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INTRODUCTION

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Genome Editing

Michael M. Lacy[a,*] and Fatima N. Mirza[b,*]

[a]*Deputy Editor, Department of Molecular Biophysics and Biochemistry, Yale University, New Haven, CT;* [b]*Deputy Editor, Yale School of Medicine, New Haven, CT*

In this issue, we focus on the topic of Genome Editing, the methods by which specific changes can be introduced into the genome of an organism. The ability to intentionally alter a gene of interest has long been a goal throughout the history of genetics and biomedical research, especially as discoveries linking certain human diseases to mutations have inspired the prospect of curing inherited diseases by directly editing or replacing the patient's mutated gene. In recent years, a number of technical advances have enabled increasingly widespread applications of genome editing in biological and medical research with a number of clinical applications being developed for future use.

Many strategies have been applied to manipulate genomes for biomedical applications. They are usually referred to as "gene editing," where a specific base pair in a gene is biochemically targeted and altered, or "gene therapy," where a replacement gene is inserted into a patient's cells. The former involves delivering an editing agent, typically an engineered nuclease enzyme, sometimes along with a synthetic replacement DNA to cells or an organism, while the latter usually uses an engineered virus to insert a gene of interest into the patient's cells, compensating for the patient's own disease-causing version of the gene. The main challenges in applying these methods, either for laboratory use in cultured cells and research animals or for clinical applications in humans, are delivering the gene-modifying agents with high efficiency and avoiding off-target effects resulting from the imperfect specificity of the editing agents or dangerous immune responses. Additionally, ethical concerns have been raised about the unprecedented challenges of safety and bioethics and the potential for mis-use of these technologies. The articles in this issue review and analyze current trends in methods of genome editing for fundamental research and clinical applications, as well as the ethical, social, and legal implications of their development.

A good starting point for readers unfamiliar to the field will be Dana Carroll's perspective on the history of genome editing, which introduces a variety of techniques and the landmark discoveries that enabled them. As one of the pioneers of nuclease-mediated gene editing, Prof. Carroll provides a valuable context for the current trends and future developments of the field.

Next, an important and exciting aspect of this topic is the rapidly expanding range of techniques and applications for gene editing and gene therapy. Savell *et al*., Quijano *et al*., Chen *et al.*, McClements *et al*., and Giersch *et al*. each dedicate their manuscripts to characterizing various methods, highlighting their uses for basic research as well as potential therapeutic applications.

Several articles will discuss genome editing for ophthalmological applications in particular. Because the eye is a convenient target for genome editing due to its accessibility and because vision impairment can arise from a single mutation, patients with retinal pathology will likely be some of the first to be successfully treated with gene editing. Chan *et al*., Peddle *et al*., Chuang *et al*., and Hassall *et al*. each present reviews on various genome editing approaches for ophthalmological applications.

Another therapeutic target of interest is the liver, where many vital metabolic pathways can be disrupted by inherited mutations. Bryson *et al*. discuss new

*To whom all correspondence should be addressed: Michael M. Lacy, 367 Cedar St, New Haven, CT, 06510, email: michael.lacy@yale.edu; Fatima N. Mirza, 367 Cedar St, New Haven, CT, 06510, email: fatima.mirza@yale.edu.

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nuclease-mediated gene editing approaches that could potentially be safer and more effective than conventional gene therapy for inherited metabolic diseases of the liver.

Looking beyond the basic science principles of gene editing, it becomes important for scientists, policy-makers, and the public to understand the ethical, social, and legal framework within which this discipline exists. Cribbs *et al*., Morris, Sherkow *et al*., De Lecuona *et al*., and Halioua-Haubold *et al*. will provide a nuanced overview of these themes, ranging from the patent and regulatory landscape to the principles scientists must abide by to responsibly address the unique complications that will inevitably arise.

The development and refinement of new genome editing tools is rapidly progressing, and we recognize that the breadth of this field could not be covered fully in a single issue. In the time between accepting these manuscripts and publishing this issue, further clinical trial data has been reported. We hope that the articles presented here will provide an in-depth introduction to a variety of topics in this exciting field and provide readers from across the biological and medical sciences with a new understanding of these rapid advances and ongoing challenges.