

## FOREWORD



## Spotlight on: Translation and applications of gene editing



Chris Mason & Elisa Manzotti

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The last 24 months have seen an explosion in genome engineering techniques that are revolutionizing our ability to edit specific elements of the genome across a multitude of organisms. The discovery of CRISPR/Cas9 in particular has unlocked a relatively simple and accessible way of manipulating DNA sequences and it is this ease of use that has led to a huge surge in the number of research publications utilizing this method. However, CRISPR/Cas9 is just one technology in an expanding gene editing toolkit and our lead article by **Andrew Bassett** (University of Oxford, UK), reviews the three main nuclease platforms: Zinc Fingers, TALENs and

CRISPR/Cas9. Dr Bassett provides an overview of the mechanisms of action and discusses the advantages and challenges of each platform.

### TRANSLATIONAL IMPACT

The potential of gene editing to impact genetic disease is evident, but as with any nascent technology, there are platform-specific as well as disease-specific challenges that must be overcome before this approach enters the clinic. In this spotlight we feature three Expert Insight articles discussing the latest advances in the development of gene editing approaches for human disease.

**Marc Moore, Denis Vallese, George Dickson & Linda Poplewell** (Royal Holloway University of London, UK) discuss the exciting developments in CRISPR/Cas9-mediated genome engineering approaches for Duchenne Muscular Dystrophy. Utilizing gene editing to correct the primary genetic defect in the *DMD* gene could transform treatment of the disease from that of a palliative to potentially curative approach.

The  $\beta$ -globin disorders have been at the forefront of gene therapy development from its very inception and naturally have taken center stage in the gene editing arena. **Carsten W Lederer & Marina**

**Kleanthous** (The Cyprus Institute of Neurology and Genetics, Cyprus) review recent progress in the application of gene-editing tools and different model systems towards the establishment of new therapies for  $\beta$ -globin disorders

**Amanda Andersson-Rolf & Bon-Kyoung Koo** (University of Cambridge, UK) provide an overview of state-of-the-art stem cell culture systems, with a focus on the recent progress in 3D tissue culture of both embryonic and adult stem cells, and how genome editing technologies can be utilized to gain insights into human development and disease.

### HOT DEBATES: PATENTS & THE HUMAN GERMLINE

Alongside the discussion of the incredible advances in gene editing applications, an ongoing patent dispute plays out in the media over the CRISPR/Cas9 technology. **Hannah Smith-Willis & Beatriz San Martín** (FieldFisher, UK) help demystify the IP situation and discuss the possible implications of the outcome of this dispute. This Expert Insight also touches upon the hotly debated issue of editing the human germline. The unprecedented pace of advances in gene editing has placed this topic firmly back on the agenda, as attested to by the recent gathering of leading scientists, legal experts, ethicists and patient advocacy groups at the International Summit of Gene Editing in Washington, USA. Undoubtedly this is only the beginning of what will be an ongoing, transparent and internationally collaborative discussion prior to it inevitably entering the clinic.

### EXPERT INSIGHT PODCAST

With all the recent coverage of CRISPR/Cas9 you could be forgiven for thinking that gene editing is a 'brand new' technology; however, what we're seeing now is a culmination of decades of work and one company in particular has been charting a path towards the clinic. Sangamo Biosciences specialize in the use of zinc finger nucleases and have been developing this technology across a range of potential clinical applications including HIV, thalassemia and just this month they received FDA clearance for their IND for SB-FIX in hemophilia B, the first *in vivo* gene editing application to enter the clinic. We talk with Project Leader and Senior Scientist at Sangamo, **Fyodor Urnov** about the promising advances towards the clinic and his thoughts on the translational challenges they have faced. You can also download the interview as a **PodCast online**.

We hope you enjoy the *Cell & Gene Therapy Insights – Gene Editing Spotlight* – you can access all content free of charge on the CGTI website, in addition to a host of other useful content, videos and webinars in our **Gene Editing Resource Center**.

#### Chris Mason

*Senior Editor, Cell & Gene Therapy Insights, Professor of Regenerative Medicine Bioprocessing, Advanced Centre for Biochemical Engineering, University College London, UK*

#### Elisa Manzotti

*CEO and Founder, BioInsights  
e.manzotti@insights.bio*