DOWN-REGULATION OF MIR-126 IN HUMAN RETINAL PERICYTES AFTER EXPOSURE TO EXTRACELLULAR VESICLES IN DIABETIC-LIKE CONDITIONS

Down-regulation of miR-126 in human retinal pericytes after exposure to extracellular vesicles in diabetic-like conditions

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Study design: Loss of pericytes in the early phases of diabetic retinopathy (DR) may disrupt their stable association with endothelial cells (EC), leading to EC proliferation and, eventually, angiogenesis. We have recently shown that extracellular vesicles (EV) derived from mesenchymal stem cells (MSC) in diabetic-like conditions may play a role in vessel destabilization by interfering with the strict EC/pericyte/extracellular matrix interactions. Thus they might contribute to angiogenesis through paracrine signalling; in particular, a role for MMP-2 has been described. MicroRNAs (miR) are short RNA sequences acting as gene modulators and playing important roles in angiogenesis and inflammation. In particular, down-regulation of miR-126 was observed in experimental models of DR, in diabetic retina extracts and in chorioretinal EC in hypoxic conditions, correlating with an increase in VEGF and MMP.

Purpose: Our aim in this study was to investigate miR-126 expression in pericytes in diabetic-like conditions and the possible influence of EV.

Methods: Pericytes (HRP) were cultured in physiological (NG), stable high (HG) and intermittent high (intHG) glucose conditions for 8 days. EV were extracted from the supernatant of MSC cultured in hypoxic (hypo) and/or HG conditions and added to HRP cultured in NG for 6, 24 and 48 hrs. Real-Time PCR for miR-126 was performed on RNA extracts.

Results: HRP express miR-126 and this expression is down-regulated by 20% in intHG. miR-126 expression is not significantly modified by 6 and 24 hr-EV exposure. After 48 hrs, miR-126 is up-regulated by exposure to NG-EV (+ 100% vs ctrl, $p<0.05$). HG-EV do not influence significantly miR-126 expression, while EV obtained in hypoxic conditions (NG-hypo and HG-hypo) down-regulate miR-126 by 50 and 70%, respectively ($p<0.005$, both).

Conclusions: We show for the first time in our knowledge that HRP express miR-126 and that its expression is down-regulated in diabetic-like conditions. Moreover, exposure of HRP to EV in hypoxic conditions is able to decrease miR-126 expression, consistently with previous observations of its involvement in DR and providing further insights for our findings of EV contribution to vessel destabilization.