DNA Synthesis – An Integral Force in the Founding and Future of Precision Medicine

By Emily Leproust

Introduction

Synthetic DNA is intricately woven into the fabric of precision medicine. DNA synthesis is the process of creating short DNA strands of a defined sequence, typically using nucleoside chemical reagents. The commercialization of DNA synthesis in the 1980s put synthetic DNA into the hands of biologists, providing them with the raw material for key technologies such as polymerase chain reaction (PCR) and DNA sequencing. These technologies led to the sequencing (and resequencing) of the human genome, ushering in the era of precision medicine – a form of healthcare that uses genetic information to guide patient care towards more effective treatment modalities.

As with the microchip (see **Inset 1**), continual innovation has made DNA synthesis technology more efficient, accurate, and scalable. These advances have made it possible to fabricate large pools, or libraries, of oligonucleotides *en masse* for use in high-throughput screening technologies, including DNA microarrays and functional genomic screens; targeted sequencing; and antibody discovery. These technologies have offered deeper insights into human disease genetics while enabling the engineering of "magic bullet" therapeutics.

This article unravels the intertwined history of synthetic DNA and precision medicine (**Figure 1**). Focusing on therapeutic antibody discovery and development, this article discusses how the advent of DNA synthesis technology expanded the biopharmaceutical discovery space. We conclude with a perspective on how modern DNA synthesis is writing the future of precision medicine.

We cover in this article:

- The intertwined history of DNA synthesis and precision medicine
- Key technologies that enabled modern precision medicine
- Twist Biopharma's capabilities in antibody discovery

From double helix to experimental commodity

Three criteria needed to be met for synthetic DNA to become an experimental commodity. First, an approach needed to be developed for chemically coupling the four unique DNA bases* with high yield. Second, the speed at which DNA could be synthesized needed to be increased substantially. Finally, the method needed to be automatable to make it readily accessible to biologists (Caruthers 2011).

Early synthetic DNA chemistries failed to meet these criteria. In the late 1960s, the phosphodiester and phosphotriester chemistries developed by Khorana and Letsinger, respectively, required months to years of effort to synthesize a quantity of a 10 base oligo (10-mer) of a defined DNA sequence of sufficient quality for experimental purposes. The next iteration, Letsinger's phosphite triester approach, came in 1975, and fulfilled the first two criteria (efficiency and speed) but failed the third (automation) because it required the use of highly unstable intermediates.

The third criteria was finally met with two innovations from the Caruthers laboratory, originally published in 1979. First, a small tweak to the synthesis intermediates improved their stability.

1953
Watson & Crick solve the structure of DNA with help from Franklin & Wilkins

WATSON JD, CRICK FH. Molecular structure of nucleic acids; a structure for deoxyribose nucleic acid. Nature. 1953 Apr 25;171(4356):737-8. doi: 10.1038/171737a0. PMID: 13054692.

1955
Michelson and Todd publish the first chemical synthesis of DNA (phosphotriester method)

Michelson AM, Todd AR. (1955) J. Chem. Soc., 2632.

1956
Har Gobind Khorana publishes the phosphodiester method of oligo synthesis

P. T. Gilham and H. G. Khorana. Studies on Polynucleotides. I. A New and General Method for the Chemical Synthesis of the C5′-C3″ Internucleotidic Linkage. Syntheses of Deoxyribo-dinucleotides1. J. Am. Chem. Soc. 1958, 80, 23, 6212–6222

1959
Gerald Edelman and Rodney Porter independently publish the molecular structure of antibodies

Edelman, G.M. (1959). Dissociation of γ-globulin. Am. Chem. Soc. 81, 3155–3156.

Porter, R.R. (1959). The hydrolysis of rabbit γ-globulin and antibodies with crystalline papain. Biochem. J. 73, 119–126.

1965
Robert Letsinger adapts the concept of solid-phase synthesis to oligos

Letsinger RL, Mahadevan V. (1965) J. Am. Chem. Soc. 87(15), 3526-7.

1969
Letsinger publishes the phosphotriester method of oligo synthesis

Letsinger, RL.; Ogilvie, KK. Nucleotide chemistry. XIII. Synthesis of oligothymidylates via phosphotriester intermediates. J Am Chem Soc. 1969 Jun; 91(12): 3350. doi:10.1021/ja01040a042.

1972
Khorana & colleagues describe the assembly of the first synthetic gene from synthetic oligos

Khorana HG, Agarwal KL, Buchi H, Caruthers MH, Gupta NK, Kleppe K, Kumar A, Otsuka E, RajBhandary UL, Van de Sande JH, et al. 1972. Studies on polynucleotides. 103. Total synthesis of the structural gene for an alanine transfer ribonucleic acid from yeast. J Mol Biol 72: 209–217.

1973
Stanley Cohen & Herbert Boyer invent recombinant DNA technology

Cohen, S.; Chang, A.; Boyer, H.; Helling, R. (1973). "Construction of biologically functional bacterial plasmids in vitro". Proceedings of the National Academy of Sciences of the United States of America. 70 (11): 3240–3244.

1975
George Köhler invents hybridoma technology in César Milstein's lab

Köhler, G. & Milstein, C. Continuous cultures of fused cells secreting antibodies of predefined specificity. Nature 256, 495–497 (1975).

1975
Letsinger publishes the phosphite-triester method of oligo synthesis

Letsinger RL, Finnan JL, Heavner GA, Lunsfold WB. (1975) J. Am. Chem. Soc. 97, 3278-9.

1977
Sanger develops Sanger sequencing method

Sanger F; Nicklen S; Coulson AR (December 1977). "DNA sequencing with chain-terminating inhibitors". Proc. Natl. Acad. Sci. U.S.A. 74 (12): 5463–7.

1981
Matteucci and Caruthers describe the use of silica-based supports for solid-phase oligo synthesis

Matteucci MD, Caruthers MH. (1981) J. Am. Chem. Soc. 103, 3185-91.

1981
Caruthers publishes phosphoramidite method of oligo synthesis

Beaucage SL, Caruthers MH. (1981) Tetrahedron Lett. 22, 1859-62.

1983
Kary Mullis et al., invent PCR

Saiki RK, Scharf S, Faloona, Mullis KB, Horn GT, Ehrlich HA, Arnheim Enzymatic amplification of β-globin genomic sequences and restriction site analysis for diagnosis of sickle-cell anemia. Science. 1985;230:1350–4.

1984
Boulianne et al. produce the first chimeric (mouse/human) antibody, a precursor to humanized antibodies

Boulianne GL, Hozumi N, Shulman MJ (1984) Production of functional chimaeric mouse/human antibody. Nature 312:643–646

1986
The first therapeutic mAb muromonab-CD3 (Orthoclone OKT3) enters the market

Kung P, Goldstein G, Reinherz EL, Schlossman SF (1979) Monoclonal antibodies defining distinctive human T cell surface antigens. Science 206:347–349

1989
The first antibody library, generated by PCR

Ward ES, Güssow D, Griffiths AD, et al (1989) Binding activities of a repertoire of single immunoglobulin variable domains secreted from Escherichia coli. Nature 341:544–546

1990
McCafferty et al. invent phage display technology

McCafferty J, Griffiths AD, Winter G, Chiswell DJ (1990) Phage antibodies: filamentous phage displaying antibody variable domains. Nature 348:552–554

1991-1994
Affymetrix invents of array-based oligo synthesis using photolithographic methods

Fodor SPA, Read JL, Pirrung MC, Stryer L, Lu AT, Solas D. Light-directed, spatially addressable parallel chemical synthesis. Science. 1991;251:767–773.

Pease AC, Solas D, Sullivan EJ, et al (1994) Light-generated oligonucleotide arrays for rapid DNA sequence analysis. Proc Natl Acad Sci U S A 91:5022–5026

1993
First semi-synthetic antibody library (using degenerate primers)

Hoogenboom HR, Winter G (1992) By-passing immunisation. Human antibodies from synthetic repertoires of germline VH gene segments rearranged in vitro. J Mol Biol 227:381–388

1995
Stemmer publishes the polymerase cycling assembly method of gene synthesis

Stemmer WP, Crameri A, Ha KD, et al (1995) Single-step assembly of a gene and entire plasmid from large numbers of oligodeoxyribonucleotides. Gene 164:49–53

1999-2001
Nimblegen and LC Sciences develop micromirror-based array synthesis of oligos

Singh-Gasson S, Green RD, Yue Y, et al (1999) Maskless fabrication of light-directed oligonucleotide microarrays using a digital micromirror array. Nat Biotechnol 17:974–978

Gao X, LeProust E, Zhang H, et al (2001) A flexible light-directed DNA chip synthesis gated by deprotection using solution photogenerated acids. Nucleic Acids Res 29:4744–4750

2000
Knappik et al. generate the first fully synthetic antibody library (HuCAL) using trinucleotide-directed mutagenesis

Knappik A, Ge L, Honegger A, et al (2000) Fully synthetic human combinatorial antibody libraries (HuCAL) based on modular consensus frameworks and CDRs randomized with trinucleotides. J Mol Biol 296:57–86

2000
Massively Parallel Signature Sequencing (MPSS) Lynx Therapeutics (USA) Company launched the first of the NGS technologies

2000
A draft of the human genomic sequence is published

2001
Array synthesis of oligos by inkjet printing

Hughes TR, Mao M, Jones AR, et al (2001) Expression profiling using microarrays fabricated by an ink-jet oligonucleotide synthesizer. Nat Biotechnol 19:342–347

2005
Launch of first next-gen sequencer

Margulies, M., Egholm, M., Altman, W. et al. Genome sequencing in microfabricated high-density picolitre reactors. Nature 437, 376–380 (2005)

2005-2006
Commercial launch of Solexa/Illumina sequencer

2007
CombiMatrix (then CustomArray, now Genscript) develops a semiconductor-based method for array synthesis of oligos by semiconductors

Ghindilis AL, Smith MW, Schwarzkopf KR, et al (2007) CombiMatrix oligonucleotide arrays: genotyping and gene expression assays employing electrochemical detection. Biosens Bioelectron 22:1853–1860

2009
First use of next-generation sequencing for B cell repertoire sequencing (using Roche 454

Weinstein JA, Jiang N, White RA 3rd, Fisher DS, Quake SR. High-throughput sequencing of the zebrafish antibody repertoire. Science. 2009;324:807–10.

2012
Jennifer Doudna and Emmanuelle Carpentier repurpose CRISPR/Cas9 for gene editing

2019
First VHH (Caplacizumab) approved by FDA

https://www.nejm.org/doi/full/10.1056/NEJMoa1806311

Figure 1: The intertwined history of synthetic DNA and precision medicine

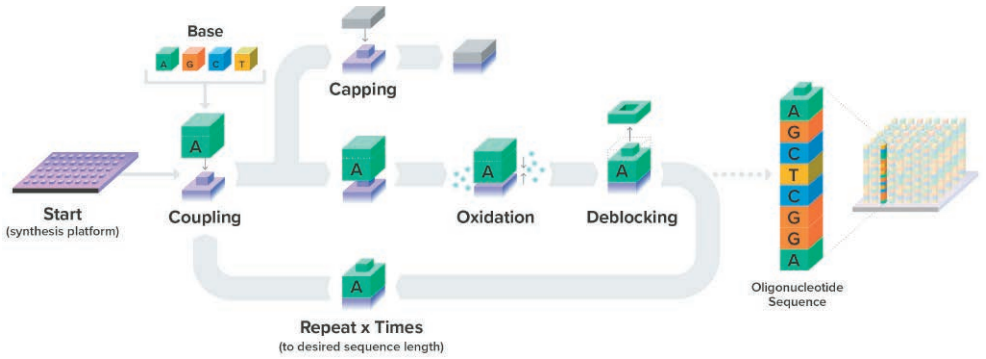

Figure 2: Oligonucleotide synthesis by cyclic phosphoramidite chemistry. Invented in 1979, phosphoramidite chemistry is still the method of choice for almost all oligo synthesis available on the market today.

Second, the use of silica-based solid supports in lieu of organic supports not only increased the number of molecules that could be synthesized at once, but also enabled solvents and reagents to be applied to an in-flow design, mitigating the need for purification following every addition of a new base (**Figure 2**). Caruthers soon founded Applied Biosystems to commercialize the first phosphoramidite DNA synthesizer, and synthetic DNA became accessible to non-chemists.

The commoditization of DNA was undoubtedly helped by the development of methods for manipulating and sequencing DNA in the 1970s. DNA synthesis and DNA sequencing, two pillars of precision medicine, improved our ability to link genes to diseases while providing the initial means to engineer highly targeted therapeutics.

From genes to genomes

The field of human disease genetics was revitalized by the emergence of methods for manipulating and sequencing DNA in the 1970s. With these techniques, researchers could more rapidly identify the causal genes underlying monogenic diseases and then sequence them. The subsequent automation of the Sanger sequencing method enabled the sequencing of the entire human genome by the year 2000, ushering in the era of precision medicine.

DNA microarrays

These new sequencing capabilities spurred the development of technologies capable of interrogating large numbers of sequences, namely, DNA microarrays. In 1991, Fodor and colleagues invented a method for synthesizing custom patterns of oligos directly on a glass wafer (i.e., a chip; Fodor *et al.* 1991). Soon commercialized by Affymetrix, the method utilized a new photolabile chemistry, allowing oligo synthesis to be carried out by a photolithographic process not unlike the one used to fabricate microelectronics (Lenoir and Giannella 2006). Photolithography essentially miniaturized solid-phase oligo synthesis, with the only limitation of a given oligo pattern size being the diffraction of light. A few years later, DNA chips would become cheaper and faster to manufacture, not to mention more feature rich, with the introduction of new DNA microarray fabrication methods, including those commercialized by Nimblegen (now Roche;Singh-Gasson *et al.* 1999), Agilent (Hughes *et al.* 2001), and CombiMatrix (subsequently CustomArray and now Genscript; Ghindilis *et al.* 2007).

The DNA chip was revolutionary for the burgeoning field of precision medicine because it was the first technology capable of rapid, relatively inexpensive genome-scale analysis. Mutational analysis; gene mapping, identification, and annotation; and RNA expression analysis could now be performed on a much larger scale. By the mid-2000s, researchers had used microarrays to distinguish blood cancers, predict disease outcomes using genetic biomarkers, and discover disease mechanisms (Panda *et al.* 2003; Claussnitzer *et al.* 2020).

Next Generation Sequencing (NGS)

The advent of next-generation sequencing in the early-2000s built on the success of the DNA chip. NGS was groundbreaking as it added massive parallelization to DNA sequencing (Heather and Chain 2016). Unlike DNA chips, which provided relative quantitation of predefined sequences, NGS enabled absolute quantitation of all sequences in a sample. With the throughput of sequencing massively increased, scientists and clinicians could begin defining common sequence variants underlying common diseases like asthma and depression.

Some DNA chip manufacturers allied themselves to the NGS market by fabricating microarrays designed to isolate specific regions of the genome for sequencing (Ledford 2008). This cost-saving and sensitivity-boosting process is known as target enrichment. Roche Nimblegen and Agilent were the first to synthesize such DNA chips (Metzker 2010). This solid-phase approach to target enrichment, however, did not scale well and required an abundant amount of starting genetic material, which can be difficult to obtain from clinical samples. To alleviate these issues, the same manufacturers also created solution-based target enrichment reagents by releasing array-synthesized

INSET 1

Silicon-powered DNA synthesis: The path from microchips to precision medicine

When Jack Kilby and Robert Noyce produced the first silicon microchip in 1960 (Lojek 2007), a technological revolution began. Whereas computers of the past were constrained by material and operational limitations, the silicon microchip possessed superior mechanical and electrical properties in a form factor that enabled mass production. What followed was the dawn of the digital era – and of our modern world.

The silicon microchip represents a nexus point in computing technology from which a cascade of world-changing technological advancements followed. Many such nexus points can be seen throughout history and across diverse industries, one of which is the advent of DNA synthesis technology.

A parallel set of developments to the microchip can be linked to 1953, the year Watson, Crick and Franklin postulated the double helical structure of DNA. In turn, that set of connections kindled a technological revolution that would ultimately transform our understanding of, and our ability to treat, human diseases. But for this revolution to happen, DNA synthesis would need to become routine so that synthetic DNA could become a widespread tool (e.g., the DNA microarray) for biological research and eventually lead to the modern concept of precision medicine.

Building on this history, Twist Bioscience has developed a proprietary semiconductor-based synthetic DNA manufacturing process featuring a high-throughput silicon platform that allows us to miniaturize the chemistry necessary for DNA synthesis. This miniaturization allows us to reduce the reaction volumes by a factor of 1,000,000 while increasing throughput by a factor of 1,000, enabling the synthesis of 9,600 genes on a single silicon chip at full scale. Traditional synthesis methods produce a single gene in the same physical space using a 96-well plate (see **Figure 1**).

https://www.twistbioscience.com/technology

oligos from their chips (Metzker 2010). Doing so made the probes much easier to handle, multiplex, and use with clinical samples.

Recently, Twist Bioscience leveraged its silicon array-based DNA synthesis platform, capable of simultaneous synthesis of over 1 million DNA oligos, to generate double-stranded DNA hybridization probes for target enrichment (**Figure 3**). By enabling capture of both strands of DNA, this innovation improves the sensitivity of targeted sequencing applications.

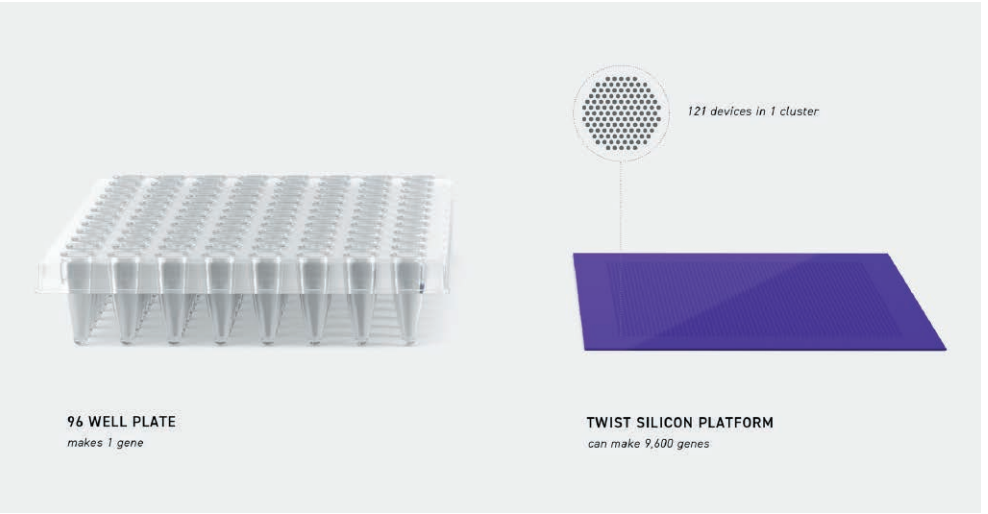

Figure 3: Twist Bioscience's Silicon Platform utilizes a silicon wafer for the miniaturized synthesis of oligonucleotides using phosphonamidite chemistry. On the surface of the chip, 9600 clusters of 121 devices are arrayed. Using nanofluidic liquid handling, a unique oligonucleotide can be synthesized on a single device. Oligonucleotides can be converted into Genes, Gene Libraries, Oligo Pools, NGS probes and DNA data storage devices.

Functional Genomics

Since the advent of NGS, DNA sequencing technologies have catalogued an immense wealth of genomic information. But more than sequencing reads are needed to inform clinical decision making. The genome must be understood *functionally* if it is to be leveraged therapeutically. The gene-function knowledge gap precipitated by high-throughput sequencing technologies spawned a new field – functional genomics – as well as new technologies like synthetic lethality screens, RNA interference screening, CRISPR screening, and massively parallel reporter assays (Claussnitzer *et al.* 2020). These approaches use complex libraries of defined DNA sequences to perturb gene function genome-wide, allowing causal gene-function relationships to be elucidated at scale. Overall, these strategies have hastened the translation of genomic insights into disease mechanisms – and therapeutic targets.

Synthesizing magic bullets

The advent of recombinant DNA technology in the 1970s did more than facilitate gene identification efforts prior to the sequencing of the human genome. It also enabled synthetic genes to be propagated and expressed in highly scalable microorganisms like *E. coli*, paving the way for new methods of producing and eventually screening biologics (biological therapeutics) at scale.

By mimicking biology, biologics have the potential to deliver "magic bullets" for a wide range of human diseases (**Figure 4**).

The first recombinant therapeutic to be approved by the U.S. Food and Drug Administration (FDA) in 1982 was humulin, or human insulin, developed by Eli Lilly in collaboration with Genentech. Before humulin, insulin was largely derived from animal pancreases. This was problematic as different lots varied in their potency, supply would eventually fall short of demand, and animal insulin produced allergic reactions in many diabetic patients (Lemprière 2021). By synthesizing the human insulin gene, Eli Lilly could mass produce the nonimmunogenic human form in bacteria. The effort involved the individual synthesis of 29 oligos, which were then enzymatically ligated together to form the full-length gene (Lemprière 2021).

The first FDA-approved therapeutic monoclonal antibody (mAb), Orthoclone OTK3, was less successful. Orthoclone OTK3 was generated by hybridoma, a technology in which a mortal antibody-producing cell (a B cell) is fused with an immortal one, providing a continual source of mAbs. Despite its approval as a therapeutic, the mouse antibody sometimes elicited serious immune reactions in kidney transplant patients. A lack of knowledge and technology precluded the chemical synthesis of antibody genes at this time.

A breakthrough in the development of antibody-based therapies came toward the end of the 1980s, when scientists began using PCR to isolate antibody genes from the genome in high numbers. Soon after, scientists devised methods for screening libraries of antibody fragment genes in bacteriophages through so-called phage displays, which gave scientists the ability to mine the human genome for magic bullets a full decade before it was fully sequenced.

Array-based oligo synthesis has been leveraged to fabricate fully synthetic human antibody libraries (Benhar 2007). And the human antibody repertoire has been sequenced using NGS, providing new insights into antibody repertoires and structures while also offering a rich source of natural sequences for library construction. Today, three key technologies are used to generate candidate antibody therapeutics (**Figure 5**). Mouse immunization and hybridoma generation, Synthetic library generation and phage display, and the capture of B-cells from a recovered patients followed by antibody synthesis. The latter two technologies are built on high throughput DNA synthesis technologies to rapidly build antibody libraries and antibody hits respectively.

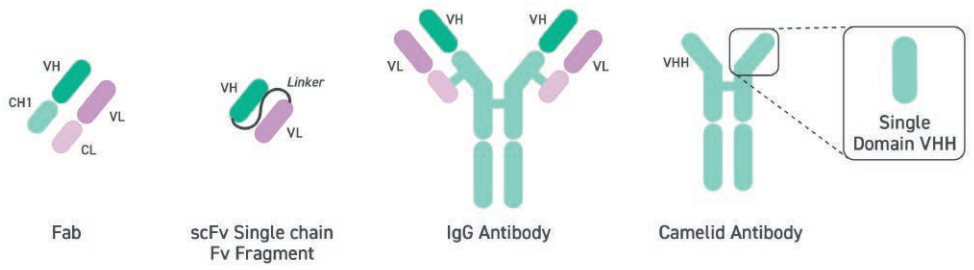

Figure 4: Common types of therapeutic antibody generated through recombinant technologies. The antigen-binding fragment (Fab) is the part of the antibody that interacts with the antigen; it is the most common format in therapeutic use today. Single-chain variable fragments (scFv) are engineered from variable regions of the heavy and light chains. Single-domain VHH antibodies are derived from the heavy-chain antibodies of llamas. Fab, scFv, and VHH antibodies can be reformatted as IgGs or Fc-fusions to confer Fc-related functionality.

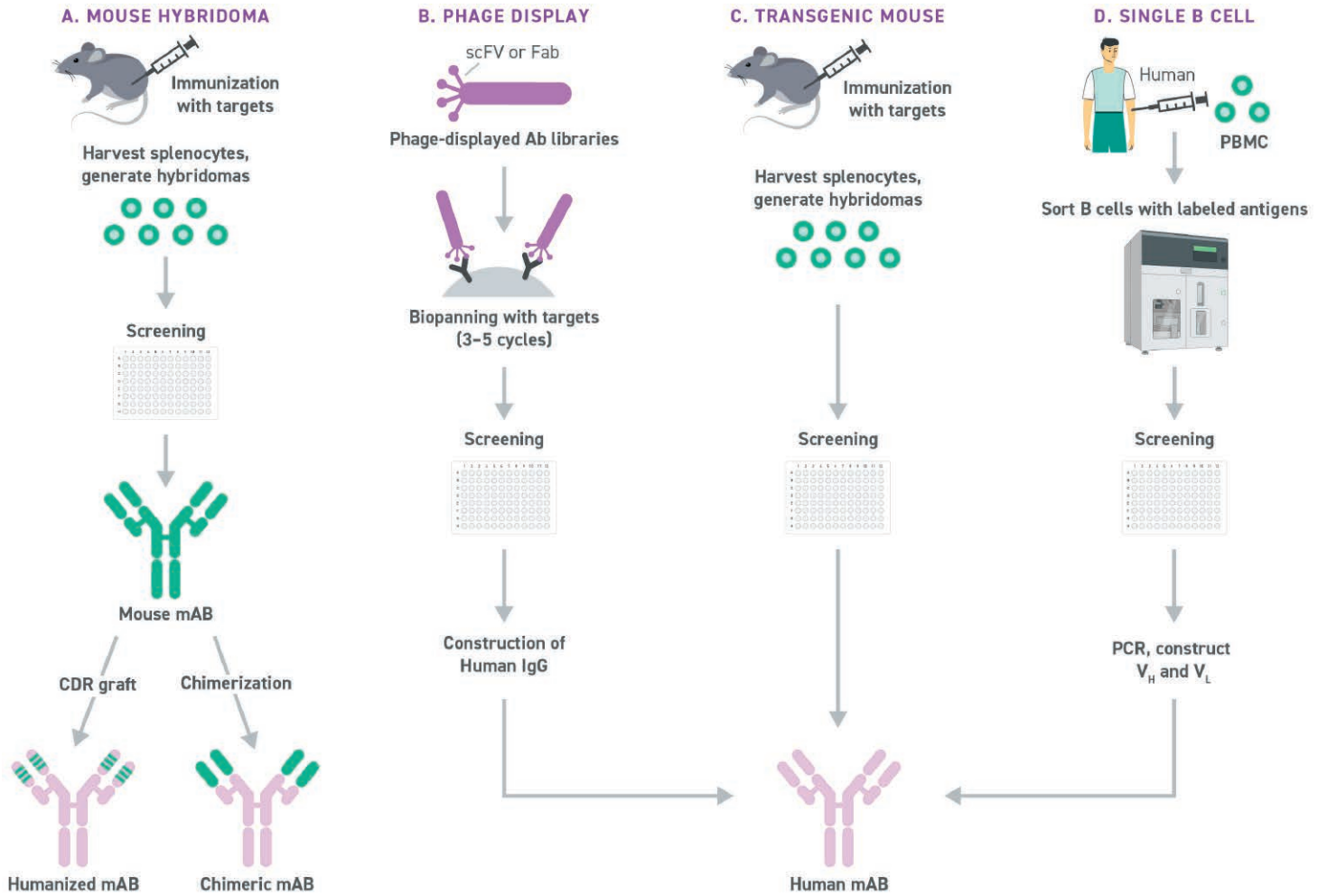

Figure 5: Key technologies for high throughout antibody therapeutic discovery. A. Mouse immunization and hybridoma generation, including CDR grafting or immunization to minimize therapeutic rejection. **B.** A synthetic library of antibody binding domains is displayed on the surface of phage, which can be panned for binders in high throughput. **C.** Humanized mouse immunization and hybridoma generation. **D.** Single B-cells are harvested from a patient that has recovered from a disorder and sorted for binders. Effective binders are re-constructed.

Twist Biopharma's Contribution – the Antibody Library of Libraries

To expand the antibody discovery space, Twist Biopharma, a division of Twist Bioscience, is leveraging its silicon-based DNA synthesis platform to build the Library of Libraries: an ever-growing collection of fully-synthetic antibody libraries. The collection has 15 ready-made therapeutic-area agnostic libraries (**Table 1**), each of which contains ~10-100 billion antibody clones. The libraries are built from precisely and uniformly synthesized oligos and quality controlled by NGS, increasing library quality and therefore reducing the time and investment needed to obtain a desirable hit.

Indeed, Takeda Pharmaceuticals recently licensed access to the libraries for the discovery, validation, and optimization of antibodies in Takeda's pipeline of biologics for oncology, rare diseases, neuroscience, and gastroenterology. As of 2021, the Library of Libraries has more than tripled the commercial antibody discovery space (**Table 1**).

Twist Biopharma is also exploring new ways to implement its library technology and discovery platform even beyond antibodies. Twist has partnered with Serotiny for the purpose of discovering novel Chimeric Antigen Receptors (CAR) for CAR T-Cell therapies.

Conclusion

The past half century has witnessed a period of explosive innovation in molecular biology: not only did scientists learn how to read, write, and comprehend DNA, they worked out how to harness newfound DNA-based technologies to understand better the molecular basis of disease and to create highly targeted therapies. Precision medicine is the culmination of these efforts.

Despite all of this progress, the majority of FDA-approved mAbs discovered using phage display originate from only two libraries (Frenzel, Schirrmann, and Hust 2016): a scFv library from Cambridge Antibody Therapeutics (acquired by MedImmune, now AstraZeneca) and a Fab library from Dyax (acquired by Shire, now Takeda). Synthetic DNA is beginning to augment this limited resource. With new antibody formats, features, and technologies at their disposal, antibody engineers can now consider targets once deemed out-of-reach of antibodies, including ion channels and G protein-coupled receptors. Synthetic DNA holds the keys to unlocking these transformative therapies – it's time we open the door!

Table 1: The Twist Biopharma Library of Libraries

Library	Format	Framework	Type
Hyperimmune Original	Fab	VH3-23/VK1-39	Naive, general discovery
Hyperimmune Common Light Chain	Fab	VH3-23, fixed Trastuzumab light chain	Naive, general discovery
VHH Ratio	VHH	Consensus llama	Naive, general discovery
VHH Shuffle	VHH	Consensus llama	Naive, general discovery
VHH hShuffle	VHH	Humanized DP-47-like VHH	Naive, general discovery
VHH hShuffle HI	VHH	Humanized DP-47-like VHH	Naive, general discovery
VHH hShuffle GPCR	VHH	Humanized DP-47-like VHH	Target-class specific
GPCR 2.0	scFv	VH1-69 (50%), VH3-30 (50%) VK1-39 (25%), VL1-51 (25%), VL2-14 (25%), VK3-15 (25%)	Target-class specific
GPCR 3.0	scFv	VH3-23 (50%), VH1-69 (50%) VL2-28 (85%), VL1-51 (15%)	Target-class specific
Ion Channel	scFv	VH1-69 (50%), VH3-30 (50%) VK1-39 (25%), VL1-51 (25%), VL2-14 (25%), VK3-15 (25%)	Target-class specific
Carbohydrate	scFv	VH3-23/VK4-1	Target-class specific
AI Hypermutated	scFv	VH3-23/VK1-38, VH3-23/VK3-20, VH1-69/VK1-39, VH1-69/VK3-20	Naive, general discovery, AI-guided design
Minotaur	scFv	VH3-23/VK1-39, VH4-59/VK1-39	Naive, general discovery, long HCDR3s
Structural	scFv	VH3-23/VK1-39	Naive, general discovery, structure-guided design based on crystallized antibodies
Ancestral	scFv	VH3-23/VK1-39	Naive, general discovery, structure-guided design based on patented antibodies

About Twist Bioscience Corporation

Twist Bioscience is a leading and rapidly growing synthetic biology and genomics company that has developed a disruptive DNA synthesis platform to industrialize the engineering of biology. The core of the platform is a proprietary technology that pioneers a new method of manufacturing synthetic DNA by "writing" DNA on a silicon chip. Twist is leveraging its unique technology to manufacture a broad range of synthetic DNA-based products, including synthetic genes, tools for next-generation sequencing (NGS) preparation, and antibody libraries for drug discovery and development. Twist is also pursuing longer-term opportunities in digital data storage in DNA and biologics drug discovery. Twist makes products for use across many industries including healthcare, industrial chemicals, agriculture and academic research.

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Emily Leproust, PhD
CEO and Co-Founder of Twist

As an early pioneer in the high-throughput synthesis and sequencing of DNA, Dr. Leproust is disrupting markets to enable the exponential growth of DNA-based applications including chemicals/materials, diagnostics, therapeutics, food and digital data storage. In 2020, BIO presented her with the Rosalind Franklin Award for Leadership. Foreign Policy named her one of their 100 Leading Global Thinkers and Fast Company named her one of the Most Creative People in Business. Prior to Twist Bioscience, she held escalating positions at Agilent Technologies where she architected the successful SureSelect product line that lowered the cost of sequencing and elucidated mechanisms responsible for dozens of Mendelian diseases. She also developed the Oligo Library Synthesis technology, where she initiated and led product and business development activities for the team. Dr. Leproust designed and developed multiple commercial synthesis platforms to streamline microarray manufacturing and fabrication. She serves on the Board of Directors of CM Life Sciences and is a co-founder of Petri, an accelerator for start-ups at the forefront of engineering and biology. Dr. Leproust has published over 30 peer-reviewed papers – many on applications of synthetic DNA, and is the author of numerous patents. She earned her Ph.D. in Organic Chemistry from University of Houston and her M.Sc. in Industrial Chemistry from the Lyon School of Industrial Chemistry.

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* Adenine (A), Cytosine (C), Guanine (G), Thymine (T)

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