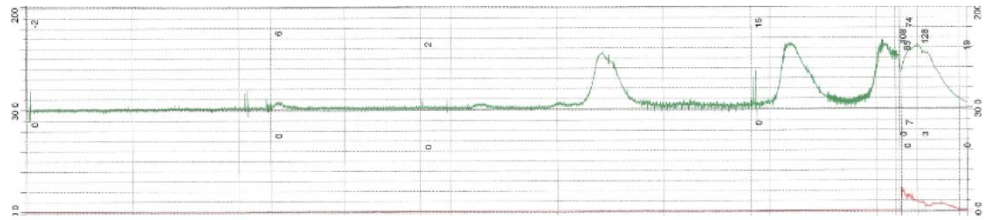
Supplementary Figures

A



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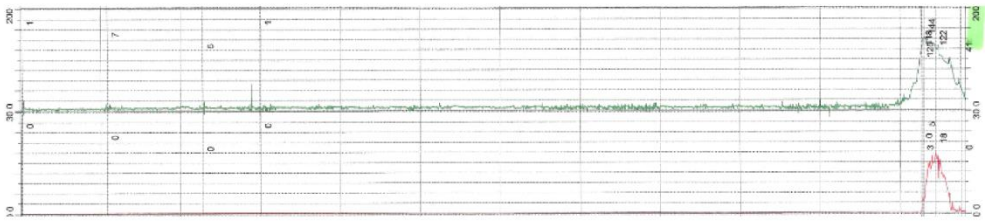

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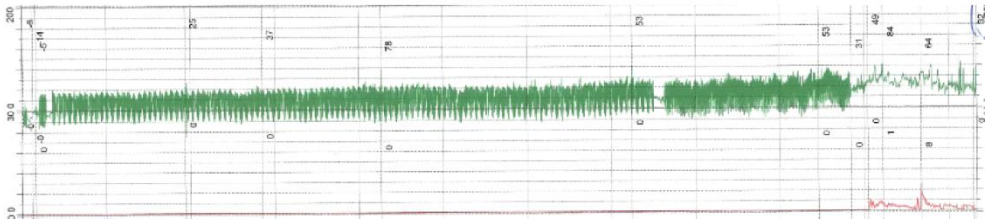

Figure S1. Urodynamic recording of BOO-induced LUTD patients. (**A**) DO group. BOO patients with increased detrusor pressure and reduced urine flow during pressure flow in combination with involuntary detrusor contractions during filling phase (phasic and/or terminal). (**B**) BO group. BOO patients without involuntary detrusor contractions during filling phase (phasic and/or terminal). (**C**) UA group. Patients where detrusor contractions could not be demonstrated during urodynamic study (underactive or acontractile detrusor). Shown are representative recordings from each patients' group.

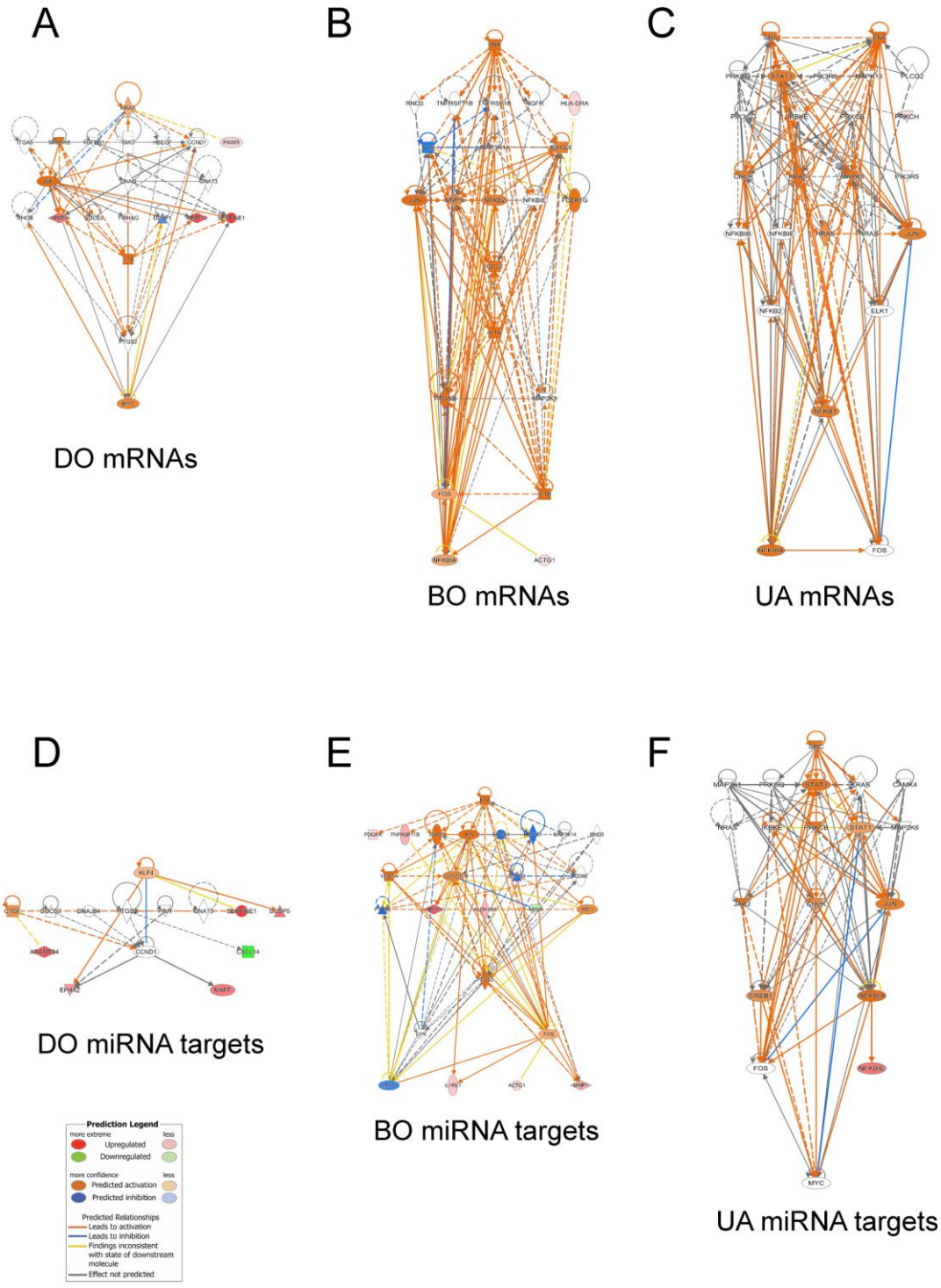

Figure S2. Upstream regulator analysis of DO, BO and UA groups based on top 30 elements in mRNA-based and miRNA target-based pathways. Upstream regulator analysis networks illustrating the interaction of top 30 pathway elements (mRNAs) in mRNA datasets or expressed miRNA targets datasets (miRNA targets) of patients' groups. (**A**) mRNA dataset of DO patients. JUN with 12 targets is the most interactive element. (**B**) mRNA dataset of BO patients. TNF with 21 targets in our mRNA dataset was the most interactive element. (**C**) mRNA dataset of UA patients. TNF with 11 targets was the most interactive element. (**D**) Expressed miRNA targets dataset of DO patients. KLF with 5 targets is the most interactive element. (**E**) Expressed miRNA targets dataset of BO patients. FOS with 16 targets in our mRNA dataset is the most interactive element. (**F**) Expressed miRNA targets dataset of UA patients. KRAS with 7 targets was the most interactive element.

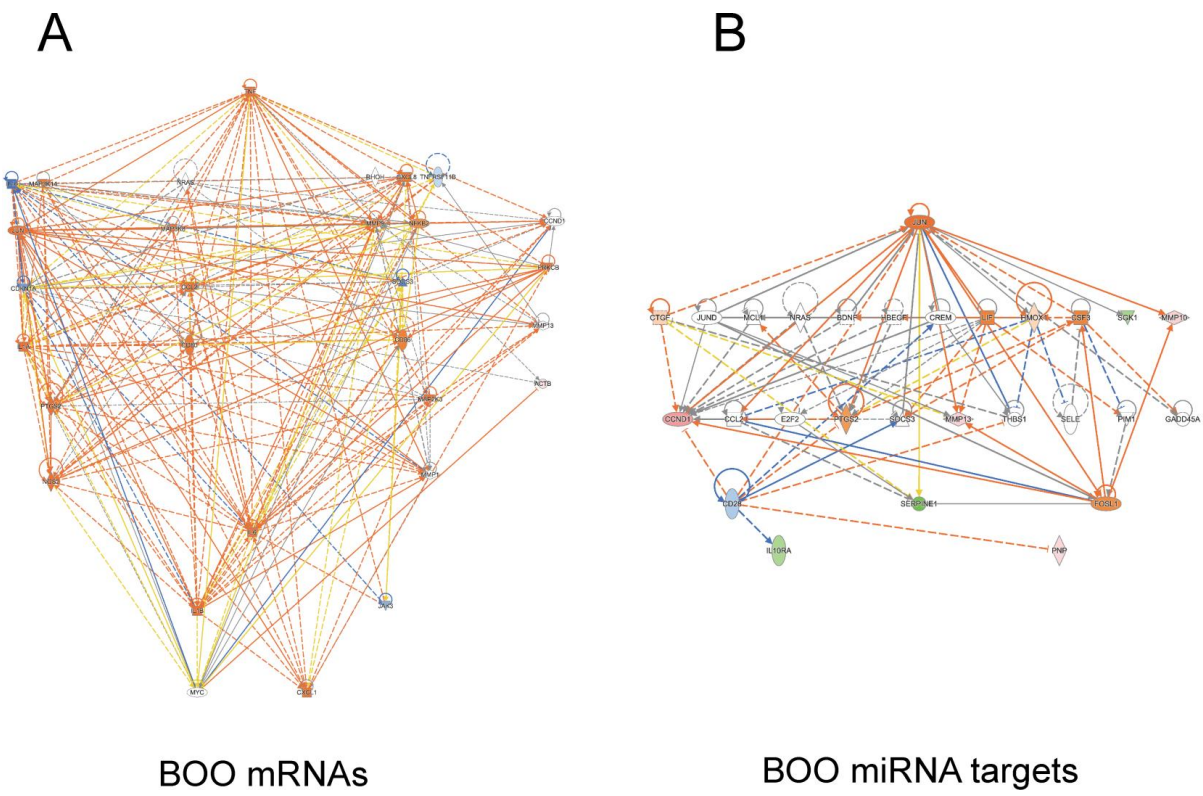

Figure S3. Upstream regulator analysis of all BOO patients based on top 30 elements in mRNA-based and expressed miRNA target-based pathways. (**A**) mRNA dataset of all BOO patients. TNF was the most effective element. (**B**) Expressed miRNA targets dataset of abundant significant miRNAs in all BOO patients. JUN is the top upstream element.

Supplementary Tables

Table ST1. Urodynamic evaluation of patients with BOO-induced LUTD

Sample	Sex	Age	Volume desire to void	Bladder Capacity	Pdet Qmax	Pdet max	Qmax	Retention	Retention / Capacity	Remarks
DO #1	M	54	190	335	43	71	2	310	0.9	
DO #2	M	70	210	460	68	76	7	160	0.3	
DO #3	M	68	23	322	50	82	0	322	1.0	
DO #4	M	62	80	103	103	106	9	5	0.0	
DO #5	M	59	190	385	65	94	8	60	0.2	
DO #6	M	61	50	250	100	180	6	170	0.7	
BO #1	M	60	75	590	133	157	15	270	0.5	
BO #2	M	63	190	340	68	70	6	190	0.6	
BO #3	M	63	200	490	130	180	8	200	0.4	
BO #4	M	76	395	905	51	65	5	480	0.5	
BO #5	M	72	335	530	57	95	5	290	0.5	
BO #6	M	69	130	450	90	99	6	115	0.3	
UA #1	M	83	210	741	0	5	0	780	1.1	acontractile
UA #2	M	80	150	560	45	30	10	500	0.9	hypocontratile
UA #3	M	71	450	610	0	0	0	610	1.0	acontractile
UA #4	M	80	470	580	0	0	0	580	1.0	acontractile
UA #5	M	65	305	900	32	36	13	425	0.5	hypocontractile
UA #6	M	66	650	1500	0	0	0	1500	1.0	acontractile

Groups (n = 6 patients per group): DO = BOO patients with urodynamically determined bladder overactivity, BO = BOO patients without bladder overactivity, UA = underactive bladder

Abbreviations: Pdet max = maximum detrusor pressure, Pdet Qmax = detrusor pressure at maximum flow, Qmax = maximum flow, Residual = post-void residual.

Table ST2. miRNAs and their targets encoding contractile and fibrotic proteins

	CNN1	CTGF	HBEGF	HGF	JUNB	MYC	RND1	SNAI1	TGFB2	TGFBR1	TGIF2	VEGFA
DO	152-3p 199b-5p	26b-5p	--	26b-5p	199b-5p	--	199b-5p	199b-5p	152-3p	--	182-5p 486-3p	199b-5p 374a-5p
BO	10a-5p	133a-3p 26b-5p 30c-5p	145-5p 29c-3p	26b-5p	199b-5p 30c-5p	145-5p	199b-5p	199b-5p 30c-5p	133a-3p 145-5p 490-3p	133a-3p 145-5p 490-3p	497-5p 29c-3p 490-3p	199b-5p 29c-3p 497-5p
UA	15b-5p	26b-5p 30c-5p	let-7b-5p 203a 29c-3p	199a-3p 203a 26b-5p	199b-5p 30c-5p	let-7b- 5p	199b-5p	199b-5p 30c-5p	199b-5p 203a 29c-3p	let-7b-5p 320a	199a-3p 29c-3p	199b-5p 429 203a 29c-3p

Table ST3. Test result variables: prediction probability

Markers	AUC[1]	Sensitivity	Specificity	Significance[1]	Lower Bound[3]	Upper Bound[3]
NRXN3	**0.93**	0.83	0.89	0.002	0.83	1
BMP7	**0.95**	0.83	0.79	0.001	0.87	1
UPK1A	**0.88**	0.83	0.79	0.006	0.73	1
hsa-miR-103a-3p	**0.86**	1.00	0.85	0.009	0.70	1
hsa-miR-10a-3p	**0.81**	0.83	0.73	0.023	0.56	1
hsa-miR-199a-3p	**0.87**	1.00	0.73	0.008	0.726	1

[1] AUC: Area Under the curve
[2] Null hypothesis: true area = 0.5
[3](95% confidence interval (CI)

Table ST4. Urodynamic parameters of the patients included in the blinded study

Diagnosis	Capacity (ml)	Pdet Qmax (cmH2O)	Residual (ml)	Qmax (ml/s)	BCI	Number of contraction during filling
BO	522.5+/-20	96.5+/-11	228.3+/-24	7.3+/-1	133.1+/-9	0
DO	458+/-31	65+/-8	227.6+/-31	6.8+/-1	51.3+/-9	2.6+/-0.4
UA	873.8+/-78	13.1+/-4	811.1+/-76	2.1+/-1	8.7+/-4	0

Samples, processed in the blinded study, originated from BOO patients belonging to the following groups: DO = BOO patients with urodynamically determined bladder overactivity (n=13), BO = BOO patients without bladder overactivity (n=7), UA = underactive bladder patients (n=20).
Shown are the group average values ± SEM.

Abbreviations: Pdet max = maximum detrusor pressure, Pdet Qmax = detrusor pressure at maximum flow, Qmax = maximum flow, Residual = post-void residual, BCI = bladder contractility index (Pdet Qmax + 5 x Qmax).

Table ST5. Patients in blinded study, decoding based on the three-mRNA and three-miRNA signatures and urodynamic diagnosis

Code	Decode	Diagnosis
BOO1	BOO1_UA	UA
BOO2	BOO2_UA	UA
BOO3	BOO3_UA	UA
BOO4	BOO4_UA	UA
BOO5	BOO5_DO	DO
BOO6	BOO6_DO	DO
BOO7	BOO7_DO	DO
BOO8	BOO8_BO	BO
BOO9	BOO9_BO	BO
BOO10	BOO10_UA	UA
BOO11	BOO11_UA	UA
BOO13	BOO13_UA	UA
BOO45	BOO45_BO	BO
BOO44	BOO44_BO	BO
BOO17	BOO17_UA	UA
BOO18	BOO18_UA	UA
BOO19	BOO19_UA	UA
BOO20	BOO20_UA	UA
BOO21	BOO21_DO	DO
BOO22	BOO22_DO	DO
BOO23	BOO23_DO	DO
BOO24	BOO24_DO	DO
BOO25	BOO25_UA	UA
BOO26	BOO26_UA	UA
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BOO31	BOO31_DO	DO
BOO32	BOO32_DO	DO
BOO33	BOO33_BO	BO
BOO34	BOO34_BO	BO
BOO37	BOO37_DO	DO
BOO38	BOO38_DO	DO
BOO39	BOO39_DO	DO
BOO40	BOO40_DO	DO
BOO41	BOO41_UA	UA
BOO42	BOO42_UA	UA

Table ST6. Top 10 canonical pathways implicated in BOO patients' groups

Pathways predicted based on mRNA dataset			Pathways predicted based on expressed miRNA targets		
Canonical Pathway Name	**-log(p-value)**	**z-score**	**Canonical Pathway Name**	**-log(p-value)**	**z-score**
		DO			
ERK5 Signaling	6.88	2.828	Protein Kinase A Signaling	3.72	-0.333
PI3K/AKT Signaling	4.43	1.89	Sphingomyelin Metabolism	3.13	NaN
Protein Kinase A Signaling	3.7	0.775	RhoA Signaling	2.42	NaN
Colorectal Cancer Metastasis Signaling	3.51	2.111	PI3K/AKT Signaling	2.4	NaN
Cholecystokinin/Gastrin-mediated Signaling	3.42	2.646	GADD45 Signaling	2.36	NaN
Corticotropin Releasing Hormone Signaling	3.17	1.342	Pyridoxal 5'-phosphate Salvage Pathway	2.34	NaN
TGF-β Signaling	2.99	2.449	Cardiac β-adrenergic Signaling	2.28	0
Neuregulin Signaling	2.97	1.342	D-myo-inositol-5-phosphate Metabolism	2.14	NaN
IGF-1 Signaling	2.75	1	3-phosphoinositide Degradation	2.13	NaN
Wnt/β-catenin Signaling	2.74	0.816	VDR/RXR Activation	2.1	NaN
		BO			
Dendritic Cell Maturation	11.8	3.889	ILK Signaling	5.54	1.941
IL-6 Signaling	11.3	3.4	IL-6 Signaling	4.62	1.897
Leukocyte Extravasation Signaling	9.79	3.128	PPAR Signaling	4.58	-2.333
Production of Nitric Oxide and Reactive Oxygen Species in Macrophages	8.9	2.117	Acute Phase Response Signaling	4.58	1.508
CD28 Signaling in T Helper Cells	8.1	1.941	IL-8 Signaling	4.22	3.464
OX40 Signaling Pathway	8.09	0.378	HMGB1 Signaling	3.75	2.828
HMGB1 Signaling	7.96	3.71	Toll-like Receptor Signaling	3.65	0.816
PKCθ Signaling in T Lymphocytes	7.39	2.4	ERK5 Signaling	3.21	2.236
ILK Signaling	7.35	1	CD40 Signaling	3.14	1.342
MIF Regulation of Innate Immunity	6.94	1.732	IGF-1 Signaling	2.93	0
		UA			
CD28 Signaling in T Helper Cells	14.4	5.603	p53 Signaling	6.69	1.091
B Cell Receptor Signaling	14	5.893	Glioblastoma Multiforme Signaling	6.61	-0.354
iCOS-iCOSL Signaling in T Helper Cells	14	4.964	B Cell Receptor Signaling	6.4	4.768
Role of NFAT in Regulation of the Immune Response	13.8	5.68	ERK5 Signaling	6.4	2.982
Dendritic Cell Maturation	13.2	6.671	IGF-1 Signaling	6.23	1.528
PKCθ Signaling in T Lymphocytes	12.7	5.598	Estrogen-mediated S-phase Entry	6.08	1.155
Tec Kinase Signaling	11.7	5.515	Tec Kinase Signaling	5.8	3.157
Toll-like Receptor Signaling	11.5	4.131	PI3K Signaling in B Lymphocytes	5.61	3.286
PI3K Signaling in B Lymphocytes	11.3	4.719	IL-6 Signaling	5.59	4.271
IL-6 Signaling	10.9	5.357	Cardiac Hypertrophy Signaling	5.44	3.28

Table is sorted based on -log(p-value) of individual pathways, calculated using the right-tailed Fisher Exact Test. Positive z-score indicates activation and negative z-score represents inhibition of a pathway. Input - differentially expressed mRNAs and expressed miRNA targets of abundant regulated miRNAs (abs. fold change ≥1.5, p-value <0.05 and adjusted p-value< 0.15).

Table ST7. Top 10 canonical pathways using all BOO patients' datasets.

Pathways predicted based on mRNA dataset			Pathways predicted based on expressed miRNA targets		
Canonical Pathway Name	**-log(p-value)**	**z-score**	**Canonical Pathway Name**	**-log(p-value)**	**z-score**
HMGB1 Signaling	8.37	3.771	**HMGB1 Signaling**	4.01	1.633
IL-6 Signaling	7.04	3.153	**SAPK/JNK Signaling**	3.72	0
Acute Phase Response Signaling	6.59	3.153	**ERK5 Signaling**	3.62	2
Role of IL-17F in Allergic Inflammatory Airway Diseases	6.18	3.162	**Hepatic Fibrosis / Hepatic Stellate Cell Activation**	2.90	NaN
TREM1 Signaling	5.56	2	**Colorectal Cancer Metastasis Signaling**	2.90	1.414
Colorectal Cancer Metastasis Signaling	5.41	3.411	**Bladder Cancer Signaling**	2.97	NaN
Leukocyte Extravasation Signaling	4.93	3.5	**NRF2-mediated Oxidative Stress Response**	2.94	1.89
B Cell Receptor Signaling	4.58	4.123	**IL-8 Signaling**	2.88	1.89
Dendritic Cell Maturation	4.48	3.5	**p53 Signaling**	2.74	NaN
p53 Signaling	4.35	1.134	**HIF1α Signaling**	2.66	NaN

Table is sorted based on -log(p-value) of individual pathways, calculated using the right-tailed Fisher Exact Test. Positive z-score indicates activation and negative z-score represents inhibition of a pathway. Input - differentially expressed mRNAs and expressed miRNA targets of abundant regulated miRNAs (abs. fold change ≥1.5, p-value <0.05 and adjusted p-value< 0.15).

Supplementary figure legends

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Figure S2. Upstream regulator analysis of DO, BO and UA groups based on top 30 elements in mRNA-based and miRNA target-based pathways

Upstream regulator analysis networks illustrating the interaction of top 30 pathway elements (mRNAs) in mRNA datasets or expressed miRNA targets datasets (miRNA targets) of patients' groups.
(**A**) mRNA dataset of DO patients. JUN with 12 targets in our mRNA dataset was the most interactive element. KRAS with 9 ILA1 with 8 MYC with 7 and MAP3K8 with 5 targets were among top targeting pathway element in DO mRNA dataset.
(**B**) mRNA dataset of BO patients. TNF with 21 targets in our mRNA dataset was the most interactive element.
(**C**) mRNA dataset of UA patients. TNF with 11 targets was the most interactive element. TNF and NFKBIA were predicted to be activated.
(**D**) Expressed miRNA targets dataset of DO patients. KLF with 5 targets in our mRNA dataset was the most interactive element. KLF and CTGF were predicted to be activated.
(**E**) Expressed miRNA targets dataset of BO patients. FOS with 16 targets in our mRNA dataset was the most interactive element.
(**F**) Expressed miRNA targets dataset of UA patients. KRAS with 7 targets was the most interactive element. STAT3, JAK2 and NFKBIA were predicted to be activated.

Figure S3. Upstream regulator analysis of all BOO patients based on top 30 elements in mRNA-based and expressed miRNA target-based pathways

(**A**) mRNA dataset of all BOO patients. TNF was the most effective element.
(**B**) Expressed miRNA targets dataset of abundant significant miRNAs in all BOO patients. JUN is the top upstream element.