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A pheno-morphological screen for microRNAs which regulate the phenotypic Switch in Human Aortic Vascular Smooth Muscle Cells

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VSMC can switch between a differentiated (contractile) state and a dedifferentiated (synthetic) phenotype in response to extracellular stimulation by mechanical stress.
To investigate the cell biology involved, we investigated the role of miRNAs. The current study was based on the assessment of cellular pheno-morphology with the parameters Elongation, CSI (cell shape index) and Ratio of con/syn. While always two phenotypes in parallel could be detected the Ratio (con/syn) approached 0 when all cells are in the synthetic phenotype and 1 when all cells were in the quiescent phenotype). We established and performed a high-throughput screening of miRNA (based on cellular morphology) and miRNA-Seq methods to screen for phenotypic-switch-related miRNAs, which can act as mediators and modulators of the respective phenotypes in VSMCs. From both approaches six miRNAs (miR-132, miR-138, miR-141, miR-145, miR-150, and miR-22) were filtered as the candidates which induce the phenotypic switch from synthetic to contractile in VSMCs. After analysis by KOBAS and Metascape 13 common pathways (hsa05200, hsa04310, hsa05161, hsa05169, hsa05135, hsa04140, hsa05165, hsa04380, hsa04620, hsa04926, hsa05162, hsa05225, and hsa05202) related to the six miRNAs were identified.
To the best of our knowledge this is the first study, which uses a high-throughput screening approach based on the cell morphology to isolate miRNAs which are involved in the phenotypic switch of VSMCs. In future investigations this approach will be upscaled to perform a genome wide screen. Using systems biology, these findings may be used as basis for future in-depth research.