Supplementary Figure 1

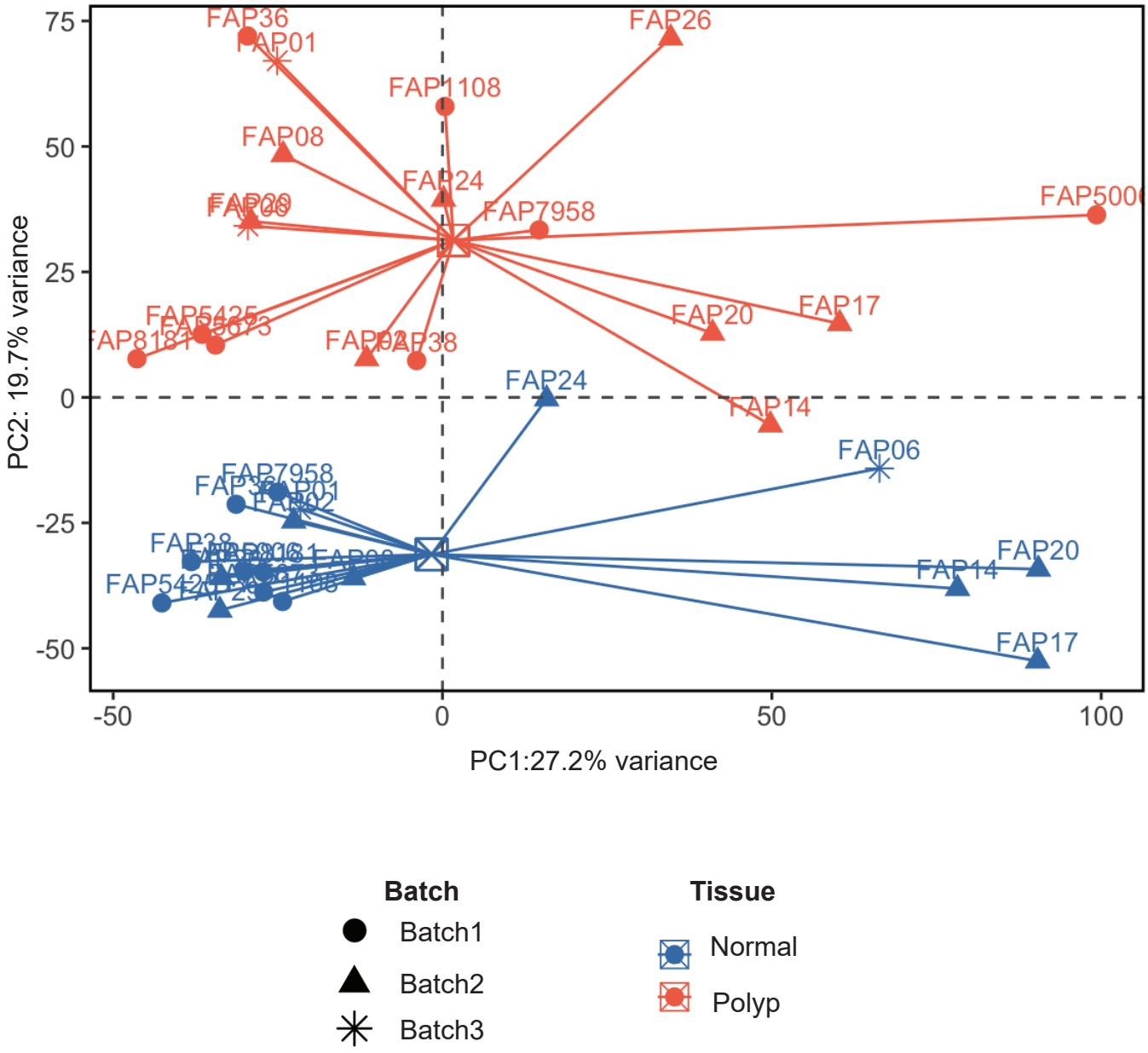


Figure S1. First (x-axis) and second (y-axis) principal components obtained from PCA output of human adenoma and normal colorectal mucosa specimens were plotted separately as a scatter plot to visualize sample distribution after dimension reduction of normalized whole transcriptome data. Each dot represents one sample. Adenoma sample is indicated with red, and normal colorectal mucosa is indicated with blue. Different shapes, circles, triangles, and asterisk, represent the sample batch. The centroids of both groups were marked as squares and connected to individual samples within each group.

Supplementary Figure 2

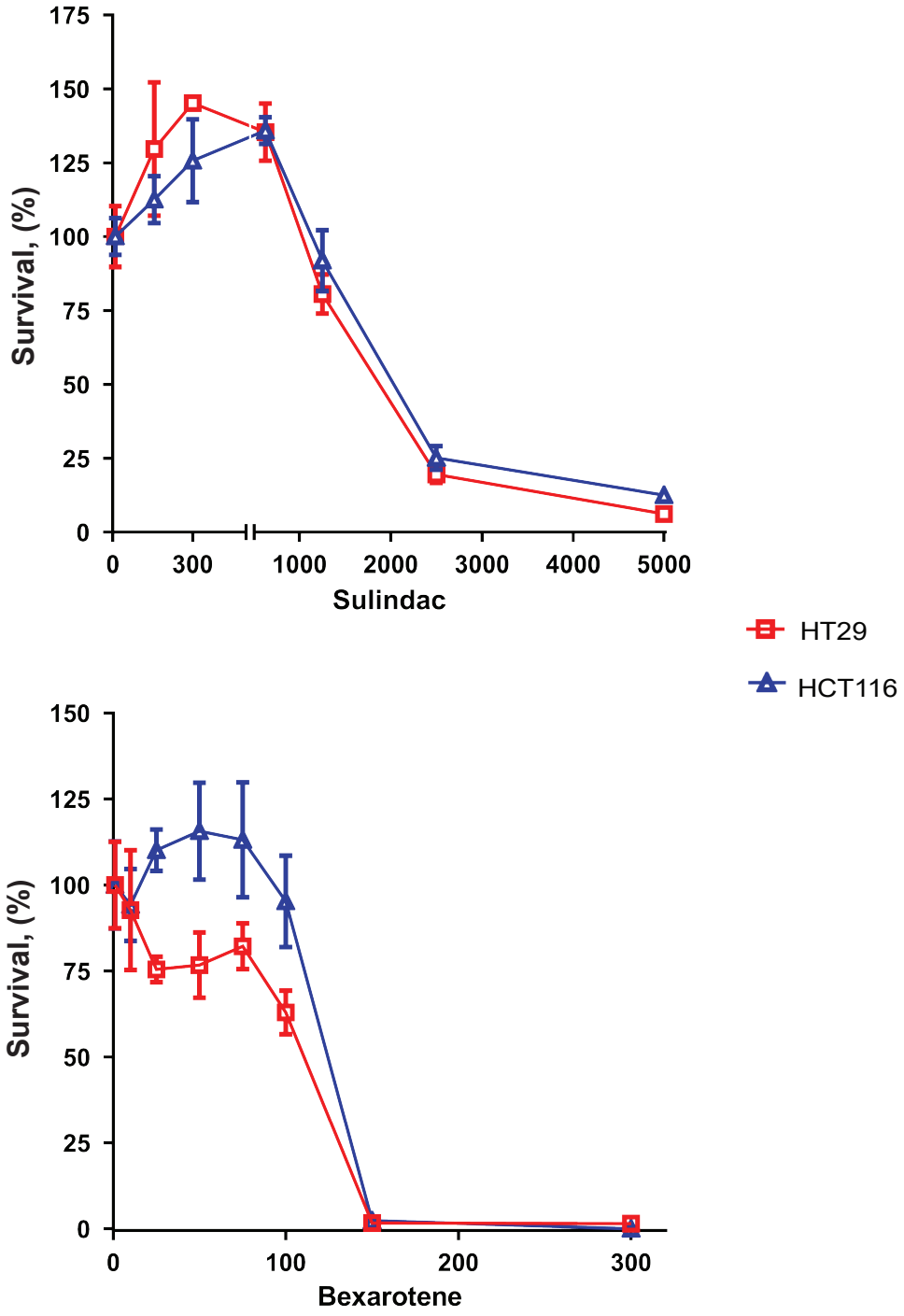


Figure S2. Drug sensitivity and IC_{50} calculations in two colorectal cancer cell lines, HT29 and HCT116. Cell lines were treated with serial concentrations of sulindac (**Top**) and bexarotene (**Bottom**) in a range from 0 (control) to 5 millimolar and from 0 (control) to 300 micromolar, respectively.

Supplementary Figure 3

A

HCT116

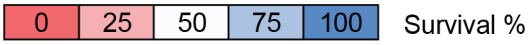
Sulindac \ Bexarotene	140 µM	120 µM	100 µM	80 µM	60 µM	40 µM	0 µM
2100 µM	0.5	1.5	1.8	1.9	5.1	7.1	10.7
1800 µM	0.6	1.1	1.3	1.2	7.0	9.2	14.1
1500 µM	1.2	1.5	1.0	2.1	9.2	13.3	17.1
1200 µM	1.2	1.1	1.4	2.7	14.9	22.5	28.0
900 µM	0.5	1.4	2.1	5.4	22.9	49.5	60.8
600 µM	1.4	1.1	1.8	5.9	46.9	77.5	118.3
0 µM	1.4	1.9	1.6	48.9	90.1	88.6	100.0

Sulindac (µM)	Bexarotene (µM)	Combination Index
1500	**40**	**0.708**
1200	**40**	**0.672**
900	**40**	**0.62**
600	**40**	**0.562**

B

HT29

Sulindac \ Bexarotene	140 µM	120 µM	100 µM	80 µM	60 µM	40 µM	0 µM
2100 µM	0.9	1.5	2.3	9.4	20.4	26.1	35.2
1800 µM	0.7	1.4	2.4	10.7	25.5	40.1	49.4
1500 µM	0.6	0.9	2.6	11.1	35.4	49.6	69.1
1200 µM	0.7	1.6	2.2	11.0	54.6	61.6	84.4
900 µM	0.0	0.0	0.5	12.5	60.0	62.1	98.1
600 µM	0.0	0.0	1.1	15.5	85.7	103.8	120.8
0 µM	0.0	1.4	4.9	57.7	72.5	96.2	100.0



Sulindac (µM)	Bexarotene (µM)	Combination Index
1500	**40**	**0.623**
1200	**40**	**0.606**
900	**40**	**0.577**
600	**40**	**0.542**

Figure S3. The efficiency of sulindac and bexarotene drug combination in HCT116 and HT29 cells assessed using the combination index (CI) from the Chou-Talalay method. CI is a quantitative measure of the degree of drug interaction in terms of additive effect (CI=1), synergism (CI<1), or antagonism (CI>1) for a given set of concentrations. (**A**) Cell viability and CI of sulindac and bexarotene drug combination for HCT116 cells; (**B**) Cell viability and CI of sulindac and bexarotene in HT29 cells.

Supplementary Figure 4

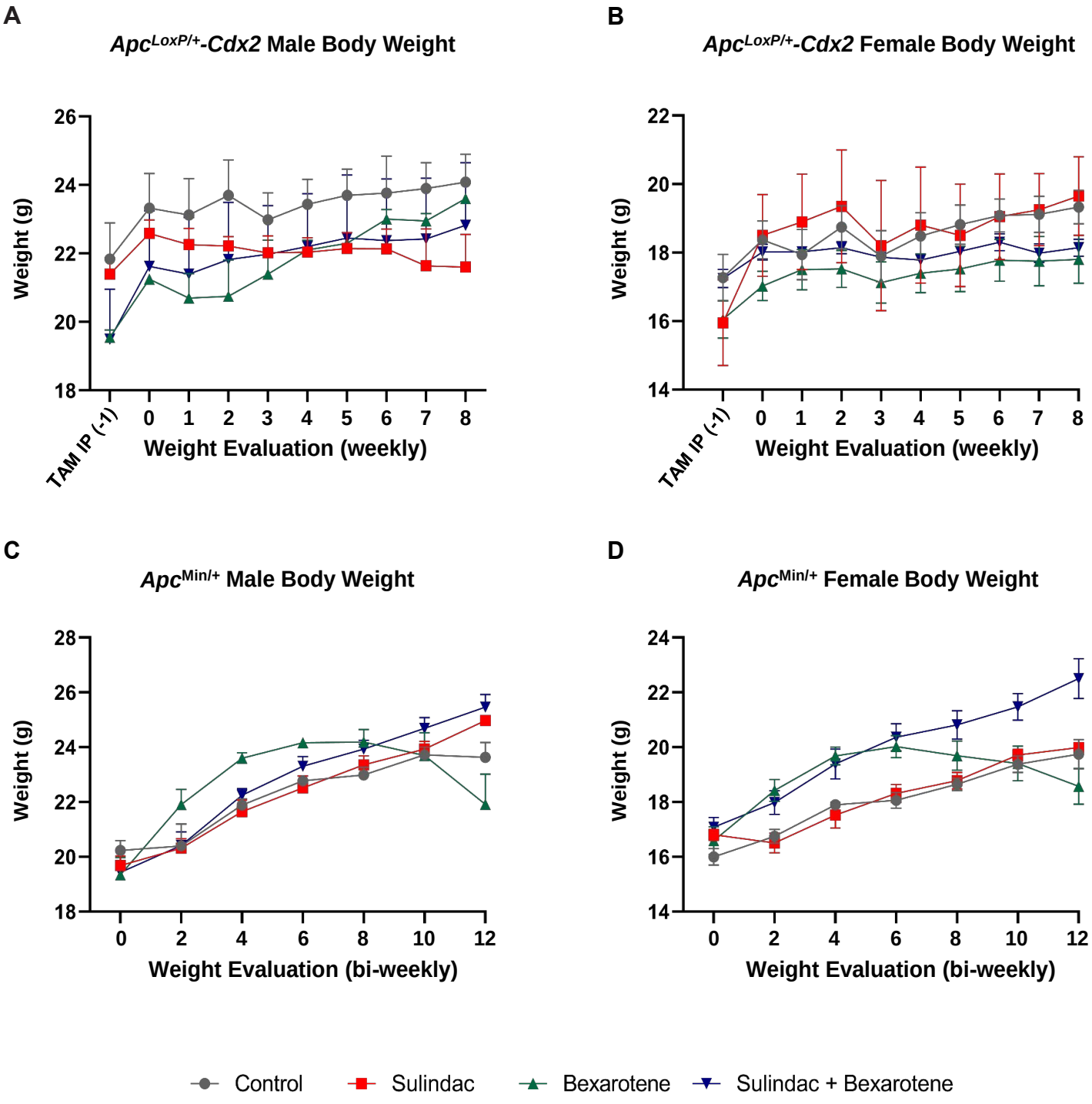


Figure S4. Mouse body weights of *Apc*$^{Min/+}$ and *Apc*$^{LoxP/+}$*-Cdx2* mice graphed by sex and stratified by treatment group. No significant deviations in body weight across all treatment groups were observed in male (**A**) and female (**B**) *Apc*$^{LoxP/+}$*-Cdx2* mice during the pre-clinical trial. No significant deviations in body weight across all treatment groups were observed in male (**C**) and female (**D**) *Apc*$^{Min/+}$ mice during the pre-clinical trial. *Apc*$^{Min/+}$ mice treated with bexarotene alone appeared to lose body weight after 10 weeks of intervention in both males and female, but this decline was not significant nor indicative of toxicity-related AEs.

Supplementary Figure 5

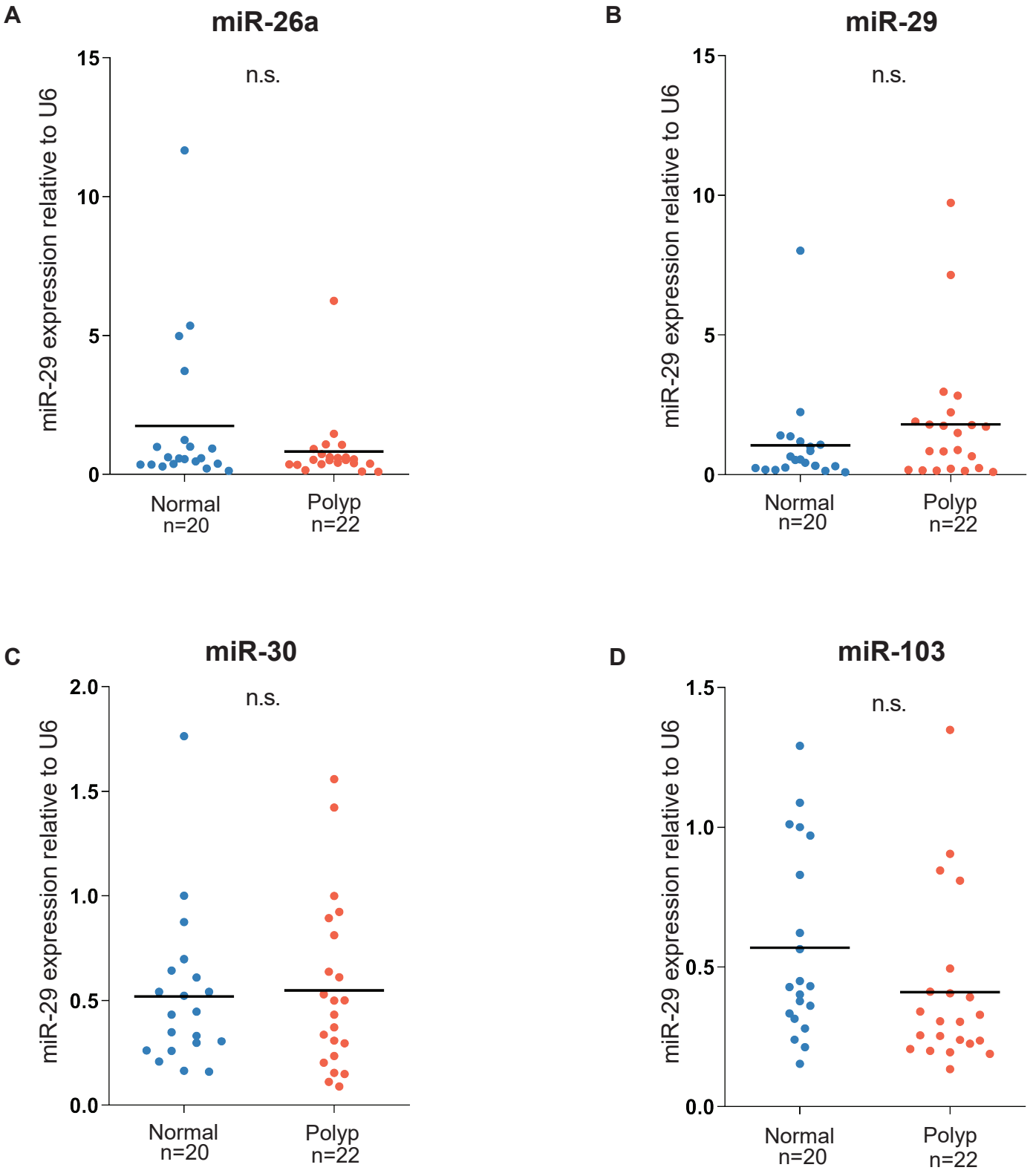


Figure S5. The expression levels of miR-26a, miR-29, miR-30, and miR-103 using qRT-PCR in normal mucosa (n=20) and polyp tissue (n=22) of the FAP patients. The expression level of each miRNA was normalized to U6 RNA expression.