THE ROLE OF MICRORNAS IN OXIDATIVE STRESS REGULATION

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MicroRNAs (miRNAs) are small, 22-24 nucleotides long, noncoding RNAs that act as pivotal posttranscriptional regulators in various biological processes. Interaction of miRNAs with their target RNAs in most cases leads to the suppression of gene expression, by promoting degradation of RNAs or inhibiting translation. These interactions mainly occur with 3′ untranslated regions (UTR), but can also occur with 5′ UTR or with the coding part of the target RNA molecule. It is estimated that miRNAs regulate more than 30–60% of protein coding genes in the human genome. Oxidative stress refers to an imbalance between reactive oxygen species (ROS) generation and body's capability to detoxify the reactive mediators or to fix the relating damage. ROS can regulate miRNA transcription, maturation, and function. ROS directly modulate the activity of vital proteins that control posttranscriptional events in the biogenesis of miRNAs (Di George critical region-8 protein; Dicer). A certain group of transcription factors involved in the regulation of miRNA expression is upregulated under oxidative stress and directly activates the transcription of a subset of miRNAs. ROS have been directly implicated in epigenetic alternations such as DNA methylation and histone modifications that control specific microRNA transcription (1). On the other hand, miRNAs may in turn modulate the redox signalling pathways, altering their integrity, stability, and functionality, thus contributing to the pathogenesis of multiple diseases: cancer, neurodegenerative diseases, diabetes mellitus (2), ROS-related cardiac diseases, including myocardial infarction, ischemia/reperfusion injury, cardiac hypertrophy and heart failure, and are also considered as potential therapeutic targets and novel diagnostic tools.

References

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ULOGA MIKRORNK U REGULACIJI OKSIDATIVNOG STRESA

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MikroRNK (miRNK) predstavljaju male, nekodirajuće RNK, dužine 22-24 nukleotida, koje regulišu ekspresiju gena na post-transkripcionom nivou. Interakcija miRNK sa ciljnim informacionim RNK (iRNK) u većini slučajeva dovodi do supresije ekspresije gena, degradacijom ciljne iRNK ili inhibicijom translacije. Ove interakcije se dešavaju na nekodirajućim 3'krajevima iRNK, ali mogu da se dese i na 5' kraju ili čak na kodirajućem regionu ciljne iRNK. Smatra se da na ovaj način, u humanom genomu, miRNK kontrolišu oko 30-60% gena koji kodiraju proteine. Oksidativni stres je stanje u kome postoji neravnoteža između stvaranja reaktivnih vrsta kiseonika (slobodni radikali, ROS) i njihovog neutralisanja od strane antioksidativne zaštite organizma. Pokazano je da ROS mogu da utiču na procese transkripcije i sazrevanja miRNK kao i na njihovu funkciju. ROS direktno modulišu aktivnost glavnih proteina koji učestvuju u post-transkripcionoj obradi u procesu biogeneze miRNK (Di George critical region-8 protein i Dicer). Pod uticajem oksidativnog stresa može se aktivirati transkripcija određenih familija miRNK, dejstvom na transkripcione faktore koji učetvuju u tom procesu. Takođe, ROS utiču na epigenetske mehanizme regulacije ekspresije miRNK, kao što su DNK metilacija i modifikacija histona (1). Sa druge strane, miRNK mogu da utiču na aktivnost redoks signalnih puteva, menjajući njihovo funkcionisanje. Na taj način miRNK doprinose patogenezi mnogih bolesti kao što su: različite vrste kancera, neurodegenerativne bolesti, dijabetes melitus (2), bolesti srca, uključujući infarkt miokarda, povredu nastalu ishemijom/reperfuzijom, srčanu hipertrofiju i srčanu insuficijenciju. Takođe, miRNK se razmatraju kao potencijalni dijagnostički markeri i novi terapijski ciljevi.

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