PREDICTION AND ANALYSIS OF MICRO-RNAS (miRs) ASSOCIATED WITH BRADYKININ-MEDIATED ANGIOGENESIS

Albuquerque, M.T.O.M., Carvalho, C.V., Rosa, H., Monteiro, H.P.

1Departamento de Medicina – Pós-Graduação em Medicina Translacional, UNIFESP, São Paulo, Brazil; 2Departamento de Ginecologia, UNIFESP, São Paulo, Brazil 3Departamento de Bioquímica – Centro de Terapia Celular e Molecular, UNIFESP, São Paulo, Brazil

Angiogenesis is a vital process that consists in the formation of new vessels from preexisting vessels. Bradykinin (BK) activates the endothelial nitric oxide (NO) synthase (NOS) in human umbilical vein endothelial cells (HUVEC). NO-derived from eNOS participates in angiogenesis by stimulating the induction of VEGF expression and the activation of the NO/EGFR/ERK1/2 MAP kinases signaling pathway. In addition, endothelial responses are potentially modulated by microRNAs (miRs) expression. MiRs regulate gene expression through translation, repression or homologous mRNA degradation. This work aims to identify miRs involved in the cell signaling pathway modulated by NO during angiogenesis. BK stimulated intracellular NO production and in vitro vessel formation in HUVEC cultivated in Matrigel®. Specific inhibitors of the VEGF NO/EGFR/ERK1/2 MAP kinases signaling pathway significantly reduced the formation of vessels and decrease endogenous NO production. We developed an in silico analysis and identified nine pro-angiogenic miRs (miR-27b, -miR-92a, miR-126, miR-130a, miR-132, miR-210, miR-296) and seven anti-angiogenic miRs (miR-15a/b, miR-16, miR-20a/b, miR-21, miR-221 and miR-222) that regulate the expression of the VEGF NO/EGFR/ERK1/2 MAP kinases pro-angiogenic signaling pathway. Analyzing miRs global expression in HUVECs by miRNA PCR Array(MIHS-103ZAQiagen), revealed seven miRs highly expressed: let-7a-5p, miR-16-5p, miR-20a-5p, miR-21-5p, miR-125b-5p, miR-126-3p, miR-222-3p and nine with reduced expression, including miR-15a-5p, miR-15b-5p, miR-20b-5p, miR-130a -3p and miR-210-3p. These findings corroborates with our in silico analysis. In conclusion, results are very promising and may help to elucidate the mechanism of interaction between miRs and the signaling proteins involved in BK-mediated angiogenesis.

Key words: angiogenesis, microRNAs, nitric oxide

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