**MicroRNA-223** **negatively regulates the osteogenic differentiation of periodontal ligament derived cells by directly targeting growth factor receptors**

**Running title:** miR-223 inhibits PDLSCs osteogenesis

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**Supplementary table 1**. The primer sequences used in the present study.

|  |  |  |
| --- | --- | --- |
| **Species** | **Gene name** | **Primer sequence (5′-3′)** |
| **Forward primer** | **Reverse primer** |
| **Human** | GAPDH | GCACCGTCAAGGCTGAGAAC | ATGGTGGTGAAGACGCCAGT |
|  | OPN | CGCAGACCTGACATCCAGT | GGCTGTCCCAATCAGAAGG |
|  | OCN | GTAGTGAAGAGACCCAGGCG | CTCCTGAAAGCCGATGTGGT |
|  | Runx2 | AGGCAGTTCCCAAGCATTTCATCC | TGGCAGGTAGGTGTGGTAGTGAG |
|  | FGFR2 | GCATCGCATTGGAGGCTA | TGTGATTGATGGACCCGTATT |
|  | TGFβR2 | GTATCGCCAGCACGATCCCA | CTCGTCATTCTTTCTCCATACAGC |
|  | U6 | GGTCTCGCTTCGGCAGCACA |
|  | miR-223 | TGTCAGTTTGTCAAATACCCCAAA |

**Supplementary table 2**. The clinical characteristics of the participants.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Control group** | **Periodontitis group** | **p-Value** |
| **Number of subjects**  | 20 | 20 |  |
| **Age (year)** | 42.55 ± 8.66 | 41.95 ± 8.12 | 0.82 |
| **Gender (F/M)** | 10/10 | 9/10 | 1.00 |
| **Mean PI** | 0.40 ± 0.26 | 2.00 ± 0.40 | < 0.001 |
| **Mean GI** | 0.15 ± 0.24 | 1.90 ± 0.38  | < 0.001 |
| **Mean BI** | 0.00 ± 0.00 | 3.08 ± 0.57 | < 0.001 |
| **Mean PD (mm)** | 2.17 ± 0.34 | 4.51 ± 1.11 | < 0.001 |
| **Mean AL (mm)** | 0.34 ± 0.13 | 3.60 ± 1.02  | < 0.001 |

Data are presented as mean ± standard deviation, or number of subjects.

AL, attachment loss; BI, bleeding index; GI, gingival index; PD, pocket depth; PI, plaque index.

**Supplementary table 3**. The target genes of miR-223.

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| FBXW7 | PHF19 | WDR77 | SRP19 | MAP4 | TMEM47 | PRKCE | TGFBR3 | RBBP4 | STYX | SESN3 |
| RHOB | **ARMC1** | **SSRP1** | **PFN2** | **PHF20L1** | **EPSTI1** | **NRF1** | **ZBTB41** | **LRP12** | **RRAS2** | **PSD3** |
| LELP1 | **SLC25A32** | **CTNNA2** | **XKR6** | **MPZ** | **PKP4** | **CNOT2** | **JMY** | **RORB** | **SH3D19** | **TNRC6B** |
| PTS | **NDP** | **XPR1** | **POU2F1** | **MARCH3** | **SOX11** | **ERC1** | **PLEKHA3** | **SLC35F1** | **SOX6** | **ZIC1** |
| TBC1D17 | **ATP10D** | **DESI2** | **ERO1LB** | **MYBL1** | **PDE4D** | **VAV3** | **CNDP1** | **PFKFB3** | **RAB10** | **TBC1D15** |
| RP11-192H23.4 | **PEX16** | **SHOX2** | **SCARB1** | **EIF4E3** | **RALGPS2** | **KIAA1468** | **ATL2** | **C8orf46** | **CALML4** | **ATG7** |
| WDR62 | **TNNI3K** | **ATP1B1** | **SMARCD1** | **RPS6KB1** | **USP6NL** | **MTMR2** | **TRPV2** | **MBNL1** | **RIMS3** | **FAM83D** |
| LACC1 | **MID1IP1** | **ARPP19** | **MMP16** | **CCT3** | **BAI3** | **MAFB** | **RNF4** | **FOXP1** | **DLEU1** | **MEF2D** |
| GTSF1 | **SEPT8** | **SCAF8** | **RYBP** | **LHX8** | **FGFR2** | **VMP1** | **SECISBP2L** | **HEY2** | **HNMT** | **PHKG2** |
| GALNT18 | **ARPC5L** | **POMP** | **SLC24A2** | **SCN1A** | **PDE3B** | **PLEKHH1** | **KIAA1755** | **NRXN3** | **IFNLR1** | **GPR22** |
| GTPBP8 | **FPGT-TNNI3K** | **NXF1** | **ATP2B1** | **KBTBD6** | **CCNT2** | **TSHZ3** | **ZFX** | **TOP2B** | **NCOA1** | **MCMBP** |
| CCDC149 | **RWDD1** | **ADCYAP1** | **PLAGL2** | **G3BP1** | **SPATA13** | **GPR155** | **DENND5B** | **KMT2C** | **RSBN1L** | **PPP1R15A** |
| C18orf54 | **RCN2** | **PTBP2** | **LRRC19** | **ZEB1** | **OPCML** | **WBP1L** | **GTDC1** | **CARM1** | **PRR14L** | **WDR7** |
| SNX24 | **PURB** | **KLF7** | **FAM46A** | **ZFHX3** | **HMGCS1** | **SDC2** | **AGO3** | **FRMD4A** | **SRGAP3** | **LRRC40** |
| FBXO8 | **CDK17** | **PAX5** | **SPRED1** | **PDS5B** | **LIF** | **MTSS1** | **FBXO28** | **POLR1C** | **TRMT2B** | **AGMO** |
| IL6ST | **MEF2C** | **F3** | **C10orf11** | **RAP2A** | **PRKACB** | **PLCE1** | **ANKFY1** | **WDR43** | **HDAC4** |  |
| PDZD11 | **APC** | **NUP210** | **ACTRT3** | **METAP1** | **ZXDB** | **TSC22D1** | **ZNF395** | **PDPK1** | **GLUL** |  |
| ATP7A | **LYPD6** | **ULK2** | **RASSF4** | **ZZZ3** | **RPS15A** | **IGF1R** | **PIK3C2A** | **PSMA5** | **ZBTB40** |  |
| FOXO1 | **RASA1** | **CLSTN1** | **VHL** | **BRINP3** | **TXLNG** | **CSNK1G1** | **FAM168A** | **ZNF706** | **C17orf75** |  |
| ARMCX1 | **SLC39A1** | **PURA** | **NAA50** | **CNOT1** | **ZBTB10** | **PA2G4** | **CPEB3** | **ELL2** | **UBE2A** |  |
| CYTIP | **PROKR2** | **KAT6A** | **RFTN2** | **NF2** | **TBC1D4** | **DCUN1D3** | **NUDT3** | **E2F1** | **MAP2K6** |  |
| ECT2 | **BRMS1L** | **NLRP3** | **ANKRD17** | **MFSD6** | **RBPJ** | **PAPD5** | **SP1** | **RP11-10A14.4** | **CCDC85C** |  |
| SLC4A4 | **TMEM178B** | **SLCO1A2** | **MMP19** | **FAM98A** | **TAOK3** | **NFIC** | **RC3H1** | **TGFBR2** | **TET3** |  |
| SLC37A3 | **KIAA0226L** | **GPM6B** | **STIM1** | **WASL** | **LONP2** | **EPOR** | **SH2B3** | **ABHD13** | **NOVA2** |  |
| LMO2 | **SLC8A1** | **KPNA3** | **KLF12** | **GABPB2** | **KIF4A** | **CREBZF** | **MAT2B** | **MGA** | **CLPB** |  |
| LAYN | **CRIM1** | **GFPT1** | **COPS2** | **DNAJC6** | **UBE2W** | **RNF217** | **SETBP1** | **TIAL1** | **WDR26** |  |
| INPP5B | **VAMP2** | **MBNL3** | **KLK15** | **FZD4** | **FNBP1L** | **ZXDA** | **SELT** | **HIPK2** | **SNCA** |  |
| RNF145 | **SEPT6** | **NUTF2** | **FOXO3** | **PHIP** | **ZCCHC14** | **ELF2** | **C11orf30** | **TMED7** | **VTI1A** |  |
| ACSL3 | **SREK1** | **SLC23A2** | **ST8SIA3** | **STK39** | **SCN3A** | **AEBP2** | **UHMK1** | **VPS39** | **RP11-315D16.2** |  |
| HSP90B1 | **CTSV** | **MSMO1** | **DOCK2** | **APOBEC4** | **GNA13** | **GRAMD4** | **ZBTB18** | **EBF3** | **ZNF507** |  |
| NFIA | **SRSF10** | **CSPG5** | **ITPR3** | **ZC3H6** | **C14orf142** | **ENPP5** | **KIAA0355** | **FAM46C** | **KCNMB4** |  |
| FAM199X | **PRDM1** | **TMEM64** | **ARID1A** | **MSI2** | **UCP3** | **FBXL4** | **ABCG4** | **ZNF207** | **GRHPR** |  |
| HLF | **SEPT4** | **COPS8** | **SYNCRIP** | **ZBTB4** | **NFASC** | **MAP1B** | **PDS5A** | **MYCBP** | **RGS9BP** |  |
| SP3 | **CBLB** | **HHEX** | **KANSL1L** | **OTUD4** | **UQCC1** | **TSPAN5** | **PHLPP1** | **SRPK2** | **PAX6** |  |
| DNAJB13 | **RNF34** | **INPP4A** | **ELP4** | **SCN2A** | **CEP41** | **SPTLC2** | **CBX5** | **MBOAT2** | **U2SURP** |  |
| SIAH1 | **NUCKS1** | **UBXN1** | **EYA3** | **FAT1** | **ZSCAN12** | **FDX1L** | **ZFP3** | **PCDH12** | **CAND1** |  |
| RGS1 | **ST3GAL1** | **NDNF** | **AKAP1** | **TCERG1** | **MYH10** | **MOSPD1** | **FUBP3** | **CDYL** | **EIF5B** |  |
| ACVR2A | **SORBS1** | **USP42** | **BRPF3** | **ZSWIM7** | **TMEM170A** | **GLIPR1** | **AIFM1** | **FBXO30** | **RBMS2** |  |
| SYAP1 | **NFIB** | **SGMS2** | **SMOC1** | **TMC5** | **ATXN7L1** | **ELK4** | **ABI2** | **TWIST1** | **PKNOX1** |  |
| USP16 | **RERG** | **RAB8B** | **KIAA0226** | **POLR3E** | **RBM20** | **SPPL2A** | **CHUK** | **FAM160B1** | **NLE1** |  |



**Supplementary Fig**. 1 The PPI network of miR-223 target genes.