Gene Therapy for Human Genetic Disease

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Dr. Andrés Fernando Muro, Group Leader-Mouse Molecular Genetics from International Center for Genetic Engineering and Biotechnology, Trieste, Italy was the second speaker of the BAS Plenary Session. Dr. Muro presented on the topic "Gene therapy for human genetic disease". He first discussed the pioneering work done by Friedmann and Roblin in proposing gene therapy in 1972. The preliminary criteria for gene therapy are having an adequate characterization of the genetic disorder, experience with other treatments to compare the efficacy, adequate characterization of the DNA vector, extensive studies in animal models to evaluate therapeutic benefits and adverse side effects, and testing the strategy in patients' fibroblasts. In the late 80's and early '90s gene therapy was first used to treat ADA-SCID (severe combined immunodeficiency due to adenosine deficiency). There were fatal responses as well, so it was important to improve the safety and efficacy. As a result, new vectors such as viral vectors (enveloped and non-enveloped), lipid nanoparticles (LNPs), and virus-like particles were developed. This approach was successful and there are commercially available drugs. Gene therapy can be particularly important in rare diseases. There are 6172 unique rare diseases and 71.9% (5304) of those are of genetic origin. The evidence-based estimate for the population prevalence of rare disease is 3.5 – 5.9% which equates 263 – 446 million persons affected globally. Inborn errors of metabolism (IEMs) are one of the rare diseases which accumulate toxic substances in the body. For this, adeno-associated virus (AAV) vectors are used. Then he described the bilirubin pathway followed by crigler–najjar syndrome type I which is an ultra-rare disease associated with bilirubin. He also explained the mouse model for crigler–najjar syndrome gene therapy. There were significant reductions of bilirubin levels after the gene therapy in both, mice and patients. In addition, genome editing can be used to treat these rare diseases. Prof. Muro explained how engineering nucleases can be used for genome editing. He also discussed work from other research groups where they have used gene editing to treat sickle cell anemia and thalassemia. Therefore, gene therapy and gene editing are promising therapies to treat genetic diseases. Gene editing clinical trial results obtained so far are very promising and the field will further be developed in safety and efficacy aspects.