frontiers

Supplementary Material

1 Supplementary Figures

1.1 Figure S1

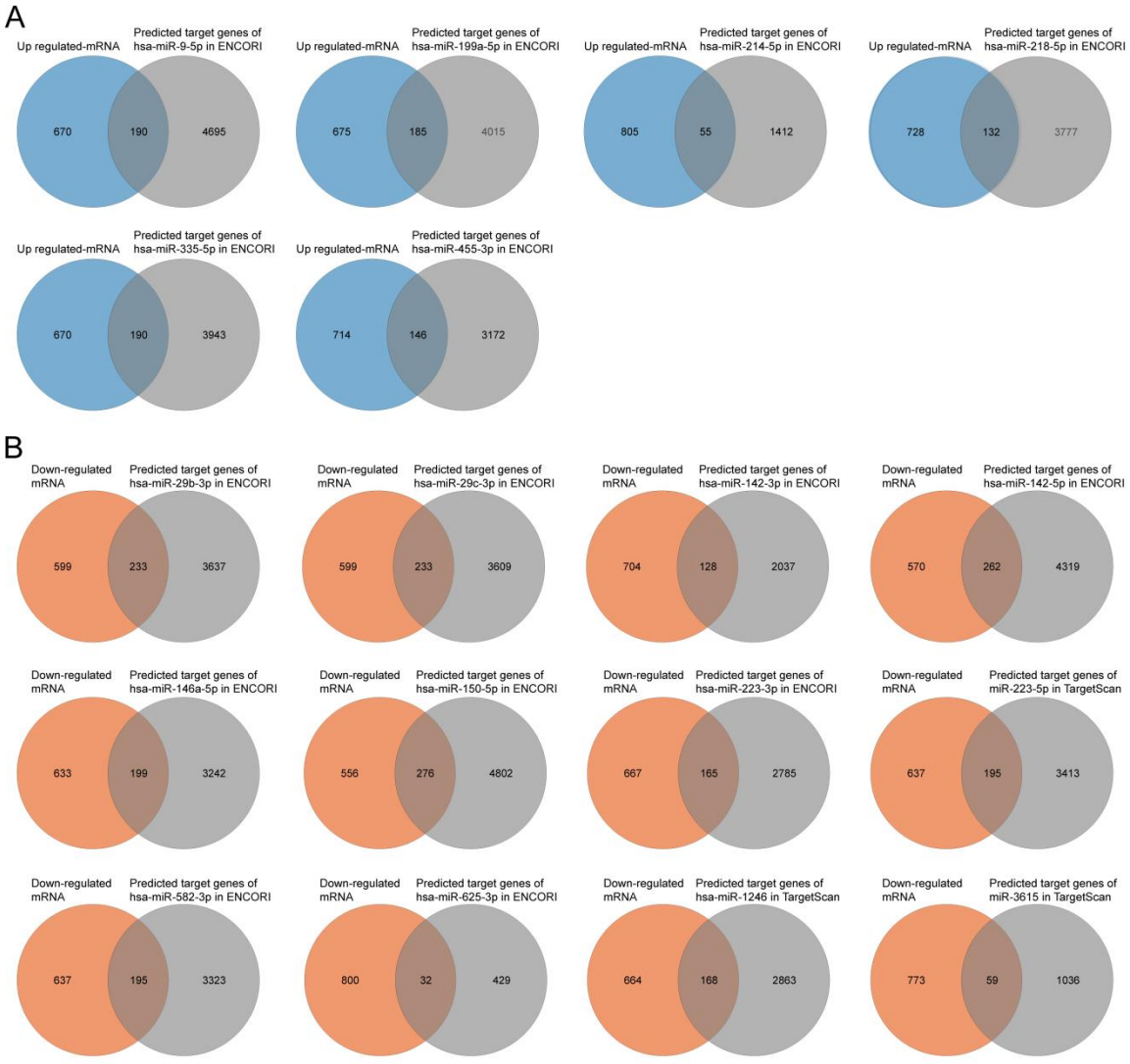


Figure S1. Intersection genes of the DE-mRNAs and the predicted target genes of DE-miRNAs. **(A)** The up-regulated mRNAs intersected with the predicted target genes of 6 down-regulated miRNAs. (**B)** The down-regulated mRNAs intersected with the predicted target genes of 12 up-regulated miRNAs.

1.2 Figure S2

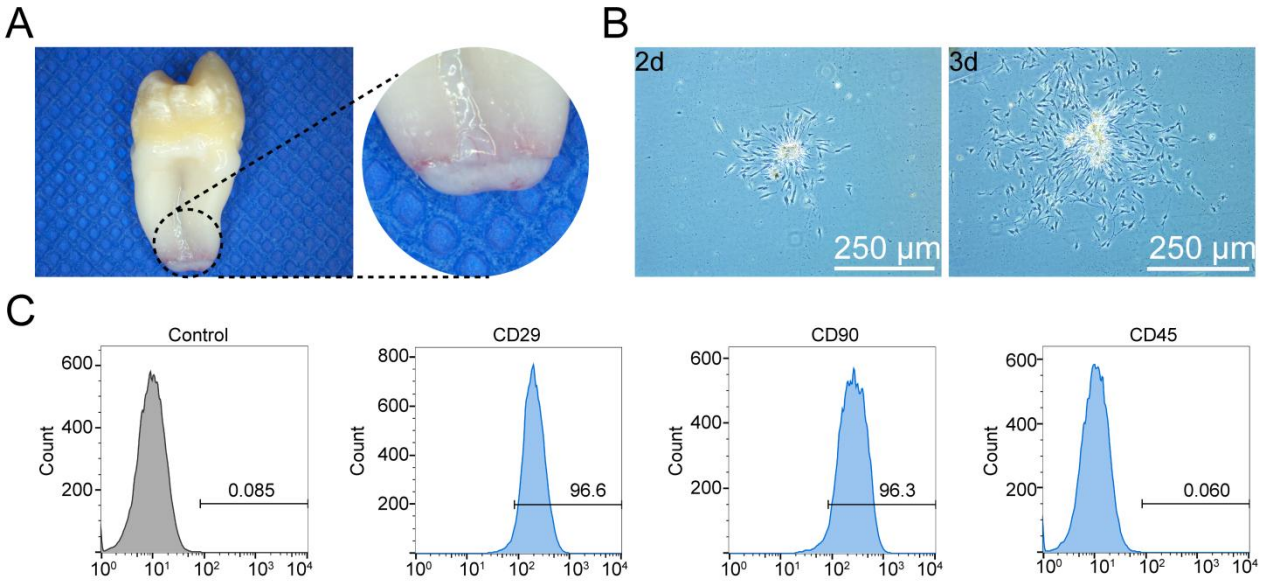


Figure S2. Isolation and identification of hSCAPs. (A) The apical papilla of immature young permanent teeth (dotted circles). (**B)** Primary hSCAPs on days 2 and 3. (**C)** Flow cytometric analysis of hSCAPs. Percentage values showed their positive expression patterns.

1.3 Figure S3

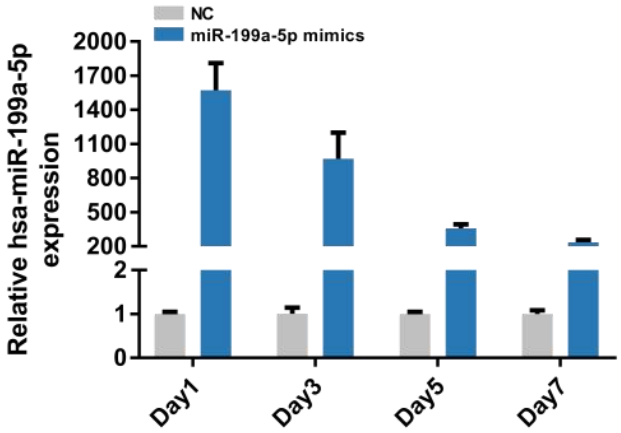


Figure S3. The relative expression level of miR-199a-5p after transfection of miR-199a-5p mimics into hSCAPs in vitro for several days.

1.4 Figure S4

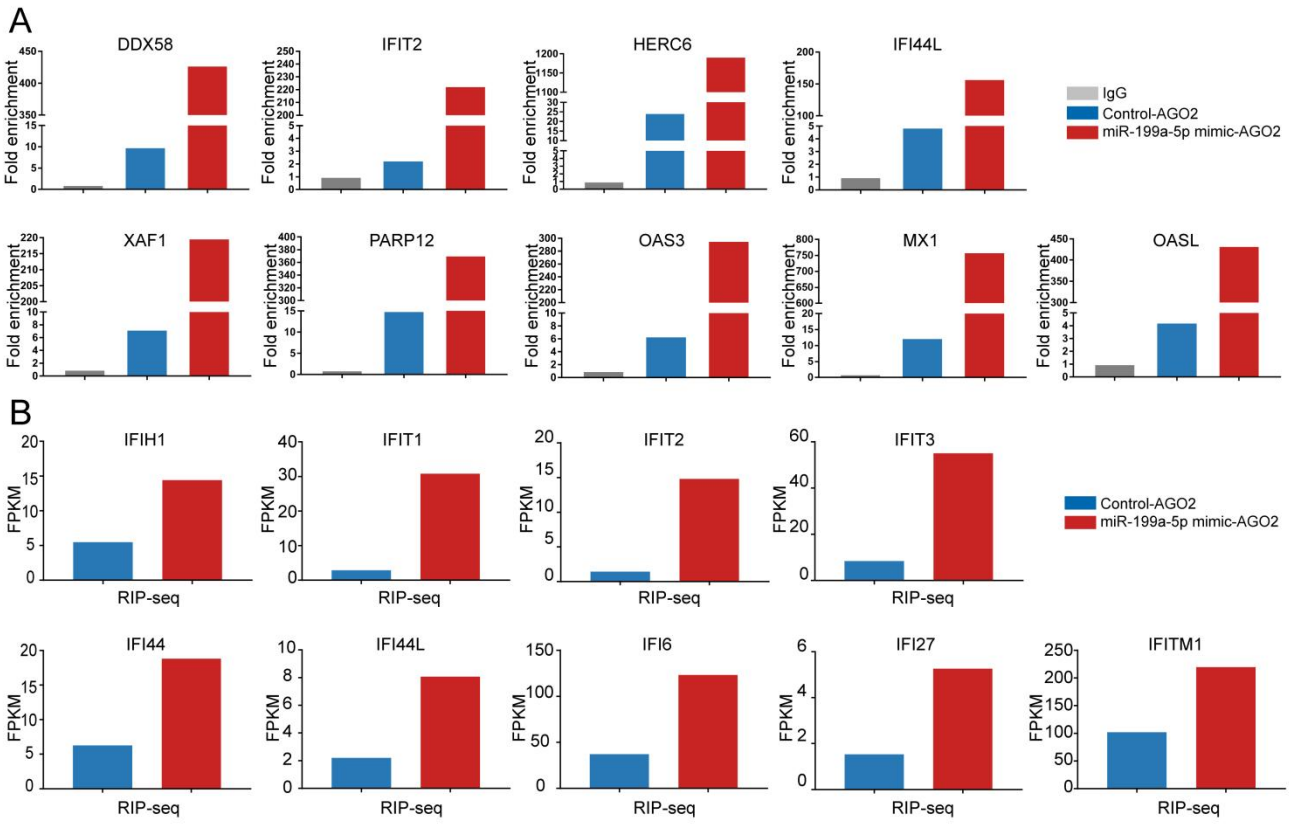
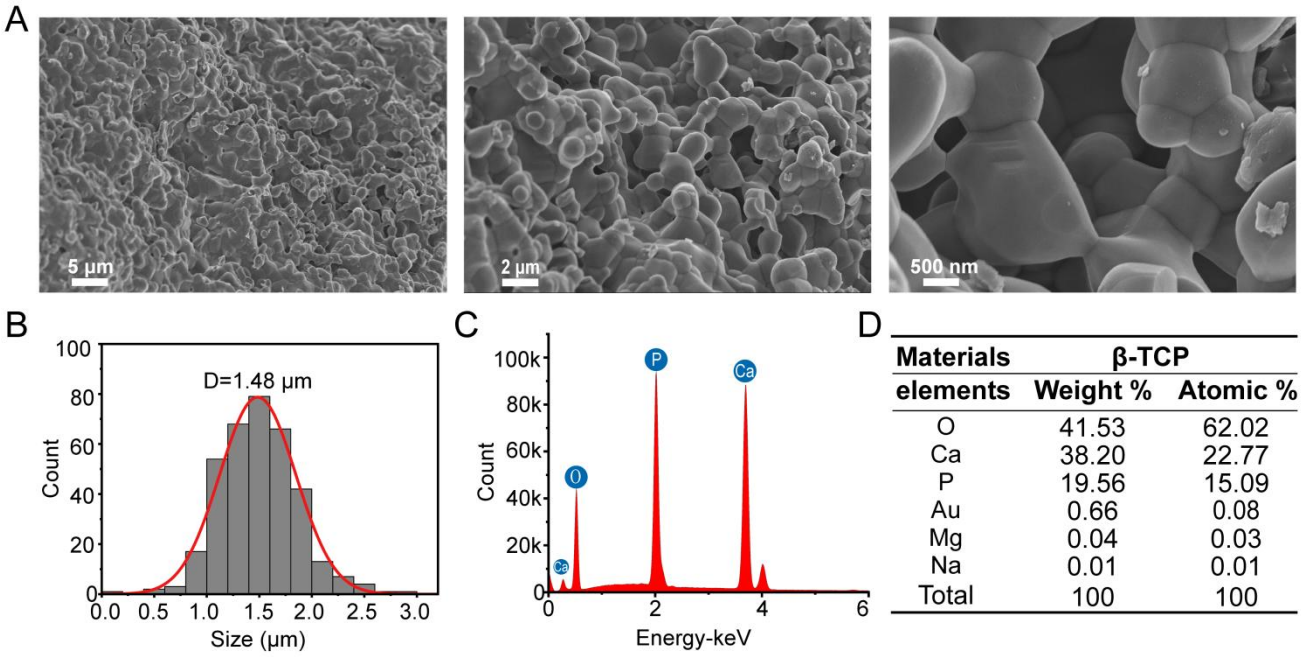


Figure S4. The relative expression level of 9 potential target genes and ISG family genes in RIP products. (A) The relative expression level of 9 potential target genes in anti-AGO2 immunoprecipitates between the miR-199a-5p overexpression group and the control group by qPCR. **(B)** ISG family genes including IFIT1, IFIT2, IFIT3, and IFI44L enriched in anti-AGO2 immunoprecipitates.

1.5 Figure S5



Materials	β-TCP	
elements	Weight %	Atomic %
O	41.53	62.02
Ca	38.20	22.77
P	19.56	15.09
Au	0.66	0.08
Mg	0.04	0.03
Na	0.01	0.01
Total	100	100

Figure S5. The physical and chemical properties of *β*-TCP ceramic particles. (A) The SEM images of *β*-TCP ceramic particles. **(B)** Analysis of particle size distribution. **(C, D)** EDS analysis of the scaffolds.

1.6 Figure S6

A

Variable	Frequency	Percent	Mean
Age (yrs) (mean±SD)			7
Patient (healthy control/AP)	36(13/23)	36.1/63.9	
Gender (M/F)	14/22	38.9/61.1	
Apical periodontitis (PAI score:3/4/5)	4/8/11	17.4/34.8/47.8	
healthy control (PAI score:1/2)	10/3	76.9/23.1	

B

PAI Score	Bone alterations in mineral structures
1	Normal periapical structures
2	Small changes in bone structures
3	Change in bone structure with mineral loss
4	Periodontitis with well-defined radiolucent area
5	Severe periodontitis with exacerbating features

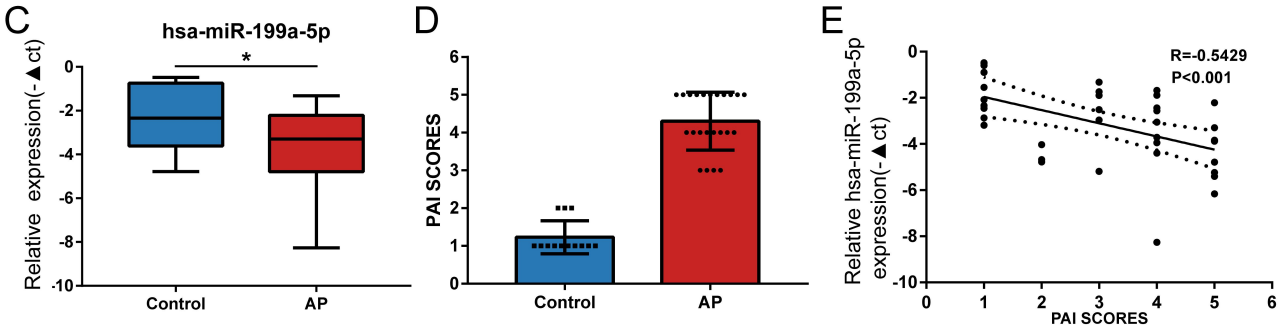


Figure S6. (A) The characteristics of the patients.**(B)** periapical index (PAI) scoring system (Venskutonis, 2016). **(C)** The relative expression of miR-199a-5p in the healthy control and AP groups. **(D)** The PAI scores in the healthy control and AP samplesgroups. **(E)** Spearman correlation analyses between the PAI scores and miR-199a-5p expression in periapical tissue samples (n = 36). Data were presented as the mean ± SD. *$p < 0.05$.

2. Supplementary Tables

2.1 Table S1. Inclusion and exclusion criteria

	inclusions criteria	exclusions criteria
Control	1. Children aged 6-8 years whose permanent anterior teeth have erupted and the corresponding deciduous teeth have not yet fallen out (i.e., Retained deciduous teeth) 2. Retained anterior deciduous teeth without caries 3. The remaining root length of the retained anterior deciduous teeth is greater than 2/3.	1. Children older than 8 years old or younger than 6 years old. 2. Children with systemic diseases: e.g. heart disease, asthma, diabetes, etc. 3. Retained anterior teeth with caries. 4. Root resorption of anterior teeth greater than 1/3.
AP	1. Children aged 6-8 years whose deciduous molar teeth have not yet undergone physiological roots resorption. 2. Indications for extraction of deciduous molars with severe periapical periodontitis: a) teeth with inflammatory root resorption and ineffective root canal treatment; b) Periapical inflammation spreading to the underlying permanent tooth germ.	1. Children older than 8 years old or younger than 6 years old. 2. Children with systemic diseases: e.g. heart disease, asthma,diabetes, etc. 3. Teeth with apical periodontitis of non-carious origins.

2.2 Table S2. sequences of hsa-miR-199a-5p mimics and antagomir

Gene	sequence(5'-3')
hsa-miR-199a-5p-mimics-ss	CCCAGUGUUCAGACUACCUGUUC
hsa-miR-199a-5p-mimics-as	ACAGGUAGUCUGAACACUGGGUU
hsa-miR-199a-5p-antagomir	ACAGGUAGUCUGAACACUGGGUU

2.3 Table S3. List of the primers used in the study

Gene	Sequence	Use
GAPDH	Forward GTCTCCTCTGACTTCAACAGCG Reverse ACCACCCTGTTGCTGTAGCCAA	qRT-PCR
RUNX2	Forward CCCAGTATGAGAGTAGGTGTCC Reverse GGGTAAGACTGGTCATAGGACC	
OSX	Forward TTCTGCGGCAAGAGGTTCACTC Reverse GTGTTTGCTCAGGTGGTCGCTT	
ALP	Forward GCTGTAAGGACATCGCCTACCA Reverse CCTGGCTTTCTCGTCACTCTCA	
OCN	Forward CGCTACCTGTATCAATGGCTGG Reverse CTCCTGAAAGCCGATGTGGTCA	
OPN	Forward CGAGGTGATAGTGTGGTTTATGG Reverse GCACCATTCAACTCCTCGCTTTC	
IFIT2	Forward GGAGCAGATTCTGAGGCTTTGC Reverse GGATGAGGCTTCCAGACTCCAA	
MX1	Forward GGCTGTTTACCAGACTCCGACA Reverse CACAAAGCCTGGCAGCTCTCTA	
OASL	Forward GAGTGGAAGGAAGAGGTGCTAGA Reverse TCCATATCAGCCTCAGAACATCTT	
IFI44L	Forward TGCACTGAGGCAGATGCTGCG Reverse TCATTGCGGCACACCAGTACAG	
DDX58	Forward CACCTCAGTTGCTGATGAAGGC Reverse GTCAGAAGGAAGCACTTGCTACC	
HERC6	Forward GGAGAAACGACTTCCATTGATGTG Reverse AGCTCTGAGCAGATCATCCTCG	
XAF1	Forward CCTCCATGAGGCTTACTGCCTG Reverse GAAACTCCAGCGAGGACTTCTG	
OAS3	Forward CCTGATTCTGCTGGTGAAGCAC Reverse TCCCAGGCAAAGATGGTGAGGA	
PARP12	Forward CTCTGTCACCAAACCTCCACAC Reverse GCTACTGCTGACAGTGGTCACA	

2.4 Table S4. List of the primers used in the study

Gene	Sequence	Use
hsa-miR-199a-5p	Forward GCCCAGTGTTCAGACTACCTGTT	qRT-PCR (tailed)
hsa-miR-335-5p	Forward GGTCAAGAGCAATAACGAAAAATG	
hsa-miR-9-5p	Forward CGAGTCTTTGGTTATCTAGCTGTATG	
hsa-miR-218-5p	Forward CGAGTTGTGCTTGATCTAACCAT	
hsa-miR-455-3p	Forward GGCAGTCCATGGGCATATACA	
hsa-miR-29b-3p	Forward GAGTAGCACCATTTGAAATCAGTGT	
hsa-miR-223-3p	Forward GAGTGTCAGTTTGTCAAATACCCC	
U6	Forward CTCGCTTCGGCAGCACA Reverse AACGCTTCACGAATTTGCGT	
hsa-miR-199a-5p	Forward GGCCCCAGTGTTCAGACTAC Common-Reverse ACTGCAGGGTCCGAGGTATT	qRT-PCR (Stem-loop)
hsa-miR-199a-5p	GTCGTATCGACTGCAGGGTCCGAGGTATTCGCAGTCG ATACGACGAACAG	RT (Stem-loop)
siIFIT2-1	Forward CCUGGAAUGCUUACGUAAA Reverse UUUACGUAAGCAUUCCAGG	siRNA silencing
siIFIT2-2	Forward GCCAGACAAAGCGAUUGAA Reverse UUCAAUCGCUUUGUCUGGC	
siIFIT2-3	Forward CUCAGACGUUCAGAUUUAU Reverse AUAAAUCUGAACGUCUGAG	

Reference

VENSKUTONIS, T. 2016. Periapical tissue evaluation: analysis of existing indexes and application of Periapical and Endodontic Status Scale (PESS) in clinical practice. *Giornale Italiano di Endodonzia,* 30**,** 14-21.