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Alternative splicing in diabetic nephropathy and other chronic kidney diseases

Alternative splicing (AS) has emerged in the post-genomic era as one of the main drivers of proteome diversity with at least 94% of multi-exon genes being alternatively spliced in humans. AS is therefore, one of the main control mechanisms for cell phenotype and a process deregulated in disease. Numerous reports describe pathogenic mutations in splice factors, splice sites or regulatory sequences. Additionally, in many cases there is an abnormal proportion of splice isoforms (or novel isoforms) in disease compared to the physiological pattern, without an apparent driver mutation. It has therefore become essential to study how AS is regulated in physiology, how it contributes to pathogenesis and whether we can manipulate faulty splicing for therapeutic advantage. While the disease most commonly linked to deregulation of AS in several genes is cancer, there are many in-depth reports of pathogenic splice variants in diseases ranging from neuromuscular disorders to diabetes or cardiomyopathies. In recent years, a plethora of splice variants have been implicated in chronic kidney diseases as well. Examples of these and ideas on how to manipulate them for therapeutic benefit will be presented in this talk.

Biography

Sebastian Oltean has studied Clinical Medicine at Iuliu Hatieganu Medical School, Romania and trained as a Junior Doctor in Nephrology and Dialysis before he obtained a PhD from the University of Nebraska-Lincoln in 2004. Further, he obtained his Postdoctoral training at Duke University Medical Center, North Carolina, USA, where he became interested in studying the connections between alternative splicing and cancer. Further, in 2008, he moved to the University of Bristol, where he continued to study alternative splicing in vivo, with focus towards the importance of several genes splice isoforms (e.g., *VEGF*, *FGFR2*) in cancer as well as kidney diseases and development of splice-based therapeutics. He was also appointed as an Independent Research Fellow and Principal Investigator in 2012 and developed his own research group in Bristol before moving to University of Exeter, Medical School in 2017, where he is presently a Senior Lecturer.

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