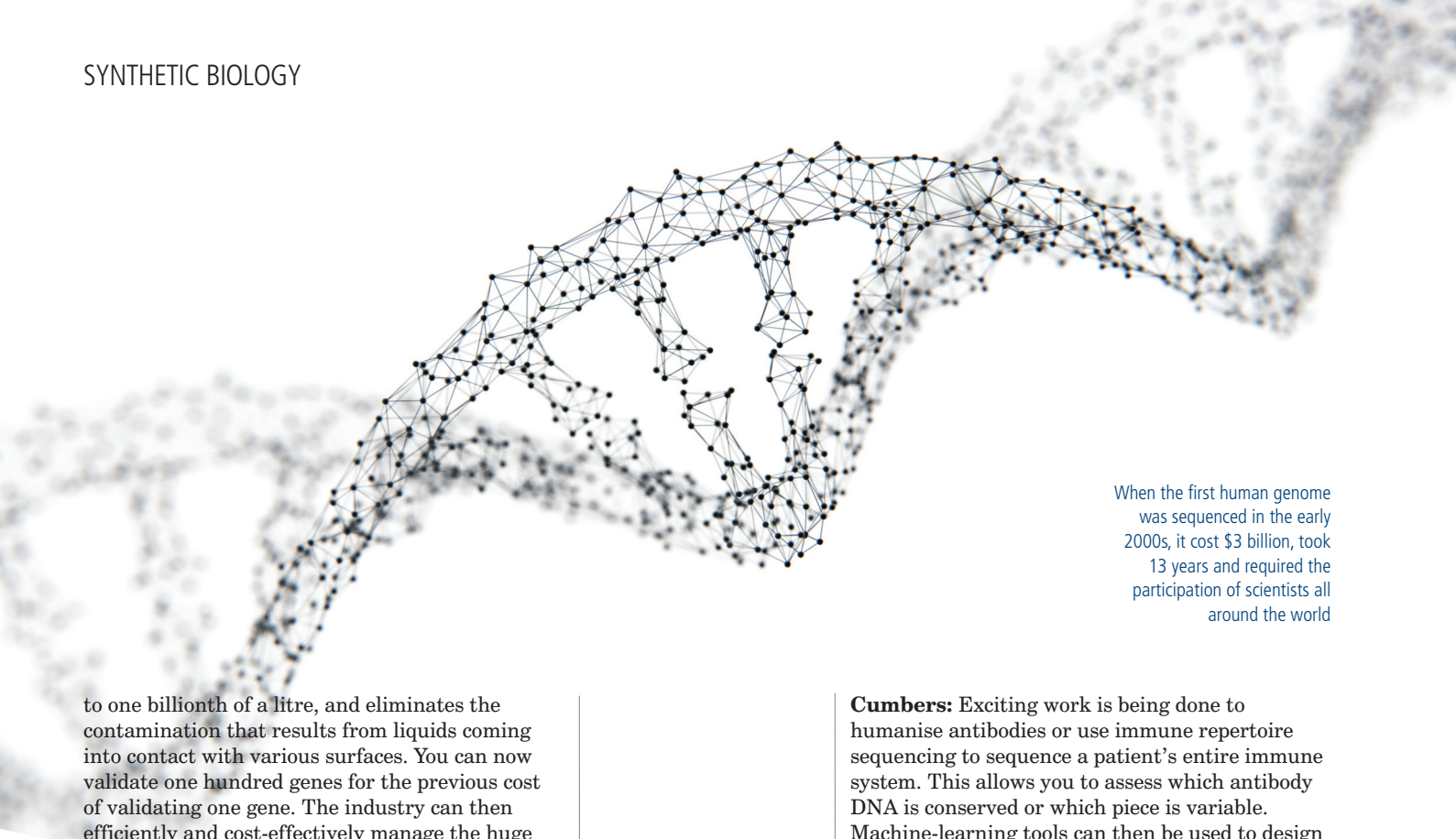

When the first human genome was sequenced in the early 2000s, it cost $3 billion, took 13 years and required the participation of scientists all around the world

to one billionth of a litre, and eliminates the contamination that results from liquids coming into contact with various surfaces. You can now validate one hundred genes for the previous cost of validating one gene. The industry can then efficiently and cost-effectively manage the huge number of experiments required for synthetic biology development work.

HA: What therapeutic developments do you see possible in the near- and longer-terms?

Leproust: Synthetic biology will allow more precision medicines to be developed and utilised. There is not one type of breast cancer, there are many types of breast cancers and we are moving towards being able to treat a patient's specific cancer and gene mutations. Immunotherapies are the first examples of this. We will be able to use the actual immune response of a patient's body and amplify it so that a patient will get treated with their own re-engineered cells, as is happening with CAR-T therapies today. Personalised medicines deliver a lot of improvements in efficacy and efficiency. Today, we are probably happy with an oncology drug that is 60% effective. With truly personalised medicine, we will be able to achieve 95–99% effectiveness. We believe fatal diseases will become chronic conditions.

Nicols: There's so much opportunity to serve patients afflicted with enzyme deficiency disorders. Although there are hundreds of these disorders, almost all of them are rare diseases; there are currently only 12 enzyme replacement therapies on the market for nine disorders. It's exciting that there are dozens of clinical trials in process for enzyme replacement therapies, and Codexis is proud to be in the mix having successfully completed our first human trial — an orally administered enzyme therapy developed for phenylketonuria (PKU) disease.

Codexis' approach is to engineer enzymes that not only work to replace the missing chemistry but also sustain better-in-human biology. Specifically, they are more stable and evoke fewer undesirable immune responses, which will allow us to treat many more diseases that could not be addressed with traditional enzyme therapeutic approaches.

Cumbers: Exciting work is being done to humanise antibodies or use immune repertoire sequencing to sequence a patient's entire immune system. This allows you to assess which antibody DNA is conserved or which piece is variable. Machine-learning tools can then be used to design antibodies that avoid unwanted immunogenicity because you've based antibodies on structures that the patient's body is used to.

Fischer-Colbrie: With the ability to completely re-engineer workflows to deliver results much more rapidly and consistently, we have the capability to deliver the proteins needed for drug discovery work. I think this will vastly improve the science; therefore, it has a real chance to accelerate drug development efforts.

HA: Do you see a role for synthetic biology in advancing small molecule pharmaceuticals?

Leproust: In organic chemistry, there are a few things that are hard to do. For instance, making a carbon–carbon bond and making a chiral product are both difficult. The amazing thing about enzymes is that they can enable carbon–carbon bonds. They can also generate chiral synthesis at high yields, in water, at room temperature, etc. It's magic if you can find the right enzyme for the right reaction. Cleaner, safer and much more efficient reactions within API manufacturing processes will ultimately allow small molecule drugs to be stronger within the market.

Nicols: We're seeing an acceleration of the use of biocatalysis in small molecule drug manufacturing. This acceleration is evident in our pipeline, which has more than doubled the number of late-stage clinical processes using biocatalysis. In some cases, we are seeing pharmaceutical manufacturers switch to biocatalysis for products already on the market to create more efficient manufacturing processes. Also, drug manufactures are selecting biocatalysis for products within the development process. Our ability to leverage our CodeEvolver platform and much more quickly engineer enzymes for extremely effective and efficient reactions is speeding the adoption of biocatalysts in small molecule drug manufacturing.