Learn How
Gene Editing Delivery Platform Development

The new synthesis: How synthetic DNA technology is transforming drug discovery

Dr Ellie Ashby, Editor-in-Chief, Drug News, Opinion | Tagged Biologics | Biotechnology, Cell and gene, DNA, Drug development, Drug discovery, Genome editing, Genome engineering, Synthetic biology, Vaccines, Vaccine development

28 May, 2022

Share
Print
Email
Comments (0)
Text size
Font

Synthetic DNA technology is transforming drug discovery, from the design of novel therapeutics to the development of vaccines and gene therapies. This article explores how advances in gene synthesis are accelerating drug development, improving precision in genetic engineering, and enabling the creation of next-generation biologics.

Synthetic DNA technology has been growing at the speed of biotechnology. Gene synthesis costs have dropped from over $10 per base pair in the early 2000s to under $0.01 per base pair today, while synthesis times have shrunk from weeks to days. Synthetic DNA technology is now being used to design novel therapeutics, develop vaccines, and engineer cells for cell and gene therapy. This article explores how advances in gene synthesis are accelerating drug development, improving precision in genetic engineering, and enabling the creation of next-generation biologics.

Leading back

Historically, drug discovery has relied largely on chemical libraries of small drug-like molecules, hoping to find a compound providing the desired effect. The rise of biologics, mRNA vaccines, and gene therapies has shifted the industry's focus toward precision medicine. Synthetic DNA technology is contributing to combinatorial and rational chemistry approaches, where additions or modifications to a molecule can be made by ordering a new DNA sequence rather than redesigning a molecule from scratch.

While this has worked in many cases, the ongoing pipeline of pharmacological compounds emerging is showing truly novel mechanisms of action, such as molecular glues and proteolysis targeting chimeras (PROTACs), which are challenging to rationally design and optimise, and will require more complex chemistry.

High-throughput screening is still used to hunt for initial promise. The success of this approach is dependent on the quality of the chemical libraries being screened. Synthetic DNA technology is being used to create more diverse and precisely designed libraries, increasing the chance of finding hits that have the right properties.

The deeper biological understanding has led to a transition from the 'one drug, one target, one disease' approach pioneered by Paul Ehrlich centuries ago. It is now widely recognised that most diseases are complex, involving many genes and pathways. Biologics have shown potential to treat some of these diseases, but are challenging to that every gene high-throughput screening approach.

Instead focus may a synthetic biologist approach to drug discovery include the breakthrough finding that immunogenicity and toxicity are not inherent properties of a molecule but rather a consequence of its sequence. Using synthetic DNA, researchers can systematically scale up promising leads and optimise them for better performance. This early-to-first-in-man and scale-up bottleneck is being AI-drug discovery, creating new chemical synthesis with unfavourable properties that increase the chance of failure in clinical trials.

The potential scope of synthetic biology is not just to improve on old techniques but to think of drug discovery in a new light. Synthetic DNA technology is being used to design novel therapeutics, develop vaccines, and engineer cells for cell and gene therapies. Researchers are also using it to produce non-antibiotic antimicrobials, such as AMPs. This early-to-first-in-man and scale-up process is growing clinically successful [1,2,3,4,5]. However, the time-lifting only currently promising these approaches from exciting discoveries to clinical reality is being shortened by the ability to rapidly design, test, and scale up DNA sequences.

Synthetic DNA in cell and gene therapy

The gene technologies for synthetic DNA today rely on plasmid-derivative synthesis, a chemical method first established in the 1980s. The process ideally yields a single, perfect sequence, but in reality, it often results in a mixture of errors. While relatively efficient, the reaction requires a large supply of complex chemicals that makes synthesis costly and environmentally wasteful. The process is also limited by the length of the synthesised DNA, with longer sequences increasing the chance of errors and decreasing yield. Nucleic acids, Building longer DNA strands, such as full plasmids, therefore, requires stitching together shorter, error-free fragments.

It is also challenging to create certain types of DNA using this process, such as palindromic sequences [6]. Or DNA sequences that form secondary structures, such as hairpins or G-quadruplexes, which can stall the process. These difficult sequences are a significant obstacle in gene therapy and synthetic biology, as they can be crucial for regulating gene expression, for example, or for tumour suppression genes, transforming genes and wound 40% of tissue specific genes [7]. Incomplete DNA synthesis can also lead to the production of truncated or mutated proteins, which can be problematic for therapeutics, efficacy, and safety.

Rather than iteratively improving current technologies, the next generation of DNA synthesisers is creating a paradigm shift in how DNA is made. Instead of relying on chemical processes, these new systems are being engineered to mimic biological processes with greater precision and efficiency. Researchers are exploring enzymatic DNA synthesis, where DNA polymerases are used to add nucleotides without the need for drive consuming and costly complex and synthesis steps and processes, such as cloning, screening and sequencing. The end result is a high quality and high-fidelity DNA sequence produced in a more sustainable manner.

As well as solving so problematic of accuracy, long strands of DNA through predetermined, the silicon chip approach also offers a significant boost in speed. The ability to synthesise longer, error-free DNA sequences directly from digital blueprints is a game-changer for drug discovery and synthetic biology, enabling the creation of more complex therapeutics and genetic circuits.

Beyond hardware, there are applications from high-throughput science to the rapid evolution and prototyping of new gene therapy pathways and therapeutics. Synthetic biology-enabled approaches are being used to develop novel therapeutics designed to rapidly approximating including LNP, CRISPR guides, vaccines and extracellular RNA.

The coming years of rapid, scalable, accessible DNA synthesis offers exciting opportunities for researchers working in drug discovery and biotechnology.

Library generation and screening

Every drug discovery campaign begins with the traditional drug discovery process by generating libraries of genetically encoded molecules. Synthetic DNA technology is being used to create these libraries, with the goal of making them more diverse, more precisely designed, and more efficiently produced. This enables researchers to cast a wider net in their identification and characterisation more straightforward, particularly in combination with DNA barcoding. One successful example comes in the form of DNA-encoded chemical libraries (DECL), where each molecule is tagged with a unique DNA barcode that allows for the identification of hits through high-throughput sequencing and polymerase-mediated.

Beyond by-bases, DNA elements are both synthetically enhanced forms the scale for an only assembling. Gene constructs is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing. The end result is a high quality and high-fidelity DNA sequence produced in a more sustainable manner.

From the ability to create synthetic gene circuits to evolving and screening enzymes for therapeutic use, arrows to target molecules, synthetic DNA is being used to unlock drug discovery pathways that were previously out of reach. Researchers are using it to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing. The end result is a high quality and high-fidelity DNA sequence produced in a more sustainable manner.

Genome engineering

Gene editing has been a game-changer for drug discovery, enabling researchers to rapidly modify the genome of cells and organisms. Synthetic DNA is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing. The end result is a high quality and high-fidelity DNA sequence produced in a more sustainable manner.

CRISPR and other gene editing tools require the production of guide RNAs, which are created from DNA templates. It is also being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing. The end result is a high quality and high-fidelity DNA sequence produced in a more sustainable manner.

Opportunities for novel therapeutics

Being with the ability to be better research in the pursuit of novel drugs, synthetic DNA technology also has a more direct role to play in the therapeutic area.

Gene and cell therapies

The most obvious application here is DNA itself, in the form of gene therapy, which is being investigated for a wide range of diseases, including cancer, rare and inherited disorders, and infectious diseases. Synthetic DNA technology, such as high purity plasmid nanopartices, and gene editing tools like CRISPR, the ability to simply synthesise DNA to order opens the door to more efficient and cost-effective manufacturing processes.

Therapeutics like mRNA vaccines, from the first authorisation in Hungary, which used synthetic DNA to produce the mRNA, specifically tend to targets from inorganic molecules to large protein complexes or even whole cells, with significant potential for treating complex diseases. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Cell therapies are a promising modality for currently incurable or hard-to-treat diseases and personalised therapies, with approximately 1,000 clinical trials currently ongoing. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

A trance of quickly producing CAR T cells would be of huge benefit and allow faster research into effective means of using CAR T cells against solid tumours, for example. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Antibodies are an attractive option for so-called 'undruggable' targets, which lack a binding pocket typically required for small molecule drugs. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Antibiotics, enzymes and molecular therapeutics

Not only are antibiotics beneficial tools in detection assays and diagnostics tests, but they are also a major drug target. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Diagnostics

Finally, synthetic DNA has a number of applications in the sphere of diagnostics. PCR-based tests for pathogens rely on oligonucleotide DNA primers. The experience of the COVID-19 pandemic has shown that being able to rapidly synthesise primers for new variants is crucial for the rapid development of diagnostic tests. Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control.

Synthetic DNA technology is being used to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, to optimise gene expression and control. Synthetic DNA technology is also being used to create libraries of synthetic antibodies and other proteins, such as cloning, screening and sequencing.

Looking forwards

The rise of synthetic DNA technology has been a transformative development, enabling researchers to rapidly design, synthesise, and test DNA sequences with unprecedented speed and precision. This has accelerated the pace of drug discovery, enabling the creation of novel therapeutics, vaccines, and diagnostics that were previously out of reach. The ability to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, has also enabled researchers to optimise gene expression and control, leading to the development of more efficient and cost-effective manufacturing processes.

The ongoing development of synthetic DNA technology is expected to further accelerate the pace of drug discovery, enabling the creation of more complex therapeutics and genetic circuits. The ability to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, will be crucial for the development of personalised medicine and gene therapies, as it will enable the creation of tailored therapeutics that are designed to target specific genetic mutations or disease mechanisms.

The ongoing development of synthetic DNA technology is also expected to have a significant impact on the manufacturing of biologics, such as vaccines and gene therapies. The ability to create libraries of genetic elements, such as promoters, enhancers, and regulatory sequences, will be crucial for the development of more efficient and cost-effective manufacturing processes, as it will enable the creation of tailored therapeutics that are designed to target specific genetic mutations or disease mechanisms.

The ongoing development of synthetic DNA technology is also expected to have a significant impact on the diagnostics market, as it will enable the creation of more sensitive and specific diagnostic tests, leading to the development of more effective and cost-effective diagnostic tests for a wide range of diseases and conditions.

Volume 23, Issue 2 > Spring 2022

2070-PCB-0002-b
evonetix

About the author

Dr Ellie Ashby, Editor-in-Chief, Drug News, Opinion | Tagged Biologics | Biotechnology, Cell and gene, DNA, Drug development, Drug discovery, Genome editing, Genome engineering, Synthetic biology, Vaccines, Vaccine development

Sign Up Free
Sign In
Subscribe Free
Subscribe Free
Sign In
Sign Up
Terms and Conditions
Privacy Policy
Contact Us
About Us
Subscribe FREE
Media Info
Events Sign Up
Log In
Terms and Conditions
Privacy Policy
Follow our social accounts
Sitemap
Sitemap
Sitemap