**Table 3. Selective literature of predicted target genes that were negatively correlated to miR-203a-3p, miR-375 and miR-31-3p, whilest significant after our meta-analysis (miR-203a-3p and miR-375) or FDR significant (miR-31-3p) after correlation.**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **miRNA id** | **Gene symbol** | **r (COPD)** | **r (Healthy)** | **Meta-analysis FDR** | **Gene function** |
| miR-375 | *ARL4C* | -0.49 | -0.52 | 1.45E-06 | Involved in tumorigenesis in lung [43, 44] |
| miR-375 | *MBNL1* | -0.50 | -0.49 | 5.52E-06 | Tumorigenesis via an isoform [45], regulates alternative splicing [46] |
| miR-375 | *SLC16A2* | -0.30 | -0.53 | 3.71E-05 | Transportation of diidothyronine, thyroxine and triiodothyronine [47] |
| miR-375 | *RLF* | -0.35 | -0.45 | 2.75E-04 | Tumorgenesis [48] |
| miR-203a-3p | *PDGFD* | -0.43 | -0.37 | 9.58E-04 | Fibroblast proliferation and survival, associated with adrenal suppression [32, 33] |
| miR-375 | *TCF12* | -0.34 | -0.39 | 1.86E-03 | Tumorgenesis in several cancers. Cell differentiation, repression of E-cadherin, cell development, differentiation of lymphocytes [49-53] |
| miR-375 | *WBP1L* | -0.25 | -0.43 | 2.20E-03 | Regulates CXCR4 signalling in leukocytes and alters B-cell development [36] |
| miR-375 | *PDE5A* | -0.49 | -0.29 | 3.13E-03 | Regulates cyclic GMP, intercellular messengers that mediate the effects of extracellular signalling molecules. [54, 55] Regulates pulmonary hypertension. |
| miR-375 | *APBB2* | -0.42 | -0.32 | 3.72E-03 | Adapter protein, signal transduction [56, 57] |
| miR-375 | *ZNF385D* | -0.54 | -0.24 | 4.87E-03 |  |
| miR-375 | *CNIH4* | -0.39 | -0.33 | 5.13E-03 | Located in the secretory pathway, it promotes the exit of GPCRs [58] |
| miR-375 | *MMD* | -0.45 | -0.27 | 7.77E-03 | Macrophages activation [59], highly expressed in non-small cell lung cancer [60] |
| miR-375 | *HAS2* | -0.40 | -0.29 | 9.63E-03 | Regulates cell adhesion, extracellular matrix formation, tumorigenesis [61, 62] |
| miR-375 | *CXCL12* | -0.39 | -0.29 | 1.03E-02 | Chemoattractant for T-lymphocytes and monocytes [63] |
| miR-375 | *LDHB* | -0.41 | -0.27 | 1.35E-02 | Involved in tumorigenesis [64], a subunit of lactate dehydrogenase |
| miR-375 | *LST1* | -0.10 | -0.39 | 2.94E-02 | Inhibition of lymphocyte proliferation [65] |
| miR-375 | *DTHD1* | -0.02 | 0.44 | 3.09E-02 | Involved in apoptosis |
| miR-375 | *TRAPPC6B* | -0.28 | -0.29 | 3.73E-02 | Vesicle transport [66], involved in the secretory pathway [67] |
| miR-375 | *APBB1IP* | -0.33 | -0.26 | 4.02E-02 | Adapter protein, signal transduction [56, 57] |
| miR-203a-3p | *EBF3* | -0.58 | -0.10 | 4.22E-02 | B-cell differentiation, bone development, neurogenesis and tumour suppressor via cell cycle arrest and apoptosis [34] |
|  |  |  |  | **FDR** |  |
| miR-31-3p | *NFATC2* | -0.58 |  | 2.74E-06 | nuclear factor of activated T cells - translocates to the nucleus upon T cell receptor (TCR) - immune response [68, 69] |
| miR-31-3p | *PLCB1* | -0.50 |  | 8.61E-05 | intracellular transduction of many extracellular signals |
| miR-31-3p | *PDE5A* | -0.48 |  | 1.40E-04 | cAMP binding - smooth muscle relaxation in the cardiovascular system [39, 40] |
| miR-31-3p | *RXFP1* | -0.48 |  | 1.43E-04 |  |
| miR-31-3p | *DLC1* | -0.47 |  | 2.52E-04 | GAP family proteins participate in signalling pathways that regulate cell processes involved in cytoskeletal changes [70]. – angiogenesis [71] |
| miR-31-3p | *TOX* | -0.45 |  | 4.06E-04 | HMG box DNA binding domain. - chromatin assembly, transcription and replication [72] - T-cell development [73]. |
| miR-31-3p | *C1QTNF7* | -0.45 |  | 4.54E-04 |  |
| miR-31-3p | *PIK3CG* | -0.42 |  | 1.15E-03 | immune response, proliferation and survival [74, 75] |
| miR-31-3p | *IL15* | -0.40 |  | 1.98E-03 | regulates T and natural killer cell activation and proliferation [76] |
| miR-31-3p | *DIRAS3* | -0.40 |  | 2.24E-03 | Inhibits RAS/MAPK signaling [77] |
| miR-31-3p | *WASF3* | -0.38 |  | 4.02E-03 | transduce signals that involve changes in cell shape, motility or function [78] |
| miR-31-3p | *LGI2* | -0.37 |  | 4.53E-03 |  |
| miR-31-3p | *KCNIP2* | -0.37 |  | 4.54E-03 | Voltage-gated potassium channels |
| miR-31-3p | *TMOD2* | -0.36 |  | 5.48E-03 | actin regulatory protein [78] |
| miR-31-3p | *RAB3C* | -0.35 |  | 8.29E-03 |  |