FAANG RNA Isolation Methods:

RNA was isolated from previously collected tissues (Burns et. al. 2018) using Trizol® (Invitrogen, Carlsbad, CA, USA) chloroform (CAS #67-66-3, Fisher Scientific, Hampton, NH, USA) phase separation followed by a column clean up using either Zymo Research (Irvine, CA, USA) or Qiagen (Hilden, Germany) columns. Tissues were homogenized in Trizol® using a Kinematica Polytron™ homogenizer (Luzern, Switzerland). Samples requiring pulverization prior to homogenization were processed with a biopulverizer (Biospec Products Bartlesville, OK, USA) or SPEX® Sample Prep Geno/Grinder® 2010 (Metuchen, NJ, USA) (**Table S1**). Homogenization using the polytron was done in bursts of 20-60 seconds with one-minute incubations on ice between bursts. After homogenization, all samples were incubated at room temperature for 5-30 minutes depending on tissue and matrix composition. Samples with high lipid or protein content were then subjected to a 12,000 x g centrifugation for 10 minutes at 4^{O}C (dirty spin). Chloroform phase separation was carried out using 200-300µL chloroform per 1mL of Trizol. The aqueous clear supernatant was then transferred to a clean tube and an equal volume of 100% ethanol added. The tubes were mixed by inversion and the mixture loaded onto Zymo Research Direct-Zol Mini or Qiagen Micro RNAeasy columns. DNA digestion was carried out on the column using the DNase enzyme and manufacturer protocol corresponding to the column. RNA was then washed and eluted according to the column manufactures instructions. RNA was stored at -80^{o}C until shipping to the University of Minnesota Genomics Center (Minneapolis, MN, USA) or Admera Health (South Plainfield, NJ, USA) for library preparation and sequencing. All tissues were prepared via TruSeq mRNA and smRNA libraries and sequenced using 125bp paired end reads and 50bp single end reads respectively.

Tissue	Homogenization			Extra Steps	Column Type	DNAse Digestion	Elution Volume
	Method	Speed (kRPM)	Duration				
Adipose: Loin	Polytron	26-28	30 sec (x3)	Yes[a]	Zymo Mini	Yes	50µL

Adrenal Cortex	Polytron	18-20	30 sec (x1)	No	Zymo Mini	Yes	100µ
Brain: Frontal Lobe	Polytron	10-12	20 sec (x2)	No	Zymo Mini	Yes	50µL
Brain: Occipital Lobe	Polytron	18-20 10-12	10 sec (x1) 10 sec (x1)	No	Zymo Mini	Yes	50µL
Brain: Parietal Lobe	Polytron	10-12	20 sec (x2)	No	Zymo Mini	Yes	50µL
Brain: Temporal Lobe	Polytron	10-12	20 sec (x2)	No	Zymo Mini	Yes	50µL
Cannon Bone Diaphysis	Geno/Grinder & Polytron	1-1.5 30+	60 sec (x6) 30 sec (x3)	Yes[b]	Qiagen Micro	No	20µL
Cartilage							
Cecum	Polytron	10-12	60 sec (x3)	No	Zymo Mini	Yes	50µL
Cerebellum Lateral Hemisphere	Polytron	10-12	20 sec (x2)	No	Zymo Mini	Yes	50µL
Cerebellum Vermis	Polytron	10-12	20 sec (x2)	No	Zymo Mini	Yes	50µL
Cornea	BioPulverizer & Polytron	30+	30 sec (x3)	Yes[a]	Zymo Mini	Yes	50µL
Cricoarytenoid Dorsalis and Lateralis Muscles	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Dorsal Root Ganglia	Polytron	10-12 14-16	20 sec (x2) 20 sec (x2)	No	Zymo Mini	Yes	50µL
Dorsum Skin	Polytron	22-24	30 sec (4x)	No	Zymo Mini	Yes	50µL
Duodenum	BioPulverizer/ Polytron	18-20 20-22	30 sec (x1) 30 sec (x2)	No	Zymo Mini	Yes	50µL
Fibroblasts					Qiagen Micro		
Gluteal Muscle	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	100µL
Heart Left Atrium	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	100µL
Heart Left Ventricle	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Heart Right Atrium	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	100µL
Heart Right Ventricle	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Hypothalamus	Polytron	10-12	20 sec (2x)	No	Zymo Mini	Yes	50µL
Ileum	Polytron	18-20	30 sec (x2)	No	Zymo Mini	Yes	70µL
Jejunum	Polytron	18-20	30 sec (x2)	No	Zymo Mini	Yes	70µL
Keratinocytes					Qiagen Micro		
Kidney Cortex	Polytron	10-12	60 sec (x3)	No	Zymo mini	Yes	50µL
Kidney Medulla	Polytron	10-12	60 sec (x3)	No	Zymo mini	Yes	50µL
Lamina	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	100µL
Left Lung	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Liver	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	80µL
Longissimus Dorsi Muscle	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	100µL
Mammary Gland	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	50µL

Mitral Valve	Polytron	18-20	30 sec (x3)	No	Zymo Mini	Yes	50µL
Ovary	Polytron	18-20	30 sec (x1)	No	Zymo Mini	Yes	100µL
Peripheral Blood Mononuclear Cells	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Pituitary	Polytron	10-12	60 sec (x3)	No	Zymo Mini	Yes	50µL
Retina	Polytron	22-24 18-20	30 sec (x7) 30 sec (x1)	No	Zymo Mini	Yes	50µL
Rib Bone Marrow	BioPulverizer/ Polytron	16-18	30 sec (x2)	Yes[a,c]	Zymo Mini	Yes	50uL
Sacrocaudalis Muscle	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL
Sesamoid	Geno/Grinder & Polytron	1-1.5 30+	60 sec (x6) 30 sec (x3)	Yes[b]	Qiagen Micro	No	20µL
Spinal Cord L6	Polytron	10-12	25 sec (x2)	No	Zymo Mini	Yes	50µL
Spinal Cord T8	Polytron	10-12	25 sec (x2)	No	Zymo Mini	Yes	50µL
Spleen	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	100µL
Suspensory Ligament	Geno/Grinder & Polytron	1-1.5 30+	60 sec (x6) 30 sec (x3)	Yes[b]	Qiagen Micro	Yes	20µL
Testis	Polytron	22-24	30 sec (x4)	Yes[a]	Zymo Mini	Yes	100uL
Uterus	Polytron	22-24	30 sec (x3)	No	Zymo Mini	Yes	50µL

[a] Additional steps: 20-minute ice incubation for Trizol homogenate followed by a dirty spin after which the cleared supernatant was transferred to a clean tube for chloroform phase separation.

[b] Additional steps: Pulverized 200 mg of tissue in Geno/Grinder (60 sec x2 at 1000 rpm, cool on dry ice or in liquid nitrogen for one minute, 60 sec x2 at 1200 rpm, cool on dry ice or in liquid nitrogen for one minute, 60 sec at 1500 rpm), then homogenized in 1mL Trizol. Transferred to a new tube and added an additional 3mL of Trizol then incubated at room temperature for 30 minutes with agitation. 10-minute dirt spin followed by addition of 300µL chloroform per 750µL cleared Trizol homogenate.

[c] Additional steps: 120mg of tissue was broken down in a Biopulverizer cooled with liquid nitrogen. Approximately 60mg of tissue was placed into one of two tubes. Following homogenization, both tubes were placed in a single spin column.