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Alternative RNA splicing and regulation of nitric oxide signaling

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Alternative splicing expands transcriptome diversity and allows cells to meet the requirements of an ever-changing extracellular environment. It has been more than 30 years since nitric oxide (NO), a gaseous free radical, was recognized as a critical physiologic signaling molecule. Since then the list of known NO-directed functions has grown substantially and includes regulation of smooth muscle function in vascular and gastrointestinal systems, inhibition of platelet aggregation and adhesion, neurotransmission and neuromodulation, regulation of cellular respiration and cytotoxicity, mitochondrial biogenesis and immune defense. However, the importance of alternative splicing in regulation of enzymatic components of NO signaling pathway started to emerge only recently. Our understanding of the mechanisms governing this process still remains very limited and awaits systematic investigation. Multiple evidences accumulated from different laboratories suggest that splicing of enzymes in the NO/cGMP pathway, including nitric oxide synthases, heterodimeric soluble guanylylcyclase and cGMP-dependent protein kinase, is very complex and strongly affects NO signaling in response to various environmental clues. New data from our laboratory demonstrate that the expression of individual splice forms of nitric oxide receptor soluble Guanylyl Cyclase varies in human healthy and diseased aortic tissue. Our research suggests a possible contribution of splicing to the impaired sGC function in vascular disorders and uncovers a potential diagnostic tool or biomarker and a target for new therapeutics. Future studies will certainly bring new exciting insights into the role that alternative splicing plays in NO/cGMP biology.

Biography

Iraida G. Sharina has completed her Ph.D. in Molecular Biology from Russian Academy of Science. She had her postdoctoral training at UT-Health Science Center in Houston as part of the research team of Dr. Ferid Murad, a Nobel Prize winner and major leader in NO field of research. She is an Assistant Professor in Department of Internal Medicine, Division of Cardiology of UT-MS. She published more than 22 research papers in high impact journals. Her current research is focusing on understanding of the genetic basis of NO/cGMP signaling.

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