CRISPR/Cas9 services for drug discovery and custom model development

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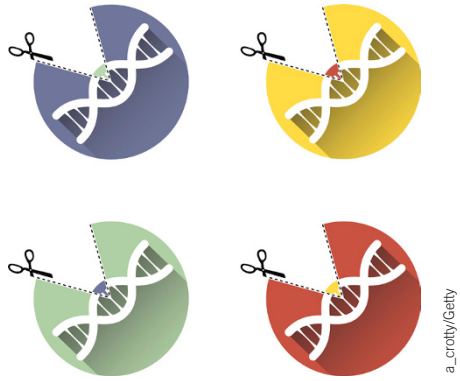
Drug discovery can be a long and expensive process, well before a potential therapy can even begin to be considered for clinical trials. Researchers must first have an idea of what they'd like to target in order to treat or prevent a given disease or condition. That involves a comprehensive understanding of the development and progression of the disease itself and then screening for potential targets or compounds to investigate their therapeutic effects; at early stages, there can be thousands to sort through. Once a candidate is identified, subsequent research must identify how and why it works and then thoroughly test it for efficacy, safety and proper dosage. This work can be conducted *in vitro* and/or *in vivo*, and may involve working with multiple contract research organizations throughout the different development phases to take advantage of the most efficient and applicable research techniques and technologies.

CRISPR/Cas9 is poised to improve the speed and efficiency of drug discovery. Previous techniques, such as intron splicing or the use of targetable nucleases, were instrumental in genetic engineering but could be time-consuming and often lacked precision, creating unintended off-target genetic changes that required additional sorting. CRISPR/Cas9, however, is both simpler and more precise. The technique, developed only a few years ago, allows researchers to directly target specific genes, whether in a screening library, cell line, or animal model. CRISPR/Cas9 can efficiently knock-out different genes in cell lines in single experiments, allowing for rapid screening of potential targets and creation of *in vitro* lines for follow-up. For *in vivo* work, this precision allows researchers to skip the multigenerational derivation steps previously required to create a genetically engineered model; they are also able to target multiple genes simultaneously.

Though a legal battle will ultimately decide where the patent for CRISPR/Cas9 will reside (*Nature* **537**, 460–461; 2016), numerous licensing agreements have been issued for commercial development using the technology. In 2014, Charles River Laboratories completed their licensing agreement for the commercial use of CRISPR/Cas9 with the Broad Institute of MIT and Harvard. At the beginning of December 2016, they announced the launch of end-to-end CRISPR/Cas9 services. Clients will be able to work with the company to use CRISPR/Cas9 for research from target discovery and validation to cell line development for high-throughput screening to the generation of transgenic mouse models for *in vivo* studies and preclinical development. In a press release, Dr. Iva Morse, Corporate Vice President and Chief Scientific Officer of Global Research Models and Services remarked, "Utilizing the CRISPR/Cas9 platform, Charles River clients can work with a single provider for both the *in vivo* and *in vitro* phases of their research."

Other large companies have also received licenses to commercialize CRISPR/Cas9 applications in the hopes of improving the development of customized genetically engineered animal models for their clients. Taconic licensed the technology directly from the Broad Institute, while the Jackson Laboratory reached their agreement through Caribou Biosciences, founded by researchers involved with CRISPR's academic development. Caribou's own license is provided by the University of California, Berkeley, which also claims the intellectual property rights to CRISPR/Cas9. The case against the Broad Institute is expected to be decided sometime in early 2017, though companies expect they will be able to license (or re-license) the technology with whichever side wins.



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Like any novel technology, there is overhead involved in applying it; with commercialization comes both operational scale and concentrated expertise. As larger companies continue to license and develop services using CRISPR/Cas9, smaller firms and research groups will be able to take advantage of those services rather than having to expend their own time and money on learning and developing the technology themselves. With CRISPR/Cas9, customized, ready-to-use genetically engineered models may be ordered on demand.