

Supplemental Table 1

Top canonical pathways representing genes that are positively regulated by both TNF- α and TonEBP, as identified by Ingenuity Pathway Analysis

Canonical Pathway	Molecules	$-\log(p\text{-value})$
Granulocyte Adhesion and Diapedesis	CXCL3, MMP3, CCL3, MMP10, CCL20, MMP13, IL1B, MMP9, CCL7, TNFRSF11B	1.16E01
Agranulocyte Adhesion and Diapedesis	CXCL3, MMP3, CCL3, MMP10, CCL20, MMP13, IL1B, MMP9, CCL7	9.86E00
Inhibition of Matrix Metalloproteases	MMP3, TIMP1, MMP10, MMP13, MMP9	7.07E00
Hepatic Fibrosis / Hepatic Stellate Cell Activation	CXCL3, TIMP1, MMP13, IL1B, MMP9, TNFRSF11B	4.87E00
HIF1 α Signaling	MMP3, MMP10, MMP13, EGLN3, MMP9	4.72E00
LXR/RXR Activation	HPX, IL1B, PTGS2, MMP9, TNFRSF11B	4.61E00
Role of IL-17A in Arthritis	CXCL3, CCL20, MMP13, PTGS2	4.4E00
TREM1 Signaling	TLR2, CXCL3, IL1B, CD83	4.2E00
Colorectal Cancer Metastasis Signaling	TLR2, MMP3, MMP10, MMP13, PTGS2, MMP9	4.14E00
Bladder Cancer Signaling	MMP3, MMP10, MMP13, MMP9	3.95E00
Communication between Innate and Adaptive Immune Cells	TLR2, CCL3L3, IL1B, CD83	3.91E00
Dendritic Cell Maturation	TLR2, IL1B, CD83, IL23A, TNFRSF11B	3.68E00
Airway Pathology in Chronic Obstructive Pulmonary Disease	CXCL3, MMP9	3.65E00
Role of IL-17F in Allergic Inflammatory Airway Diseases	MMP13, IL1B, IL11	3.57E00
Prostanoid Biosynthesis	PTGES, PTGS2	3.55E00

Supplemental Table 2

Top diseases and biological functions representing genes that are positively regulated by both TNF- α and TonEBP, as identified by Ingenuity Pathway Analysis

Category	Top Diseases and Biological Functions	p-value	# Molecules
Diseases and Disorders	Inflammatory Response	7.13E-04 - 1.00E-13	31
	Respiratory Disease	2.85E-04 - 2.78E-13	18
	Connective Tissue Disorders	5.79E-04 - 4.24E-12	23
	Inflammatory Disease	5.19E-04 - 4.24E-12	26
	Skeletal and Muscular Disorders	5.79E-04 - 4.24E-12	27
Molecular and Cellular Functions	Cell Death and Survival	7.07E-04 - 7.35E-11	32
	Cell-To-Cell Signaling and Interaction	7.13E-04 - 1.89E-10	24
	Cellular Movement	7.13E-04 - 2.17E-10	25
	Cellular Growth and Proliferation	6.73E-04 - 1.53E-09	35
	Cellular Development	6.88E-04 - 8.58E-09	34
Physiological System Development and Function	Hematological System Development and Function	7.13E-04 - 1.00E-13	30
	Tissue Morphology	5.22E-04 - 1.00E-13	29
	Immune Cell Trafficking	7.13E-04 - 1.16E-12	22
	Tissue Development	6.88E-04 - 1.16E-12	26
	Cardiovascular System Development and Function	3.55E-04 - 1.89E-10	24

Supplemental Table 3

Top networks representing genes that are positively regulated by both TNF- α and TonEBP, as identified by Ingenuity Pathway Analysis

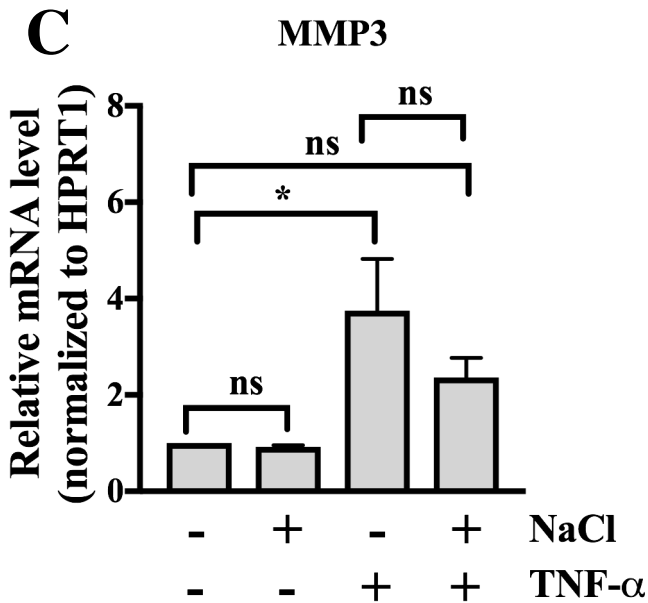
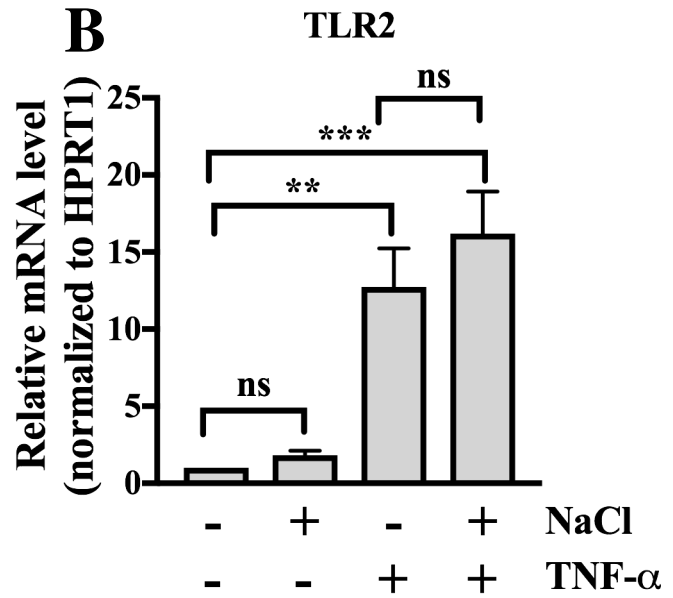
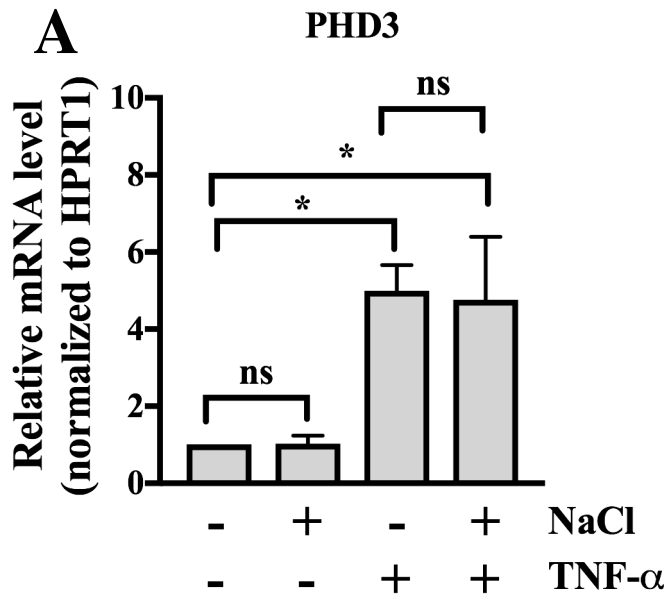
Network	Focus Molecules	Score
Hematological System Development and Function, Inflammatory Response, Tissue Morphology	19	38
Cardiac Infarction, Cardiovascular Disease, Organismal Injury and Abnormalities	13	23
Humoral Immune Response, Protein Synthesis, Tissue Development	10	16
Cellular Growth and Proliferation, Organismal Development, Connective Tissue Development and Function	7	10
Cellular Movement, Connective Tissue Development and Function, Tissue Development	5	7
Lipid Metabolism, Post-Translational Modification, Protein Degradation	1	2
Cardiovascular Disease, Embryonic Development, Molecular Transport	1	2
Cancer, Cardiovascular Disease, Cell Morphology	1	2
Connective Tissue Disorders, Developmental Disorder, Hereditary Disorder	1	2
Cellular Assembly and Organization, Cell-To-Cell Signaling and Interaction, Reproductive System Development and Function	1	2

Supplemental Table 4. Details for human tissue samples used in immunohistochemical and gene expression analyses. PM: Post-mortem.

	Sample	Source	Age	IVD Level	Average Grade	Classification	RT-qPCR	IHC
HD	1	Surgical	42	L4/L5	3	Non-degenerate	✓	✓
HD	2	Surgical	40	L5/S1	3.9	Non-degenerate	✓	
HD	3	Surgical	25	L4/L5	4.8	Degenerate	✓	
HD	5	Surgical	33	L5/S1	9	Degenerate	✓	
HD	16	Surgical	41	L5/S1	7	Degenerate	✓	
HD	17	Surgical	44	L5/S1	4	Non-degenerate	✓	
HD	21	Surgical	25	L5/S1	4	Non-degenerate	✓	
HD	22	Surgical	23	L5/S1	3	Non-degenerate	✓	
HD	23	Surgical	29	L3/L4	7.8	Degenerate	✓	
HD	24	Surgical	35	L4/L5	2	Non-degenerate	✓	
HD	25	Surgical	20	L4/L5	2	Non-degenerate	✓	
HD	26	Surgical	40	L5/S1	5	Degenerate	✓	
HD	30	PM	45	L5/S1	2	Non-degenerate	✓	
HD	31	PM	45	L3/L4	1	Non-degenerate	✓	
HD	33	Surgical	48	L4/L5	8	Degenerate	✓	
HD	34	Surgical	26	L5/S1	12	Degenerate	✓	
HD	36	Surgical	33	L5/S1	9	Degenerate	✓	
HD	40	PM	74	L2/L3	11	Degenerate		✓
HD	44	Surgical	41	L5/S1	2	Non-degenerate	✓	✓
HD	45	Surgical	36	L5/S1	8	Degenerate	✓	
HD	53	Surgical	38	L5/S1	7	Degenerate	✓	
HD	54	Surgical	28	L4/L5	6	Degenerate	✓	
HD	56	Surgical	43	L5/S1	8	Degenerate	✓	
HD	57	Surgical	44	L5/S1	9	Degenerate	✓	
HD	58	Surgical	28	L5/S1	8	Degenerate	✓	
HD	59	Surgical	35	L5/S1	6	Degenerate	✓	
HD	61	Surgical	43	L5/S1	7	Degenerate	✓	
HD	63	Surgical	42	L5/S1	5	Degenerate	✓	
HD	65	Surgical	43	L4/L5	10	Degenerate	✓	✓
HD	66	Surgical	62	L3/L4	10	Degenerate	✓	
HD	85	Surgical	49	L2/L3	8	Degenerate	✓	
HD	86	Surgical	40	L5/S1	9	Degenerate	✓	
HD	92	Surgical	38	L5/S1	7	Degenerate	✓	
HD	93	Surgical	38	L5/S1	12	Degenerate	✓	
HD	94	Surgical	66	L5/S1	10	Degenerate	✓	
HD	97	Surgical	46	L5/S1	10	Degenerate	✓	
HD	98	Surgical	65	L3/L4	11	Degenerate	✓	✓
HD	144	Surgical	37	L5/S1	5.5	Degenerate	✓	
HD	145	Surgical	38	L4/L5	11	Degenerate	✓	✓
HD	146	Surgical	47	L5/S1	7	Degenerate	✓	
HD	151	Surgical	47	L5/S1	8.5	Degenerate	✓	

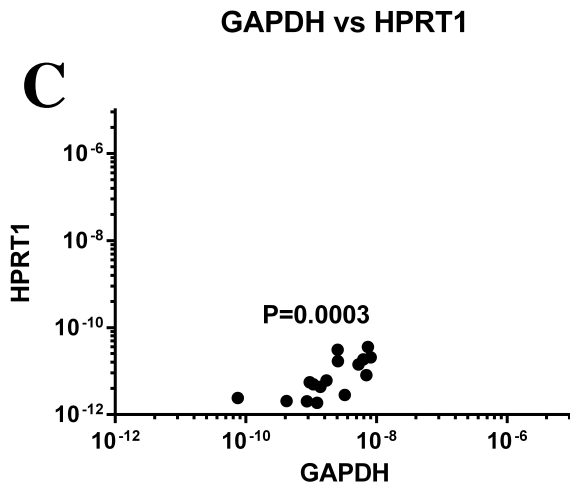
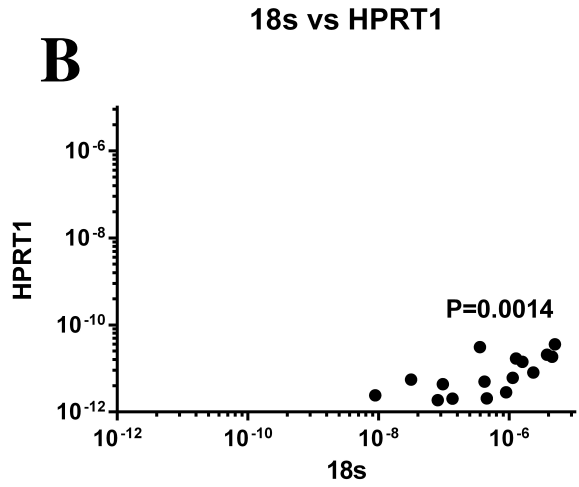
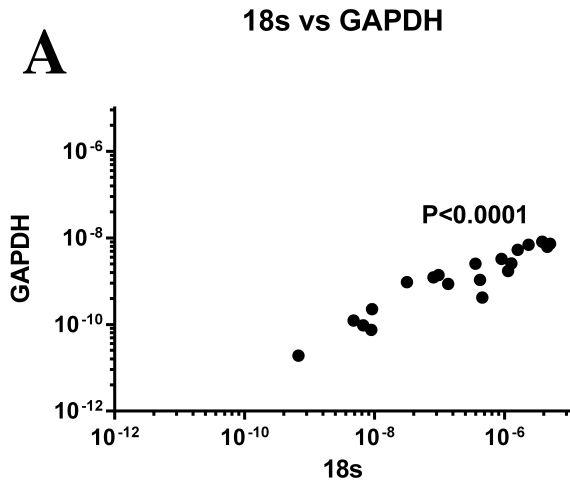
HD	153	Surgical	30	L5/S1	5	Degenerate	✓	
HD	154	Surgical	52	L4/L5	11	Degenerate	✓	✓
HD	194	Surgical	35	L4/L5	11	Degenerate		✓
HD	203	Surgical	45	L5/S1	4	Non-degenerate		✓
HD	233	Surgical	44	L5/S1	10	Degenerate		✓
HD	234	Surgical	54	L5/S1	9	Degenerate		✓
HD	254	Surgical	47	L4/L5	6	Degenerate		✓
HD	257	Surgical	46	L5/S1	3	Non-degenerate		✓
HD	266	Surgical	27	L5/S1	4	Non-degenerate		✓
HD	270	Surgical	45	L5/S1	6	Degenerate		✓
HD	287	Surgical	46	L5/S1	5	Degenerate		✓
HD	310	Surgical	37	L4/L5	5	Degenerate		✓
HD	319	Surgical	47	L5/S1	5	Degenerate		✓
HD	330	Surgical	32	L5/S1	5.5	Degenerate		✓
HD	332	Surgical	24	L5/S1	10	Degenerate		✓
HD	342	Surgical	18	L4/L5	6	Degenerate		✓
HD	346	Surgical	46	C5/C6	6	Degenerate		✓
HD	350	Surgical	38	L4/L5	9	Degenerate		✓
HD	356	Surgical	26	L5/S1	4	Non-degenerate		✓
HD	359	Surgical	40	L5/S1	4	Non-degenerate		✓
HD	360	Surgical	50	C6	5.5	Degenerate		✓
HD	374	Surgical	37	L4/L5	4	Non-degenerate		✓
HD	378	PM	33	L4/L5	2	Non-degenerate		✓

Supplemental Figure 1



Inflammatory gene response to co-stimulation with hyperosmolarity and TNF- α . A-C) While NaCl had no effect on mRNA levels of *PHD3* (A), *TLR2* (B), or *MMP3* (C), treatment with TNF- α induced levels of all three transcripts. Co-treatment with NaCl and TNF- α did not affect inducibility of *PHD3* (A) or *TLR2* (B). TNF- α -mediated induction of *MMP3* was reduced by co-treatment with NaCl.

Supplemental Figure 2



Correlation between housekeeping gene expression in human NP samples. A-C) Strong positive correlation between expression levels of 18s and GAPDH (A), 18s and HPRT1 (B), and GAPDH and HPRT1 (C).