protein—crucial especially for monoclonal antibody development research [2] (Figure 2). You have the option to choose from more than 30 available expression vectors or upload your own to our easy-to-use online portal.

You can also outsource your entire workflow with GeneArt Gene-to-Protein Services. Starting with an electronic nucleotide sequence, you can receive highly purified protein in expression systems such as mammalian and insect. These GeneArt services leverage highly advanced Gibco transient expression systems and, coupled with gene optimization, provide a complete, hands-off solution to protein production and purification.



**Watch this webinar to learn more about the end-to-end process of our gene-to-protein services**



Figure 2. Gene optimization with the GeneOptimizer algorithm significantly increases protein production.

### References

1. Hughes RA, Ellington AD (2017) Synthetic DNA Synthesis and Assembly: Putting the Synthetic in Synthetic Biology. *Cold Spring Harb Perspect Biol* 9(1):a023812.
2. Raab D, Graf M, Notka F et al. (2010) The GeneOptimizer Algorithm: using a sliding window approach to cope with the vast sequence space in multiparameter DNA sequence optimization. *Syst Synth Biol* 4(3):215-225.

The full suite of Thermo Fisher Scientific DNA and protein services offers researchers the unique opportunity to get their novel therapeutic into the clinic faster.

**Find the right custom service to fit your gene synthesis needs**