

Table S1. miRNA microarray of RNA isolated from Mewo exosomes stimulated or not with rWNT5A for 3h. The values show the relative increase (fold change) of miRNA in the rWNT5A stimulated exosomes as compared to carrier stimulated.

Probe Set ID	Sequence type	Fold change	q-value	Alternative name
ENSG00000202498	snoRNA	8.252258	0	SNORD116
hsa-mir-455	miRNA	2.4449663	0	
ENSG00000252531	snoRNA	2.222854	0	SNORA73
hsa-mir-593	Stem-loop	1.8366694	0	

Figure S1

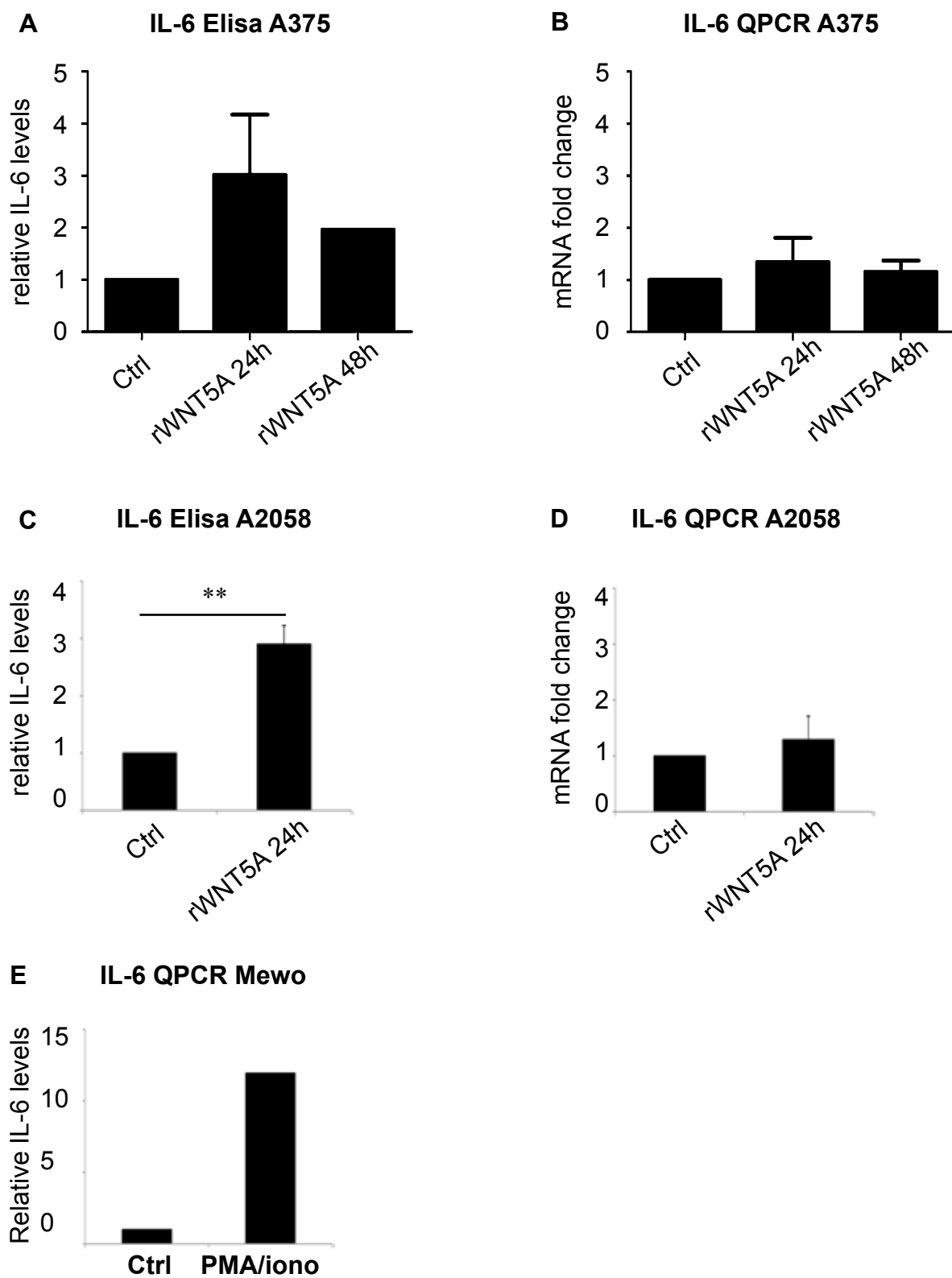


Figure S2

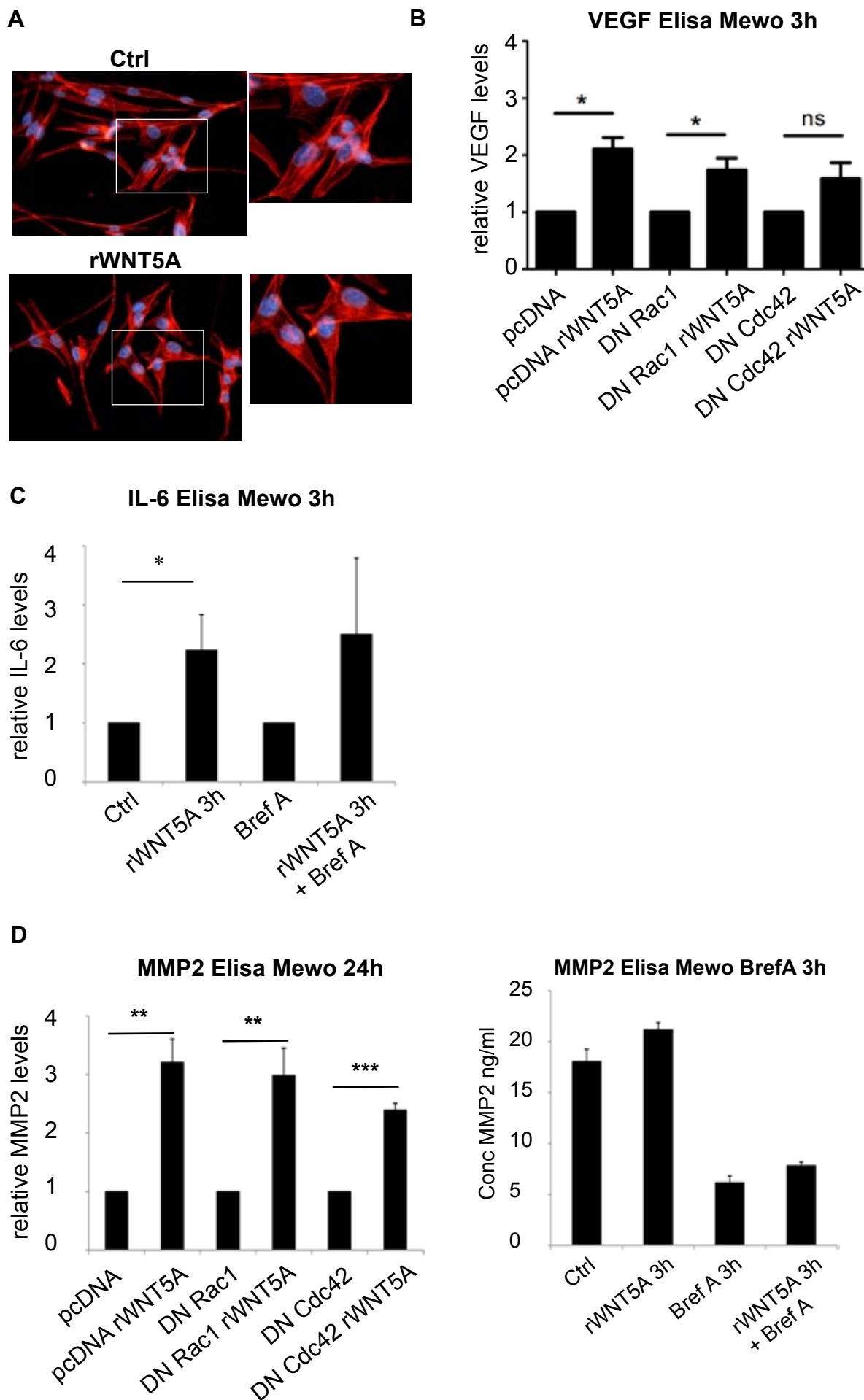
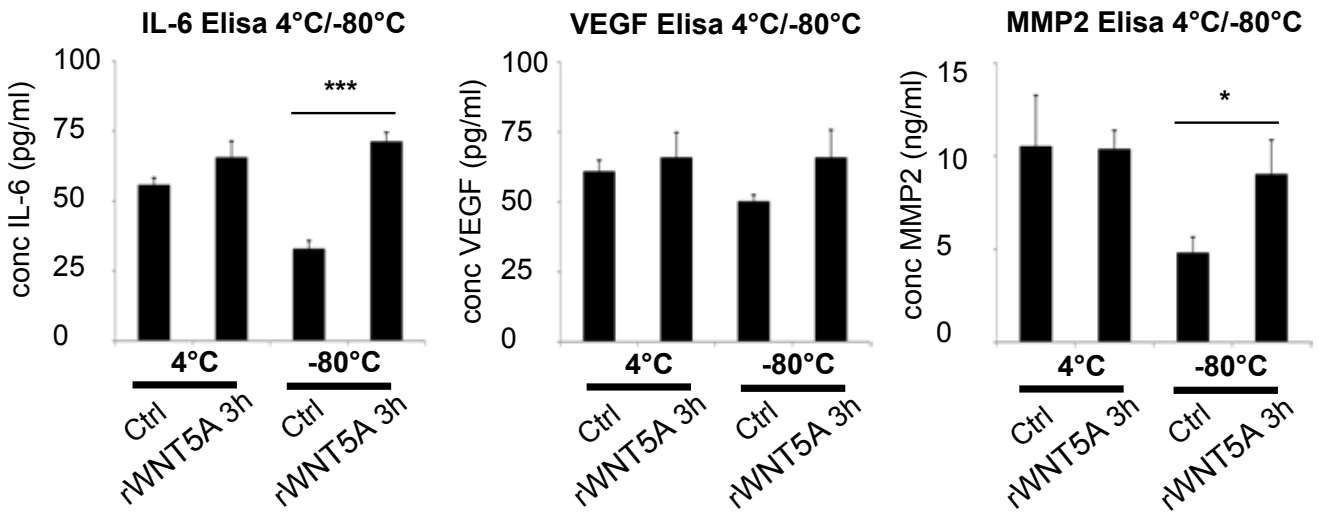
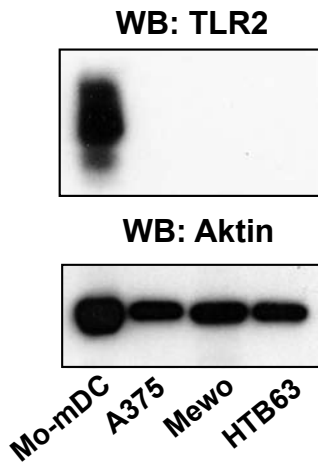


Figure S3

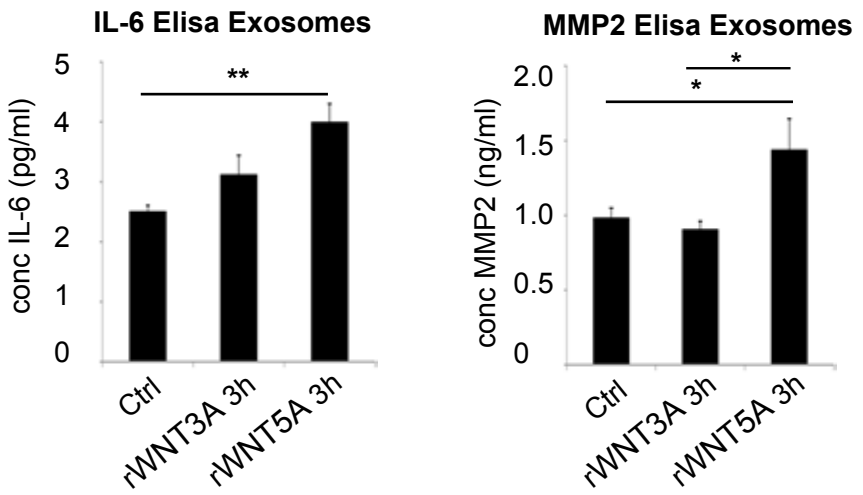
A



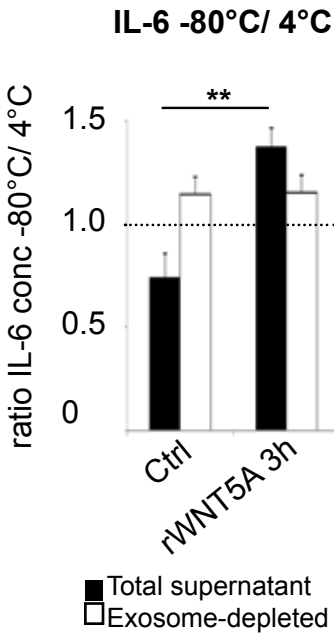
B



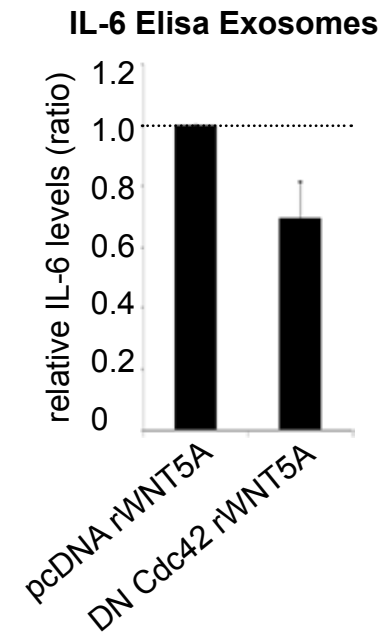
C



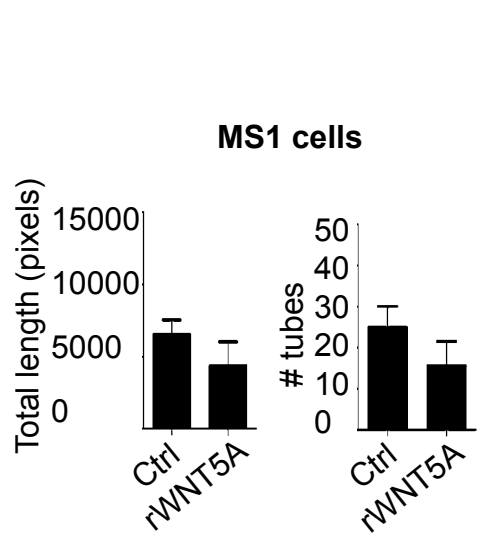
D



E



F



Supplementary Fig 4

Gene	Forward Sequence 5'-3'	Reverse Sequence 5'-3'
IL-6	GGCACTGGCAGAAAACAACC	GCAAGTCTCCTCATTGAATCC
Wnt5a	TCAGGACCACATGCAGTA	CTCATGGCGTTCACCACC
VEGF	AGGAGGAGGGCAGAATCATCA	CTCGATTGGATGGCAGTAGCT
UBC	ATTTGGGTCGCGGTTCTTG	TGCCTTGACATTCTCGATGGT
SDHA	TGGGAACAAGAGGGCATCTG	CCACCACTGCATCAAATTCATG
YWHAZ	ACTTTTGGTACATTGTGGCTTCAA	CCGCCAGGACAAACCAGTAT
MMP2	TGA TCT TGA CCA GAA TAC CAT CGA	GGC TTG CGA GGG AAG AAG TT

Supplementary Figure Legends

Figure S1

IL-6 and VEGF is increased in A375 cell culture supernatants after Wnt5a treatment.

(A) A375 cells treated with rWNT5A 0.2 μ g/ml for 24h and 48h. Elisa was used to measure differences in IL-6 (A). IL-6 n=2. Error bars represent SEM. (B) Changes in mRNA were analyzed using RT-QPCR for IL-6. At least 4 experiments were performed (n=4-7). Error bars represent SEM. (C-D) A2058 cells treated with rWNT5A 0.2 μ g/ml for 24h. Elisa was used to measure differences in IL-6 (C). IL-6 n=3. Error bars represent SD. ** p<0.01 Students t-test. (D) Changes in mRNA were analyzed using RT-QPCR for IL-6. n=4. Error bars represent SD. (E) Mewo cells treated with PMA/ionomycin for 12h was used as positive control for RT-QPCR (IL-6 shown in E).

Figure S2. (A) Mewo cells treated with rWNT5A for 3h stained with phalloidin to visualize F-actin and counter stained with DAPI. The white boxes represent magnified areas. (B) Transfection of Mewo cells with DN-Cdc42, but not -Rac1, inhibits the Wnt5a induced secretion of VEGF as measured by Elisa. The control cells were transfected with an empty vector. The data shown are ratios of rWNT5A treated (3h)/ untreated cells for each plasmid transfected and normalized against the empty vector control. n=4. * = p <0.05 by paired Student's t-test. Error bars represent SEM. (C) Mewo cells were pre-treated with Brefeldin A, Bref A, for 30min prior to Wnt5a treatment for 3h. IL-6 levels in cell-culture supernatants were detected using Elisa. n=3. *= p <0.05 by Student's t-test. Error bars represent SD. (D) Left panel; Transfection of Mewo cells with DN-Cdc42 inhibits the Wnt5a induced secretion of MMP2 as measured by Elisa. DN-

Rac1 does not. The control cells were transfected with an empty vector. The data shown are ratios of rWNT5A treated (3h)/ untreated cells for each plasmid transfected and normalized against the empty vector control. n=3. Right panel; Mewo cells were pre-treated with Brefeldin A, Bref A, for 30min prior to Wnt5a treatment for 3h. MMP2 levels in cell-culture (actual concentration) supernatants were detected using Elisa n=4. Error bars represent SEM.

Figure S3. (A) IL-6, VEGF and MMP2 levels as measured by Elisa in cell culture supernatants of Mewo cells that were treated with 0.2µg/ml rWNT5A or carrier for 3h and subsequently was freshly run on Elisa (4°C) or freeze/thawed for two cycles -80°C/4°C before analyses. The bar graphs show actual concentration for each treatment indicated. Error bars represent SD. n= 2. (B) Western blot of TLR2 in Mo-mDCs (Ctrl), A375, Mewo and HTB63 malignant melanoma cells. (C) IL-6 or MMP2 levels as measured by Elisa of frozen exosome fractions isolated from supernatant of Mewo cells that were treated with 0.2µg/ml rWNT5A, carrier or 0.1ng/ml rWnt3a for 3h. The bar graphs show the actual concentration for each treatment indicated. Error bars represent SD. n= 3. * = p <0.05; **= p <0.01; ***= p <0.001 by Student's t-test. (D) Induction of IL-6 levels in unfractionated supernatants of rWNT5A stimulated Mewo cells, as measured by Elisa of frozen/non-frozen supernatants (ratio; black bars) but not in exosome-depleted supernatants of rWNT5A stimulated Mewo cells, as measured by Elisa of frozen/non-frozen exosome-depleted supernatants (ratio; white bars). The bar graphs show the relative increase of IL-6 in frozen : refrigerated samples. SEM. n=3. **= p <0.01 by Student's t-test. (E) IL-6 levels, as measured by Elisa, of frozen exosome fractions isolated from supernatant of Mewo cells that were transfected with pcDNA3 or DN-Cdc42 plasmids and subsequently treated with carrier or 0.2µg/ml rWNT5A for 3h. The bar graphs show the relative increase of rWNT5A treated as

compared to carrier treated, for each transfection indicated. Error bars represent SEM. n=4. (F)
MS1 cells grown alone and treated with carrier or rWNT5A, total length of tubes (left), number
of tubes (right), n=3. Error bars represent SEM.

Figure S4,

Table of primers used for Q-PCR.