# Novel, synthetic DNA templates for the production of mRNA

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The manufacture of high-quality, GMP grade DNA is a major bottleneck in the production of mRNA for use in gene therapy and vaccines. In addition to worldwide lack of capacity and long lead times, complex sequences such as long homopolymeric sequences including long polyA tails are difficult to propagate in bacteria.

4basebio has developed a proprietary, scalable, fully enzymatic synthesis process for the production of linear DNA constructs via our Trueprime™ amplification technology. The process yields DNA at 1g/L, several orders of magnitude higher than plasmid fermentation yields, allowing a small footprint using benchtop equipment.

The process is size and sequence independent, allowing for large scale production of linear DNA with high yield and purity in less than a week. Unlike plasmid DNA, 4basebio DNA eliminates contamination from endotoxins or host proteins, and excludes bacterial sequences such as antibiotic resistance genes. Complex sequences including ITRs and homopolymeric sequences are easily produced without risk of deletion or recombination.

Currently, we make 4 types of DNA, each with unique application-specific benefits. For mRNA production, opDNA™ can be used directly in IVT processes, without the need for enzymatic linearisation. Using opDNA™, we were able to achieve significantly higher mRNA yields as compared to linearised plasmid, with equivalent capping efficiency and dsRNA impurities. Proinflammatory cytokine/chemokine levels in isolated primary, human PBMCs are comparable to mRNA produced from linearised plasmid, with equivalent protein expression both in vitro and in vivo.

We have demonstrated that opDNA™ templates can be used for the production of IVT mRNA. Moreover, the technology could overcome the difficulties associated with complex polyA tails for mRNA constructs, which are inherently difficult to synthesise via bacterial propagation systems. The combination of 4bb mRNA and Hermes™ non-viral delivery platform can greatly accelerate the therapeutic development of gene therapy and vaccine programmes.