Gene editing for the treatment of inherited liver disorders

S-04.2-1

G. Gonzalez-Aseguinolaza[I,II]

[I]Center for Applied Medical Research (CIMA), University of Navarra, Pamplona, Spain, [II]vivet therapeutics, Pamplona, Spain

The deliberate and precise modification of the host genome using engineered nucleases represents a groundbreaking advancement in modern medicine. The initiation of several clinical trials employing these approaches to address metabolic liver disorders, along with the recent remarkable outcomes observed in patients with Transthyretin Amyloidosis, underscores the progress in this domain and highlights the potential of these innovative therapies to safely and effectively treat such diseases. These advancements have been facilitated by significant recent technological improvements, particularly the emergence of CRISPR Cas9-based technology, which has revolutionized the field of gene editing and enabled in vivo modification of the cellular genome for therapeutic purposes. These modifications can encompass gene supplementation, correction, or silencing, opening up a plethora of therapeutic possibilities.
Moving forward, it is likely that we will witness the therapeutic potential of these strategies unfold in the coming years. In this presentation, we aim to summarize some of the preclinical data gleaned from animal models and explore the various gene editing strategies employed in the treatment of liver diseases. Finally, we will focus on the latest results obtained by our group using gene editing for the treatment of Primary Hyperoxaluria type I. The therapeutic efficacy of nucleases and nickases delivered by adeno-associated vectors will be showcased, along with interesting data on the nature of the genome modification, vector integration, and safety implications.