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Supplemental information

Exosomal miR-205-5p enhances angiogenesis and nasopharyngeal carcinoma metastasis by targeting *desmocollin-2*

Wenjuan Yang, Shiming Tan, Lixia Yang, Xiaohui Chen, Ruiqian Yang, Linda Oyang, Jinguan Lin, Longzheng Xia, Nayiyuan Wu, Yaqian Han, Yanyan Tang, Min Su, Xia Luo, Yiqing Yang, Lisheng Huang, Zifan Hu, Yi Tao, Lin Liu, Yi Jin, Hui Wang, Qianjin Liao, and Yujuan Zhou

Supplementary figure legends:

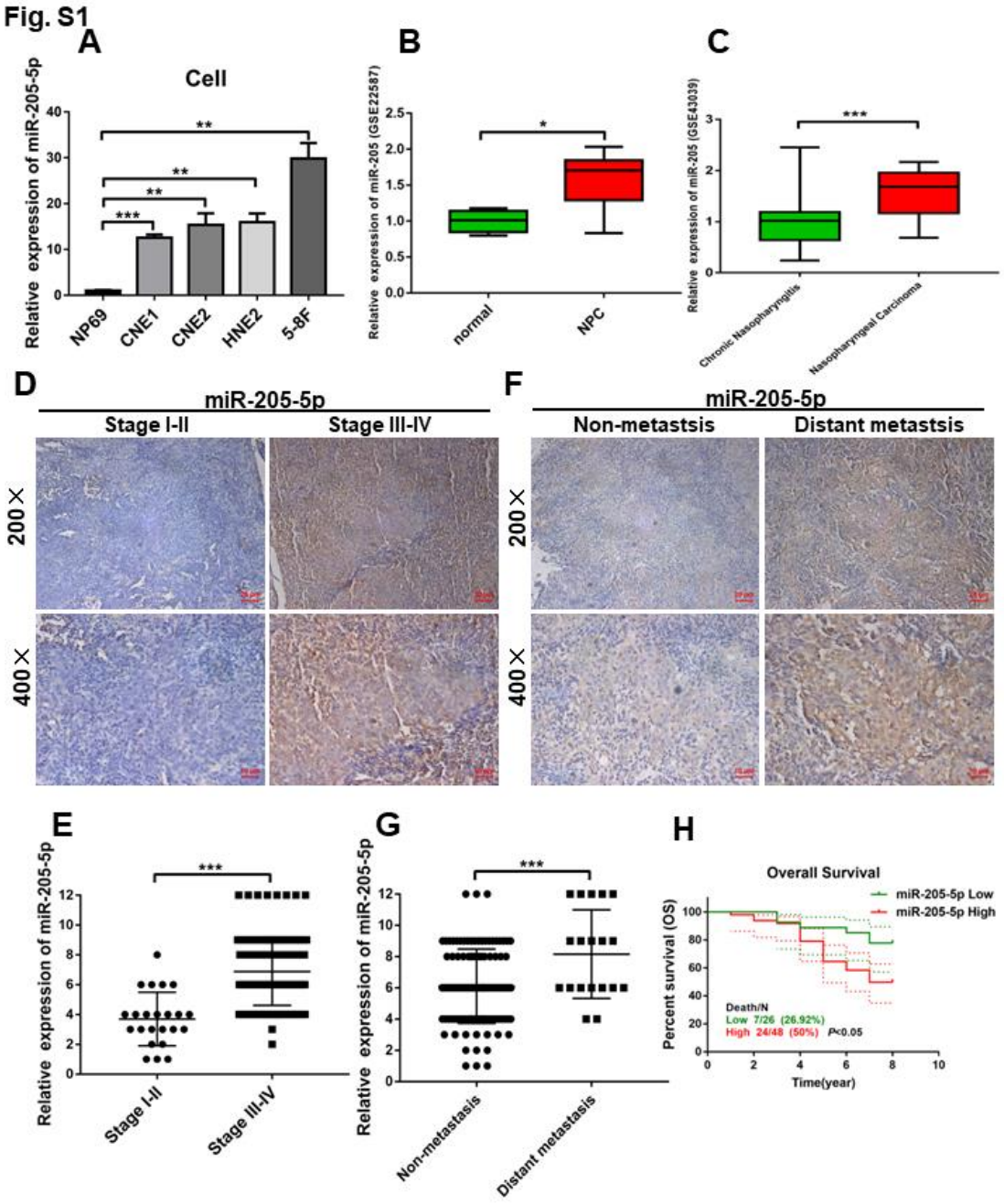

Figure S1. Up-regulated miR-205-5p transcripts are linked to tumor progression and worse prognosis of NPC. (A) The relative levels of miR-205-5p transcripts in the indicated cell lines, determined by qRT-PCR. **(B and C)** The levels of miR-205 transcripts in NPC (n=28) and control (n=24) tissues of the GSE22587 and GSE43039. **(D, E)** ISH analysis of miR-205-5p transcripts in stage I-II (n=23) and stage III-IV

(n=112) of NPC tissues. The scale bar in 200× images represents 50 μm. The scale bar in 400× images represents 10 μm. **(F, G)** ISH analysis of miR-205-5p transcripts in NPC (n=135) and distant metastatic NPC (n=19) tissues. The scale bar in 200× images represents 50 μm. The scale bar in 400× images represents 10 μm. **(H)** High levels miR-205-5p transcripts were associated with worse overall survival of NPC patients (n=48 for high; n=27 for low). Data are representative images (magnification x 200 and x 400) or expressed as individual values, mean ± SD or mean ± 49.6% interquartile range (IQR) from three separate experiments. * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

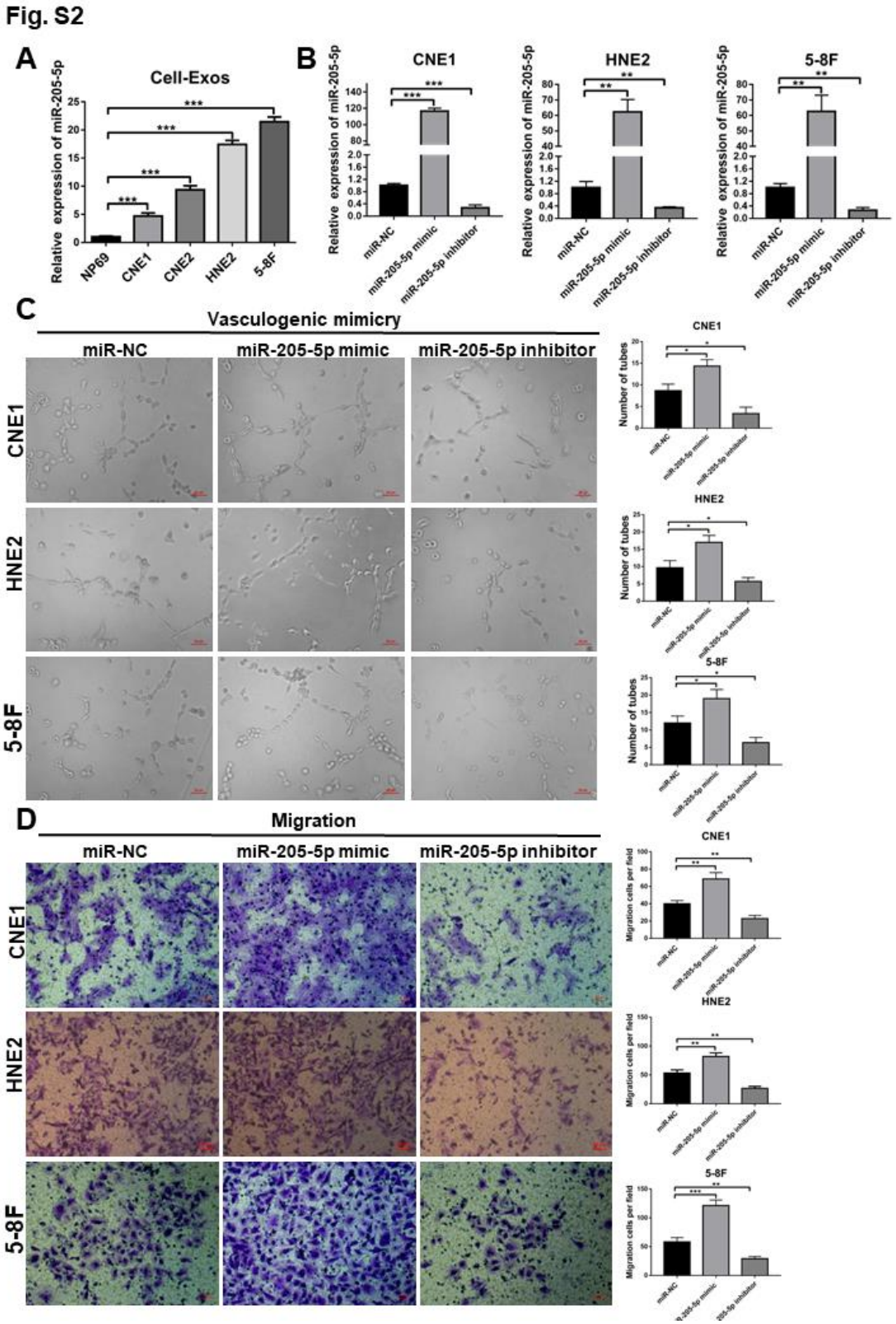

Figure S2. MiR-205-5p promotes the VM and migration of NPC cells.

(A) The relative levels of exosomal miR-205-5p in the supernatants of cultured cells, determined by qRT-PCR. **(B)** qRT-PCR verification of miR-205-5p over-expression

and silencing in NPC cells. **(C, D)** Altered miR-205-5p transcripts affected the VM, migration and invasion of the indicated NPC cells. These data indicated that miR-205-5p over-expression significantly enhanced the VM and migration of the indicated NPC cells *in vitro*. Scale bar, 20 μm. Data are representative images or expressed as mean ± SD of each group from three separate experiments. * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

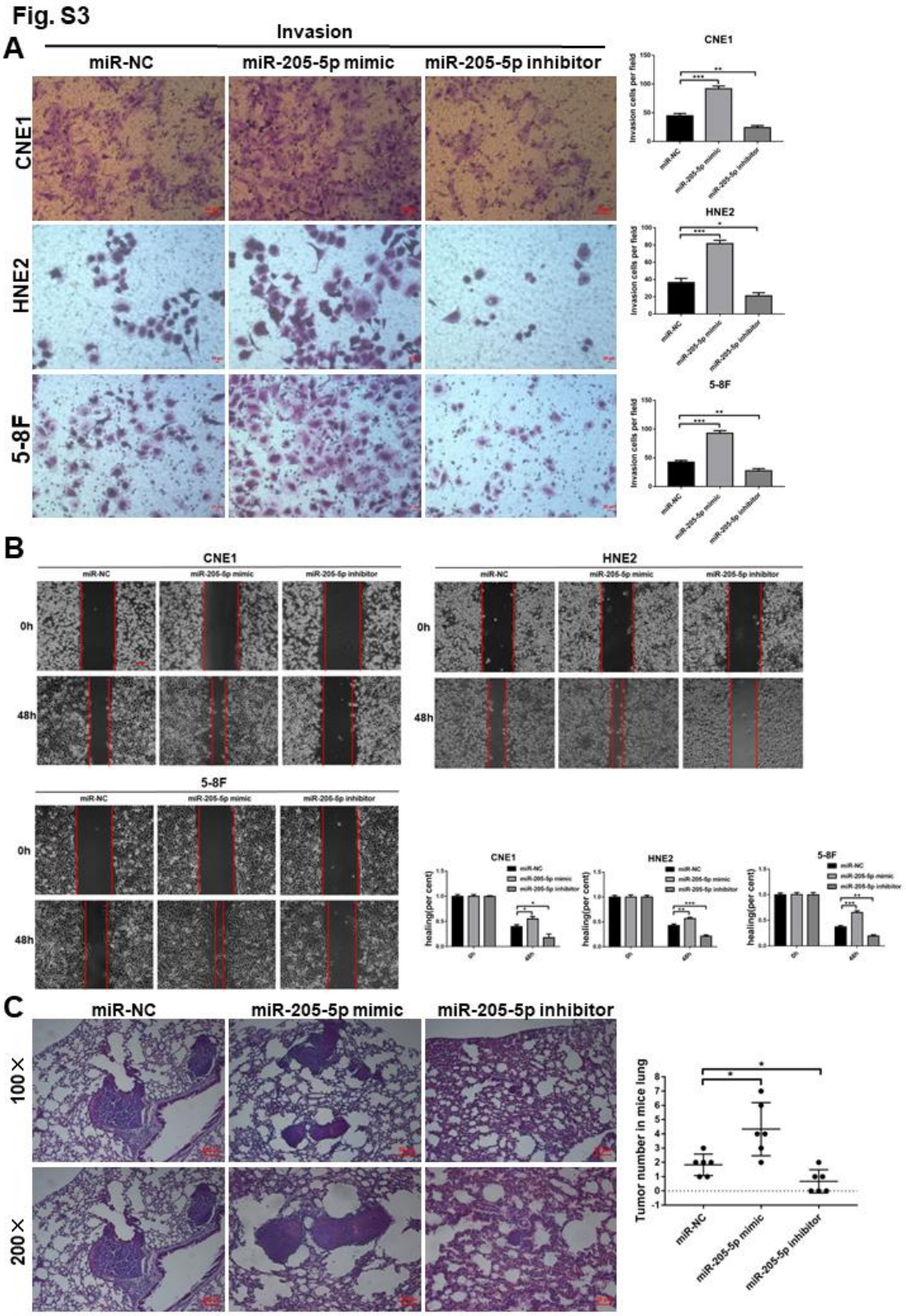

Figure S3. MiR-205-5p enhances the metastatic behaviors of NPC cells.

Altered levels of miR-205-5p transcripts modulated invasion **(A)**, wound healing (**B**) of NPC cells. The scale bar in (A) represents 20 μm. The scale bar in (B) represents

100 μm. **(C)** Altered levels of miR-205-5p transcripts affected the lung metastasis of 5-8F tumors in mice (N=6 per group)**.** These data indicated that miR-205-5p over-expression significantly enhanced the invasion and would healing of the indicated NPC cells *in vitro* and lung metastasis of 5-8F tumors *in vivo* while miR-205-5p inhibition had opposite effects. Data are representative images (magnification x 200) or expressed as mean ± SD of each group from three separate experiments. The scale bar in 100× images represents 100 μm. The scale bar in 200× images represents 50 μm. * $P<0.05$, ** $P<0.01$, *** $P<0.001$.

Fig. S4

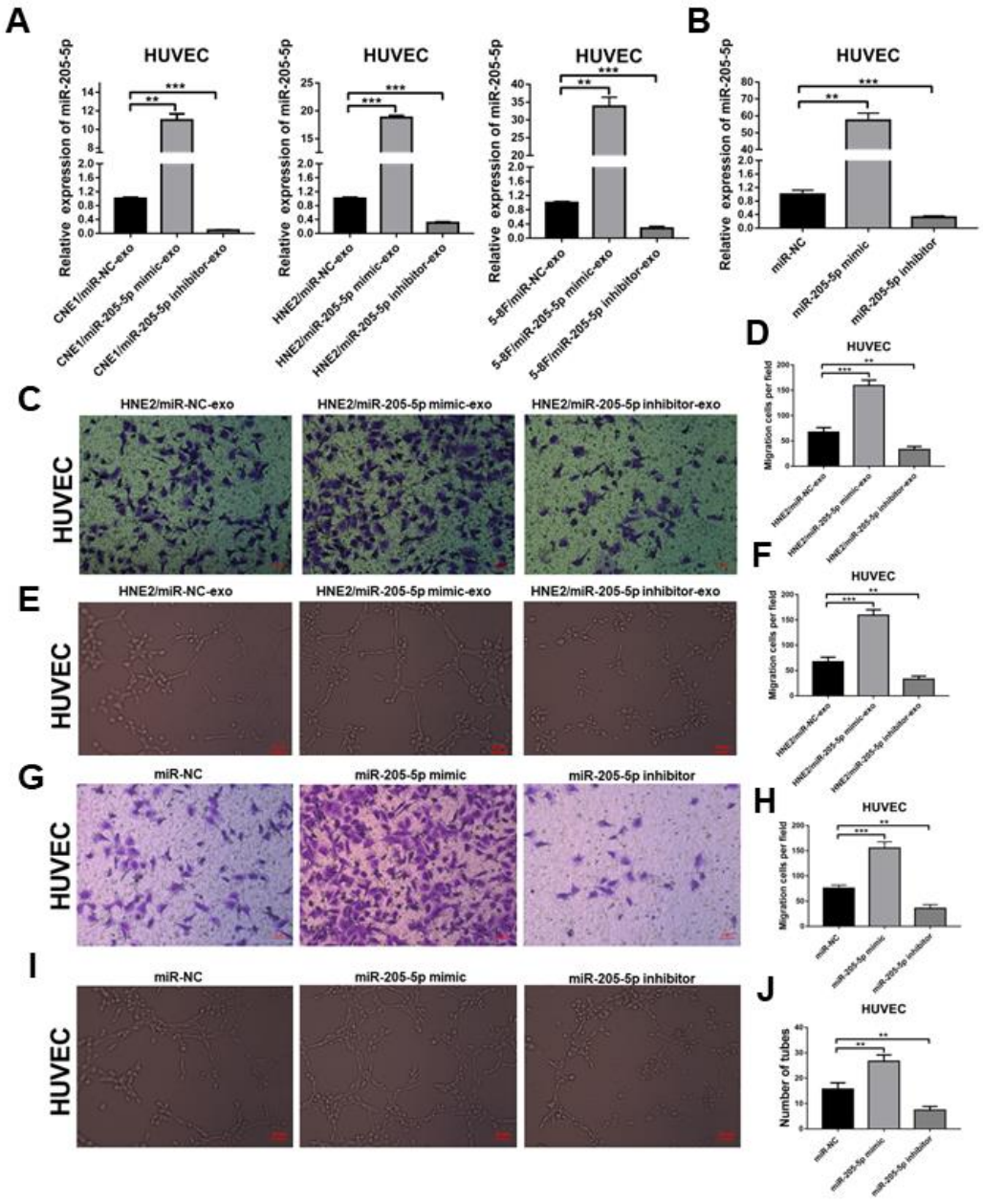

Figure S4. Exosomal miR-205-5p from different groups of NPC cells modulates the migration and tube formation of HUVECs. (A) Treatment with exosomes from the different groups of NPC cells altered the relative levels of miR-205-5p transcripts in HUVECs. **(B)** qRT-PCR verification of the efficiency of transfection with the indicated miRNA in HUVECs. **(C-F)** Treatment with exosomes from the miR-205-5p mimic-transfected HNE2 cells enhanced the migration and tube formation of HUVECs while treatment with exosomes from the miR-205-5p inhibitor-transfected HNE2 cells had opposite effects. Scale bar, 20 μm. **(G-J)** Transfection with miR-205-5p mimic significantly increased the migration and tube formation of

HUVECs while transfection with miR-205-5p inhibitor had opposite effects. Scale bar, 20 μm. Data are representative images or expressed as mean ± SD of each group from three separate experiments. ** P<0.01, *** P<0.001.

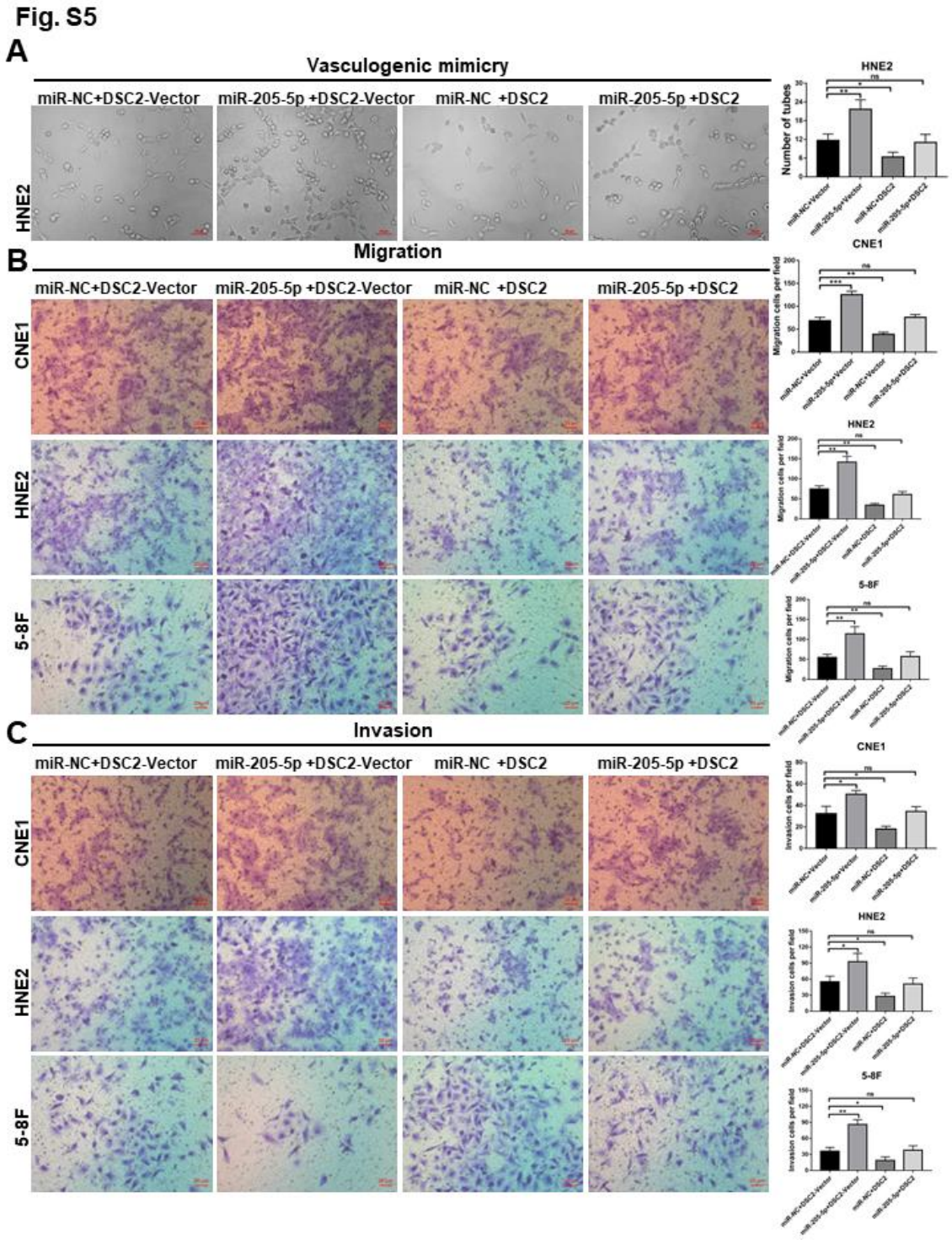

Figure S5. DSC2 over-expression abrogates the miR-205-5p-enhanced VM, migration and invasion in NPC cells.

(A-C) DSC2 over-expression abrogated the miR-205-5p-enhanced VM, migration and invasion of NPC cells. Data are representative images or expressed as mean ± SD of each group from three separate experiments. Scale bar, 20 μm. * *P*<0.05, ** *P*<0.01, *** *P*<0.001.

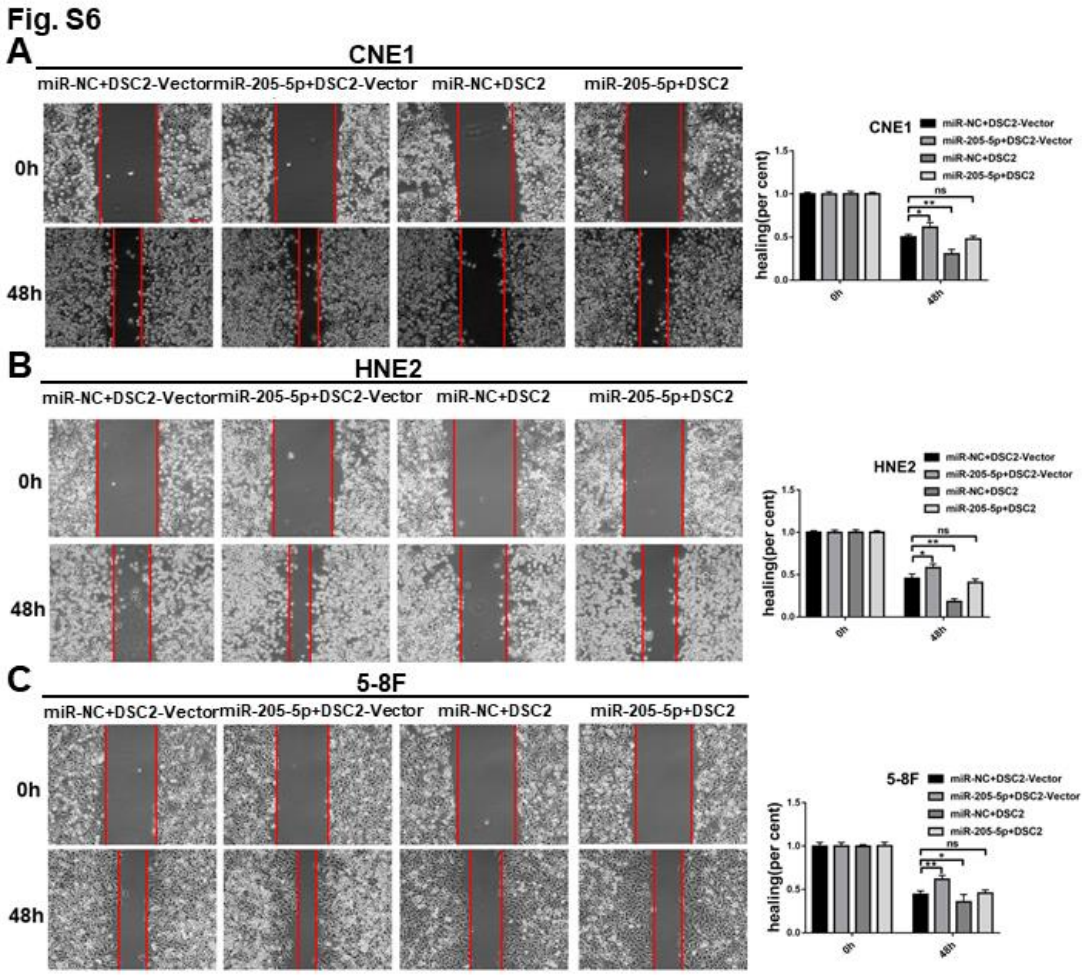

Figure S6. DSC2 over-expression abrogates the miR-205-5p-enhanced wound healing in NPC cells.

(A-C) DSC2 over-expression abrogated the miR-205-5p-enhanced wound healing in NPC cells. Data are representative images or expressed as mean ± SD of each group from three separate experiments. Scale bar, 100 μm. * *P*<0.05, ** *P*<0.01.

Fig. S7

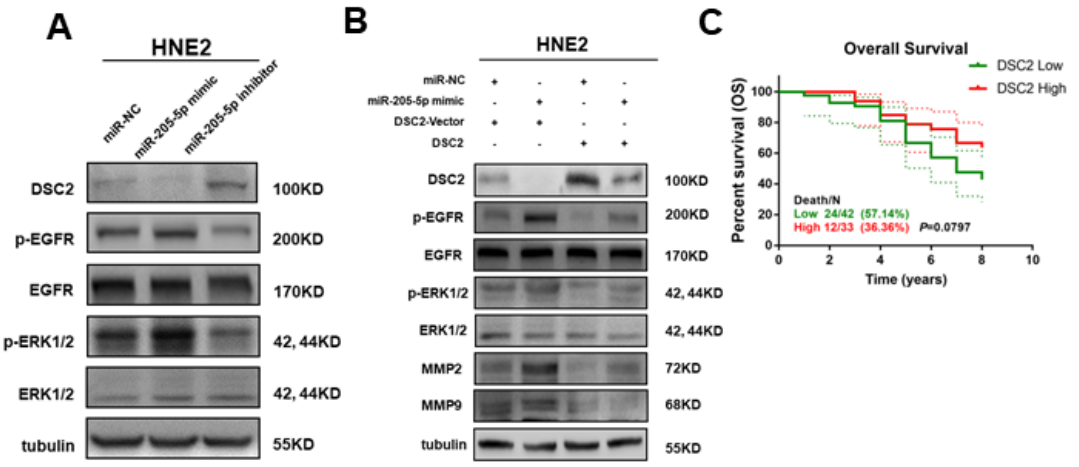

Figure S7. MiR-205-5p targets *DSC2* to enhance the EGFR/ERK signaling in HNE2 cells. (A) Western blot analysis of the relative levels of DSC2, EGFR, ERK1/2 expression and, EGFR and ERK1/2 phosphorylation in the indicated HNE2 cells. **(B)** DSC2 over-expression abrogated the miR-205-5p-enhanced EGFR/ERK1/2 activation and MMP2/MMP9 expression in HNE2 cells. **(C)** Higher levels of DSC2 expression were associated with a better overall survival of NPC patients.

Supplementary Tables:

Table S1. The association of clinical parameters with exosomal miR-205-5p in NPC patients

Items	Cases (n=88)	Exosomal miR-205-5p low	Exosomal miR-205-5p high	Chi-square	*P* value
Age (years)					
≤60	75	31	44	1.833	0.176
>60	13	8	5		
Gender					
Male	65	26	39	1.879	0.17
Female	23	13	10		
TNM stage					
T stage (T1-2)	27	19	8	10.71	0.001
T stage (T3-4)	61	20	41		
N stage (N0)	12	6	6	0.182	0.670
N stage (N1-3)	76	33	43		
Stage I, II	9	7	2	4.548	0.033
Stage III, IV	79	32	47		

Table S2. The association of clinical parameters with miR-205-5p in NPC

Items	Cases (n=75)	miR-205-5p Low	miR-205-5p High	Chi-square	*P* value
Age (years)					
≤60	63	23	40	0.774	0.379
>60	12	6	6		
Gender					
Male	55	21	34	0.02	0.886
Female	20	8	12		
TNM stage					
T stage (T1-2)	22	14	9	6.896	0.009
T stage (T3-4)	53	15	37		
N stage (N0)	10	5	5	0.625	0.429
N stage (N1-3)	65	24	41		
M stage (M0)	68	28	40	1.935	0.164
M stage (M1)	7	1	6		
Stage I, II	15	11	4	9.501	0.002
Stage III, IV	60	18	42		