Panel 42

Development of RNA based approaches to exploit alternative therapies for Lysosomal Storage Diseases

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Treatment strategies such enzyme-replacement therapy and substrate reduction, among others, are available for some Lysosomal Storage Diseases, yet still with some limitations.

In recent years, the RNA molecule became one of the most promising targets for therapeutic intervention and currently, a large number of RNA-based therapies are being investigated at the basic research level and in late-stage clinical trials. Actually, some of them are already approved for medical use (e.g. Spinal muscular atrophy and Duchenne muscular dystrophy).
RNA-based approaches can act at pre-mRNA level (by splicing modulation/correction using antisense oligonucleotides or U1snRNA vectors), at mRNA level (inhibiting gene expression by siRNAs and antisense oligonucleotides) or at DNA level (by editing mutated sequences through the use of CRISPR/Cas).

Currently, we are developing some of these therapeutic approaches for LSDs. Two main research lines are ongoing: one involves the use of antisense U1 snRNAs to overcome the effect of a splice site mutation causing Mucopolysaccharidosis type IIIC and the other is based on the use of splice switching oligonucleotides to induce the skipping and consequently circumvent the effects of the most common causal mutation in Mucolipidosis type II.