ONLINE SUPPLEMENT

Blood pressure control by a secreted FGF Binding Protein, FGFBP1

Elena Tassi[1,*], En Yin Lai[2,3,*], Lingli Li[2], Glenn Solis[2], Yifan Chen[2], Will Kietzman[1], Patricio E. Ray[4], Anna T. Riegel[1], William J. Welch[2], Christopher S. Wilcox[2], and Anton Wellstein[1]

[1]Lombardi Cancer Center, [2]Division of Nephrology and Hypertension, Georgetown University, Washington, DC 20007, USA; [3]Department of Physiology, Zhejiang University, Hangzhou 310058, China; [4]Children's National Medical Center, George Washington University, Washington DC 20001, USA

*equal contribution

Correspondence: to A.W. email: anton.wellstein@georgetown.edu; Phone +1 (202) 687-3672; Fax +1 (202) 687-4821

Running Title: Blood pressure control by FGFBP1

Contents:

Supplemental Methods

Conditional transgenic animal model.

Animal experiments were reviewed and approved by the Institutional Animal Care and Use Committee. Transgenic animals carrying a human BP1 cDNA under the control of a tetracycline response element (TRE-BP1) were mated with CMV-tTA (tet-OFF) mice as described [1]. Transgene expression was suppressed by continuous tetracycline containing diet (=BP1 OFF) and induced by switching the animals to a tetracycline-free, regular diet (=BP1 ON). Doxycycline was used as an orally available tetracycline. $FGF2^{-/-}$ mice were obtained from the Jackson laboratory who store embryos generated by the Doetschman laboratory [2].

Telemetric monitoring of blood pressure and heart rate.

The surgical procedure and telemetry have been described earlier [3]. Tempol (2 mM) and a high dose of candesartan (10 mg/kg/d [4]; gift from AstraZeneca) were administered through the drinking water. Angiotensin II was administered by minipump.

In vivo cremaster arteriole contractility.

Anesthetized (1.5 - 2% isofluorane) mice were infused with 1% albumin in 0.9% NaCl to maintain hydration. The cremaster muscle was exteriorized for intravital microscopy. Vascular diameter was measured with a video caliper in real time using computerized data acquisition. Only arterioles that showed >70% vasodilation with 0.1 mM acetylcholine and >70% constriction with 10 µM PE at the beginning and the end of the experiments were selected. Maximum vasodilation was defined as the response to 10 mM acetylcholine. Increasing concentrations of AngII or PE (~20 µl) were superfused over the vessel. At least 3 minutes were allowed between doses and no subsequent doses were applied before recovery to the baseline diameter. PD173,074 (EMD Chemicals, Gibbstown, NJ) was administered by i.p. injection at 1 mg/kg/day.

Gene expression analysis.

Gene expression analysis was performed on MOE430A Affymetrix arrays with RNA extracted using the Qiagen RNeasy kit that was provided to the Genomics Core Facility for reverse transcription, labelling, and hybridization. Readings from the arrays were analyzed as per the manufacturer's specifications.

Upstream regulators were derived from cDNA array gene expression using the Ingenuity Upstream Regulator Analysis (Qiagen, Germantown, MD) platform [6]. A 1.5-fold difference in gene expression was set as the threshold value. The upstream regulator analysis examines how many known targets are changed and the direction of the change to what is published for a given candidate upstream regulator. IPA's definition of upstream regulator includes any molecule that can affect the expression of a gene. This broad definition includes transcriptional regulators, microRNAs, kinases, phosphatases, chemical compounds, drugs, etc. This is shown in Table S1 below. For each upstream regulator the p-value signifies the overlap of altered genes in the dataset evaluated with genes known to be regulated by the respective upstream regulator. An activation z-score indicates to what extent the pattern changes observed (up or down) match with the direction of gene regulation found in the literature.

Gene Set Enrichment Analysis (GSEA [7]) is a publically available analysis software and data bases from the Broad Institute (http://software.broadinstitute.org/gsea/index.jsp) and was also applied to the cDNA array gene expression. Results from hallmark pathways are exemplified in Figure 5B and the complete list is shown in Table S2 below.

Cell culture, histochemistry and Western blot analysis.

Human HEK293 cells were maintained in DMEM with 10% FCS (Invitrogen, Carlsbad, CA). Human lung microvascular endothelial cells (HMVEC-L) and pulmonary artery smooth muscle cells

(PASMC) (Lonza, Basel, Switzerland) were maintained as suggested by the manufacturer. Immunoblot studies for phospho- and total MKK4, ERK1/2, p38, and JNK were performed with the respective rabbit polyclonal antibodies (Cell Signaling, Danvers, MA) as described [8]. Immunoblot analyses for human actin were performed with a respective mouse monoclonal antibody (Chemicon International, Temecula, CA). Immunohistochemistry was as decribed in [1] with phospho-p38 and phospho-MKK4 antibodies (Cell Signaling, Danvers, MA).

Proteomics analysis of tissue extracts.
For the mass spectrometry analysis, protein lysates from kidneys were subjected to immunoprecipitation using gamma-bind G-Sepharose beads and an anti-phosphotyrosine monoclonal antibody (4G-10, Millipore). The amount of protein input for immunoprecipitations of the kidney extracts was 3.11 mg/ml (BP1 OFF) and 3.14 mg/ml (BP1 ON) with bovine serum albumin used as the standard. The immunoprecipitated proteins were separated by 2D gel electrophoresis. After electrophoresis, gels were stained with Coomassie blue overnight and washed with ddH2O overnight to remove background staining. Stained gels were imaged using a color scanner and spots of distinct intensity cut from the gels for mass spectrometry analyses. Gel slices were subjected to tryptic digest and followed by MS and MS/MS on an ABI MALDI-TOF-TOF. Proteins in the MS or MS/MS analysis were identified based on searches of the Swiss-Prot database using the search engine Mascot as described earlier [9]. The number of matching peptides and the raw protein score were recorded as was the fold difference between BP1 ON and BP1 OFF.

Western blots and immunoprecipitation.
Detection of the BP1 protein was described earlier [10]. Briefly, organs from BP1 OFF and BP1 ON mice were homogenized in 1 ml of lysis buffer with a MagNa lyser homogenizer (Roche, Indianapolis, IN) and BP1 immunoprecipitated with 2 µg of 3E11 mouse monoclonal antibody [10] for 2 hours at 4°C. Immunoblots were performed with a rabbit polyclonal antibody to human FGFBP1 (Sigma, St. Louis, MO) and with a mouse monoclonal antibody to mouse actin (Millipore, Temecula, CA). Human recombinant FGFBP1 (R&D Systems, Minneapolis, MN) (20 ng) was a positive control.

Real-Time Polymerase Chain Reaction.
Total RNA was isolated from transgenic mouse tissues and from cultured cells using RNA STAT-60 (Tel-Test, Inc., Friendswood, TX). cDNA was synthesized with the iScript cDNA Synthesis Kit (Bio-Rad Laboratories). Quantitative real-time PCR (qRT-PCR) to quantify mRNA expression was performed using iQ SYBR Green Supermix (Bio-Rad Laboratories) as described [1].

PCR primer sequences:

BP1 sense 5'-ATGAAGATCTGTAGCCTCACC-3'
BP1 antisense 5'-TTCTGAGACCACTTTGCTGT-3'

mouse beta-actin sense 5'-GGCGCTTTTGACTCAGGATTTAA-3'
mouse beta-actin antisense 5'-CCTCAGCCACATTTGTAGAACTTT-3'

mouse AT1R sense 5' - TGCAGGTGACTTTGGCCAC - 3'
mouse AT1R antisense 5' - CCATTGTCCACCCGATGAAG - 3'

Statstics and data analysis.
Prism 5 (Graphpad Inc) was used for descriptive statistical analyses that include the assessment of normal distribution of quantitative measurements. The non-linear regression analyses of dose-response data obtained in vivo or in vitro used the functions described earlier [11] and available in Prism 5. A sinus wave function was fit to the circadian measurements. For comparisons between data sets analyzed by non-linear regression analyses, parameters from the best fit were compared using an F-test [11, 12]. The respective p-values and parameters are provided as calculated in Prism 5. ANOVA was used for multiple comparisons and t-tests for paired comparisons. *P* values <0.05 were considered statistically significant. Mean $\pm$ SEM values are depicted in the figures. For the GSEA analysis nominal p-values as well as false-discovery rate adjusted q-values are provided in Table S2.

Supplemental References

1. Tassi E, Mcdonnell K, Gibby KA, Tilan JU, Kim SE, Kodack DP, Schmidt MO, Sharif GM, Wilcox CS, Welch WJ, Gallicano GI, Johnson MD, Riegel AT, Wellstein A. Impact of fibroblast growth factor-binding protein-1 expression on angiogenesis and wound healing. *Am J Pathol*. 2011;179:2220-2232
2. Zhou M, Sutliff RL, Paul RJ, Lorenz JN, Hoying JB, Haudenschild CC, Yin M, Coffin JD, Kong L, Kranias EG, Luo W, Boivin GP, Duffy JJ, Pawlowski SA, Doetschman T. Fibroblast growth factor 2 control of vascular tone. *Nat Med*. 1998;4:201-207
3. Kawada N, Solis G, Ivey N, Connors S, Dennehy K, Modlinger P, Hamel R, Kawada JT, Imai E, Langenbach R, Welch WJ, Wilcox CS. Cyclooxygenase-1-deficient mice have high sleep-to-wake blood pressure ratios and renal vasoconstriction. *Hypertension*. 2005;45:1131-1138
4. Callera GE, Antunes TT, Correa JW, Moorman D, Gutsol A, He Y, Cat AN, Briones AM, Montezano AC, Burns KD, Touyz RM. Differential renal effects of candesartan at high and ultra-high doses in diabetic mice-potential role of the ACE2/AT2R/Mas axis. *Bioscience reports*. 2016;36
5. Chen Y, Pearlman A, Luo Z, Wilcox CS. Hydrogen peroxide mediates a transient vasorelaxation with tempol during oxidative stress. *Am J Physiol Heart Circ Physiol*. 2007;293:H2085-2092
6. Krämer A, Green J, Pollard J, Tugendreich S. Causal analysis approaches in Ingenuity Pathway Analysis. *Bioinformatics (Oxford, England)*. 2014;30:523-530
7. Subramanian A, Tamayo P, Mootha VK, Mukherjee S, Ebert BL, Gillette MA, Paulovich A, Pomeroy SL, Golub TR, Lander ES, Mesirov JP. Gene set enrichment analysis: a knowledge-based approach for interpreting genome-wide expression profiles. *Proceedings of the National Academy of Sciences of the United States of America*. 2005;102:15545-15550
8. Tassi E, Al-Attar A, Aigner A, Swift MR, McDonnell K, Karavanov A, Wellstein A. Enhancement of fibroblast growth factor (FGF) activity by an FGF-binding protein. *J Biol Chem*. 2001;276:40247-40253
9. Hu Z-Z, Kagan BL, Ariazi EA, Rosenthal DS, Zhang L, Li JV, Huang H, Wu C, Jordan VC, Riegel AT, Wellstein A. Proteomic analysis of pathways involved in estrogen-induced growth and apoptosis of breast cancer cells. *PLoS ONE*. 2011;6:e20410
10. Tassi E, Henke RT, Bowden ET, Swift MR, Kodack DP, Kuo AH, Maitra A, Wellstein A. Expression of a fibroblast growth factor-binding protein during the development of adenocarcinoma of the pancreas and colon. *Cancer Res*. 2006;66:1191-1198
11. Wellstein A, Belz GG, Palm D. Beta adrenoceptor subtype binding activity in plasma and beta blockade by propranolol and beta-1 selective bisoprolol in humans. Evaluation with Schild-plots. *J Pharmacol Expt Ther*. 1988;246:328-337
12. Wellstein A, Pitschner HF. Complex dose-response curves of atropine in man explained by different functions of M1- and M2-cholinoceptors. *Naunyn-Schmiedeberg's Arch Pharmacol*. 1988;338:19-27

Table S1. cDNA array gene expression analysis of kidneys. mRNA was extracted from kidneys 48 hour after induction of BP1 and analyzed relative to controls without induction. Ingenuity Pathway Analysis was used to identify Upstream Regulators [6]. *P*-values are shown. As available, activation z-scores are included. Negative z-scores indicate inhibitory Upstream Regulators. For genes that function as "Upstream Regulators", the 48 h gene expression relative to control (log-fold) is included [examples: 0.301 = 2-fold up; - 0.301 = 2-fold down; 0 = no change relative to control]
The data is sorted by *P* values.

Upstream Regulator	Log ratio mRNA 48h / control	Activation z-score	p-value of overlap
beta-estradiol		0.897	3.64E-29
methylprednisolone		1.988	3.51E-28
lipopolysaccharide		1.575	1.18E-25
TP53	-0.263	2.098	3.24E-25
HNF4A	-0.655	-0.578	1.22E-23
HTT	0.289	0.379	1.64E-23
dexamethasone		-0.934	1.83E-22
tretinoin		-0.522	1.09E-20
TGFB1	0	1.386	1.41E-20
nitrofurantoin		3.874	3.43E-20
TO-901317		0.532	9.86E-20
HNF1A	-0.15	-2.349	9.13E-19
TNF	-0.324	0.497	9.13E-19
pirinixic acid		2.159	5.18E-18
IL1B	-0.102	2.741	7.92E-18
ciprofibrate		5.346	8.3E-18
ACOX1	-0.349	-5.898	9.34E-18
progesterone		0.468	1.66E-17
forskolin		0.785	3.36E-16
FOS	0.617	-0.84	8.5E-16
CTNNB1	-0.639	-1.769	1.17E-15
D-glucose		0.009	1.73E-15
IL6	-0.11	1.222	2.35E-15
U0126		-1.413	2.44E-15
PPARA	0.686	2.557	2.48E-15
SP1	0.588	-1.628	2.69E-15
NR3C1	-0.978	1.002	9.16E-15
methapyrilene		2.837	2.83E-14
ethanol		1.519	3.03E-14
acetaminophen		3.372	3.93E-14
RORA	0.615	0.501	5.1E-14
dihydrotestosterone		0.599	1.53E-13
carbon tetrachloride		0.636	2.12E-13

methotrexate		-0.45	2.2E-13
Insulin		1.498	4.02E-13
ERBB2	0.207	0.838	4.55E-13
MYC	0.084	1.131	7.59E-13
L-triiodothyronine		-0.982	7.63E-13
NR1I2	-0.376	1.974	7.96E-13
APP		0.683	9.12E-13
FOXA2	-0.328	-0.26	1.14E-12
RXRA	-0.559	-0.317	1.2E-12
PRKAG3			1.28E-12
CREB1	-0.265	1.837	1.38E-12
CEBPB	1.036	-0.208	1.6E-12
EGF	0.254	1.773	1.65E-12
Sos			1.93E-12
LEP	-0.024	-0.725	4.24E-12
mifepristone		-0.547	8.97E-12
NFE2L2	0.218	1.87	9.34E-12
NFKBIA	0.792	0.656	9.68E-12
HRAS	0.109	0.957	1.15E-11
PDGF BB		2.286	1.75E-11
YY1	0.48	-0.697	2.43E-11
CLOCK	0.35	1.71	3.62E-11
phorbol myristate acetate		0.217	5.47E-11
cycloheximide		0.656	5.54E-11
CEBPA	0.092	-1.047	6.57E-11
RORC	-0.41		7.94E-11
LY294002		-1.273	9.03E-11
FSH		1.132	1.37E-10
cisplatin		2.054	1.96E-10
TCOF1	0.218		2.6E-10
Ins1	-0.197	-0.433	3.71E-10
trichostatin A		0.59	4.92E-10
8-bromo-cAMP		-0.696	5.35E-10
PRL	-0.265	0.047	6.09E-10
1,2-dithiol-3-thione		1.696	6.76E-10
PD98059		-1.472	9.4E-10
IGF1	-0.951	0.429	1.23E-09
E. coli B5 lipopolysaccharide		0.43	1.26E-09
PDX1	-0.696	1.883	1.62E-09
AR	0.228	-0.255	1.8E-09
rosiglitazone		-0.057	1.81E-09
thyroid hormone		-0.48	2.12E-09
POR	0.036	-0.366	2.6E-09

1,4-bis[2-(3,5-dichloropyridyloxy)]benzene		-1.205	3.38E-09
tunicamycin		1.371	3.82E-09
PTEN	0.72	0.228	3.93E-09
NR1I3	-0.355	-1.366	4.51E-09
lactacystin		0.777	5.23E-09
GH1		0.904	6.18E-09
streptozocin		0.994	7.01E-09
fenofibrate		2.086	7.85E-09
propylthiouracil		-0.652	7.93E-09
IL3		1.479	8.22E-09
valproic acid		1.165	1.11E-08
diethylstilbestrol		0.106	1.35E-08
benzyloxycarbonyl-Leu-Leu-Leu aldehyde		0.977	1.46E-08
Cg		1.54	0.000000015
triamcinolone acetonide		1.193	1.52E-08
cholic acid		0.972	1.61E-08
cadmium chloride		2.368	1.73E-08
NR1H4	0	0.084	1.75E-08
LIPE	-0.081	0.653	1.78E-08
PGR	-0.002	2.185	1.83E-08
17-alpha-ethinylestradiol		0.57	1.83E-08
prostaglandin E2		2.309	2.72E-08
SREBF1	-0.288	0.407	2.75E-08
methylselenic acid		-1.539	4.18E-08
JUN	0.884	-0.141	4.86E-08
camptothecin		0.609	5.25E-08
thapsigargin		3.06	5.75E-08
mercuric chloride		2.072	6.04E-08
miR-30c-5p (and other miRNAs w/seed GUAAACA)		-1.026	6.52E-08
hydrogen peroxide		1.875	7.67E-08
butyric acid		1.063	9.17E-08
TAF4	-0.398	0.124	0.000000106
gentamicin		5.633	0.000000118
miR-1-3p (and other miRNAs w/seed GGAAUGU)		-1.197	0.00000014
chenodeoxycholic acid		-0.042	0.000000146
EGFR	-0.648	0.576	0.000000159
AGT	-0.019	0.637	0.000000169
INSR	-0.492	1.693	0.000000181
cholesterol		-0.149	0.000000183
IGF2	1.549	0.496	0.000000191

IRS1	0.591	1.218	0.000000193
OSM		0.546	0.000000198
testosterone		0.625	0.000000227
trovafloxacin		1.225	0.000000245
ZBTB20	1.253	-3.441	0.000000255
CD38	-0.317	3.8	0.000000256
AKT1	0.189	0.363	0.000000268
Ca2+		1.786	0.000000285
curcumin		-1.47	0.00000029
CFTR	0.049	1.033	0.0000003
ATN1	0.377		0.000000313
CREM	0.584	2.212	0.000000348
dinoprost		0.239	0.000000363
Creb		1.14	0.000000369
RNA polymerase II			0.000000379
6-hydroxydopamine		1.552	0.000000383
NR1H3	0.149	-0.738	0.000000383
FECH	-0.337		0.000000389
miR-16-5p (and other miRNAs w/seed AGCAGCA)		-2.045	0.000000457
SP3	0.347	1.859	0.000000473
NR5A2	-0.478	1.25	0.000000485
PPARG	-0.008	0.933	0.000000493
cyclic AMP		-0.238	0.000000676
cyclosporin A		0.358	0.000000761
PSEN1	-0.372	1.211	0.00000081
FXR ligand-FXR-Retinoic acid-RXRα		-1.118	0.000000817
4-hydroxytamoxifen		0.584	0.000000824
RHO	-0.486	-1.091	0.000000841
GW 4064		-0.237	0.000000932
halofuginone		-0.13	0.00000102
cadmium		1.472	0.00000103
sirolimus		-3.999	0.00000105
tetrachlorodibenzodioxin		2.325	0.00000106
MECP2	0.461	-0.617	0.00000112
MYOD1	-0.206	-1.238	0.00000115
LEPR	-0.981	0.41	0.00000121
4-phenylbutyric acid		-1.974	0.00000129
androgen		-1.353	0.00000135
troglitazone		1.137	0.00000138
MED1	-0.193	0.294	0.00000145
anisomycin		0.085	0.00000153

EPO		2.455	0.00000156
KRAS	0.677	0.07	0.00000171
CD3		-0.157	0.00000173
GW501516		1.255	0.00000181
bromobenzene		0.842	0.00000183
dimethyl sulfoxide		-0.153	0.00000184
potassium chloride		1.013	0.00000189
thioacetamide		-0.757	0.00000192
ESR1	-0.707	0.08	0.00000201
Lh		0.115	0.00000204
selenomethylselenocysteine		-2.331	0.00000209
ERBB4	-0.153	0.501	0.00000238
fulvestrant		1.364	0.00000244
FGF2	-0.05	2.65	0.00000248
TAF4B		0.896	0.00000252
HIF1A	0.678	0.448	0.00000273
ONECUT1	-0.337	-1.974	0.00000288
tamoxifen		-0.178	0.00000344
NFkB (complex)		0.139	0.0000037
dexamethasone phosphate		2.891	0.00000374
ATF4	0.939	1.375	0.00000393
RARG	-0.502	-1.109	0.0000043
IFNG	-0.194	1.175	0.00000478
miR-155-5p (miRNAs w/seed UAAUGCU)		0.236	0.00000493
alitretinoin		-0.61	0.00000493
HGF	-0.306	1.838	0.00000508
bortezomib		1.966	0.0000052
fatty acid		0.414	0.00000533
PXR ligand-PXR-Retinoic acid-RXRα		0.032	0.00000548
T3-TR-RXR		-1.525	0.00000548
bexarotene		-0.134	0.00000566
SIM1	0.2	0.386	0.00000591
ARNT2	-0.419	0.885	0.00000602
AGN194204		2.578	0.00000609
raloxifene		-0.938	0.00000617
Gh	-0.474	-0.595	0.0000062
STAT3	0.782	-0.657	0.00000635
oleic acid		0.684	0.00000639
FGF1	-0.311	0.192	0.00000659
FGF19	-0.15	0.812	0.00000667
bisphenol A		0.592	0.00000686

Pkc(s)		2.064	0.00000711
IL1		-0.282	0.00000742
CAV1	0.089	1.082	0.00000799
PPARD	-0.132	0.954	0.00000829
prednisolone		0.725	0.00000857
arsenite		2.099	0.00000867
corticosterone		1.696	0.00000867
doxorubicin		1.093	0.00000895
NFYC	-0.004	-1	0.00000912
bucladesine		-0.027	0.00000918
5-N-ethylcarboxamido adenosine		-0.13	0.0000107
MGEA5	0.348	-0.577	0.0000111
USF2	0.116	-2.575	0.0000112
SLC13A1	-0.07	0	0.0000116
Mapk		1.699	0.0000131
GPD1	-0.455		0.0000143
paclitaxel		-0.355	0.0000147
diethylnitrosamine		2.857	0.0000147
WISP2	-0.169	0.64	0.0000151
bezafibrate		1.895	0.0000155
IL4	-0.068	1.337	0.0000155
miR-221-3p (and other miRNAs w/seed GCUACAU)		-1.291	0.0000165
NKX3-1	-0.262		0.0000177
RARA	-0.013	-0.917	0.0000194
RAF1	-0.3	2.769	0.0000202
palmitic acid		1.693	0.0000211
clofibrate		3.347	0.0000215
SLC25A13	0.043		0.0000215
HNF1B	-0.833	-0.488	0.0000219
MYCN	-0.474	1.307	0.0000222
IL5	-0.34	4.52	0.0000231
FOXA1	-0.169	-0.113	0.0000277
phenobarbital		-2.671	0.0000277
CD40LG	-0.54	0.137	0.0000292
miR-21-5p (and other miRNAs w/seed AGCUUAU)		-0.63	0.0000301
Vegf		2.357	0.0000308
IL13	-0.208	-0.016	0.0000323
FAS	-0.007	-1.054	0.0000353
THRB	-0.695	1.045	0.0000356
LRP6	0.222	0	0.0000356
CDKN2A	-0.106	1.84	0.0000357

cocaine		2.729	0.0000364
estrogen receptor		0.323	0.0000405
norepinephrine		1.566	0.0000424
EGR1	1.025	-0.053	0.0000424
Rxr		0.198	0.0000424
NCOR-LXR-Oxysterol-RXR-9 cis RA		-0.389	0.0000437
pregnenolone carbonitrile		-0.12	0.0000451
RET	-0.245	0.885	0.0000463
FOXO1	0.513	0.881	0.0000476
monorden		2.121	0.0000481
SMARCB1	0.211	-0.177	0.0000484
IGF1R	0.336	2.68	0.0000538
linoleic acid		0.436	0.0000562
metribolone		0.183	0.0000568
NR3C2		1.031	0.0000576
Histone h3		0	0.0000612
BDNF	-0.504	-0.926	0.0000631
okadaic acid		1.389	0.0000638
MAP2K1	-0.082	2.116	0.0000648
GAST	-0.129	2.544	0.0000659
HOXA10	0.052	-0.728	0.0000675
glucocorticoid		0.953	0.0000686
leucine		-1.207	0.0000697
amino acids		-2.18	0.0000697
amphetamine		1.576	0.0000701
INS	-0.329	1.66	0.0000751
MET	-1.115	-0.496	0.0000824
ETS1	-0.499	0.57	0.0000871
TERT	-0.521	0.447	0.0000873
SYVN1	0.164	1.616	0.0000888
TGFBR2	-0.624	-0.151	0.0000899
actinomycin D		-1.625	0.0000909
N-ethyl-N-nitrosourea			0.0000926
SIN3A	-0.181	0.447	0.0000929
AHR	-0.093	0.213	0.000095
ADRA1A	-0.182		0.0000954
PI3K (complex)		1.467	0.0000983
GNA12	-0.415	1.478	0.000102
kainic acid		2.138	0.000103
MTPN	1.119	0.258	0.000105
miR-124-3p (and other miRNAs w/seed AAGGCAC)		-1.323	0.000106

CP-55940		0.655	0.000107
K+		-0.907	0.000107
WNT3A	-0.654	-0.895	0.000109
Tcf 1/3/4		-1.4	0.000109
ADRB		0.192	0.000109
ELOVL5	0.106	-1.869	0.000109
dehydroisoandrosterone		-1.158	0.00011
miR-141-3p (and other miRNAs w/seed AACACUG)		-0.061	0.000111
HSF1	-0.108	1.546	0.000114
genistein		-1.887	0.000117
ZAP70	-0.699	0.158	0.000122
mannose		-0.378	0.000124
CYP1A1	0.051	2.309	0.000128
RB1	0.401	1.151	0.000128
TEAD4	-0.534		0.000129
bleomycin		-1.149	0.000134
deferoxamine		0.568	0.000136
NR4A1	0.638	-1.161	0.000137
WT1	0.076	0.667	0.000138
EGR2	0.174	0.278	0.000139
estrogen		-0.953	0.000142
ERK		1.056	0.000145
RARB	-0.371	-0.351	0.000147
flutamide		-0.851	0.000147
GNB2	0.203		0.000148
NFYB	0.354		0.000152
USF1	-0.141	-1.433	0.000156
Histone h4			0.000156
MTOR	-0.796	2.724	0.000156
NPC1	0.234	1.349	0.000158
wortmannin		-0.893	0.000159
isoproterenol		0.26	0.000161
ADRA1D			0.000162
miR-133a-3p (and other miRNAs w/seed UUGGUCC)		0.107	0.00017
arotinoid acid		-0.166	0.00017
EDN1	-0.097	1.087	0.000173
acenocoumarol		2	0.000175
USE1	0.381	-1.154	0.000175
ATF6B	0.155		0.000175
CYP4F2	-0.019		0.000175
FSHB	-0.154	0.115	0.000178

ZNF202	-0.529		0.000178
NKX2-1	-0.444	-1.643	0.00018
GCG	-0.032	1.205	0.000196
olanzapine		-1.494	0.000196
PKD1	0.213	-0.277	0.000204
PPARGC1A	1.307	0.045	0.000205
TCR		1.931	0.000208
pioglitazone		-1.046	0.000209
PRDM1	-0.18	2.633	0.00021
NR4A3	-0.592	0.614	0.00021
glucosamine		-1.295	0.00021
L-methionine		-0.853	0.000211
Hdac		-2.02	0.000215
FGF21	-0.022	1.178	0.000219
SU6656		-1.508	0.000219
simvastatin		0.137	0.000221
TCF			0.000222
methylmercury		1.739	0.000229
SMAD4	0.839	1.745	0.00023
NFYA	-0.291	1.212	0.000232
mir-451		-2.646	0.000242
ATF6	0.021	2.41	0.000252
Ubiquitin		-1.929	0.000254
GW3965		-0.156	0.000261
ATP7B	-0.408	0.277	0.00027
chloropromazine		0.003	0.00027
GNB1	0.717		0.00027
PRKACA	-0.133	0.25	0.000275
MAT1A	-1.039	0.39	0.00028
sorafenib		-0.571	0.00028
DYSF	0.07		0.000281
CDC73	0.567		0.000283
arachidonic acid		-0.084	0.000301
poly rI:rC-RNA		-0.275	0.000305
NR0B2	-0.424	0.893	0.000307
4-methylnitrosoamino-1-(3-pyridinyl)-1-butanone		1.044	0.00031
TP63	-0.498	0.252	0.000321
Zn2+		0.7	0.000321
SOCS2	0.813		0.000321
SOD2	-0.412	1.091	0.000327
FOLR1	-0.319		0.000327
TGFA	-0.519	1.04	0.00034

BAPTA-AM		-1.355	0.000343
SEL1L	-0.519	-2	0.000345
NPAS2	-0.744		0.000345
nonylphenol		0.832	0.000358
mono-(2-ethylhexyl)phthalate		2.971	0.000375
homocysteine		1.922	0.000381
phenylephrine		1.137	0.000381
CD28	-0.044	-0.011	0.000381
nifedipine		-1.625	0.000381
LHX1	0.596	0.139	0.000408
n-nitrosomethylbenzylamine			0.000417
ALDH1A2	0.164	-0.971	0.00043
mir-144		-2.646	0.000436
salirasib		-0.893	0.00044
CXCL12		0.36	0.000441
desmopressin		0.616	0.000443
POMC	-0.412	0.155	0.000443
LDL		-0.348	0.000445
CSF2	-0.178	0.421	0.000447
GNA15	-0.129		0.000453
BMP7	-0.299	1.377	0.000455
Pka		0.874	0.000455
dicarbethoxydihydrocollidine		1.063	0.000458
A23187		2.434	0.000458
PTH	-0.225	1.364	0.000458
CDH1	0.675	-0.132	0.000461
KIAA1524	-0.66	0.497	0.000469
topotecan		-1.046	0.00049
phosphate		1.303	0.000508
F2	-1.522	3.807	0.000512
ESRRA	-0.216	2.831	0.000519
bile acid		-0.066	0.000529
PTPRJ	0.555	1.069	0.000554
decitabine		1.015	0.000558
Mek		3.025	0.000575
IL17A	-0.249	-0.072	0.000586
ADRA1B	-0.428		0.000587
methylnitrosourea			0.000588
TGFB3	-0.179	0.324	0.000601
ionomycin		1.898	0.000602
carbamylcholine		2.457	0.000612
memantine		-0.453	0.000612
5-azacytidine		1.424	0.000618

XBP1	0.511	0.233	0.000632
L-histidine		-1.819	0.000637
miR-217-5p (and other miRNAs w/seed ACUGCAU)		-2.401	0.000637
5-fluorouracil		-1.781	0.000639
EZH2	-0.163	-1.49	0.000641
RETNLB	0.031	-0.75	0.000662
TBX2	0.072	-2.261	0.000662
MAPK8	0.852	0.89	0.00069
11,12-epoxyeicosatrienoic acid		0.146	0.000711
HFE	-0.312	-1.964	0.000711
HOXA9	-0.541	-0.867	0.000717
EIF2AK3	-0.366	2.333	0.000717
GPER1		0.484	0.000736
HR	-0.451	-1.195	0.000736
MAP2K1/2		3.06	0.000742
leukotriene D4		1.871	0.000742
MITF	0.344	-0.665	0.000745
CREBBP	-0.052	-0.434	0.000746
SREBF2	0.294	1.322	0.000751
lysophosphatidic acid		0.542	0.000751
resveratrol		0.421	0.000753
NOS2	-0.206	-0.115	0.000756
RXRB	0.146	-0.068	0.000782
BMS-690514		-0.302	0.000792
mir-182		-0.745	0.000792
bicalutamide		-0.971	0.000792
GTF2B	-0.165		0.000792
TERC			0.000792
triiodothyronine, reverse		1.067	0.000795
mercury		0.192	0.000795
miR-142-3p (and other miRNAs w/seed GUAGUGU)		-0.849	0.000795
HTR2A		-0.94	0.000795
6-cyano-7-nitroquinoxaline-2,3-dione		-1.214	0.000795
acetazolamide		-2	0.000795
MRAS	-0.587		0.000795
beta-carotene		-0.466	0.000802
IL2	-0.321	1.013	0.000818
tyrphostin		0	0.000834
miR-126a-3p (and other miRNAs w/seed CGUACCG)		-1.34	0.000834
P1,P4-Di(adenosine-5')		-1.387	0.000834

tetraphosphate			
MEF2D	0.616	1.569	0.000904
CLDN6	-0.598		0.000904
EPHB4	-0.046	0.535	0.000931
TP73	0.029	0.041	0.000935
TGFB2	-0.751	0.871	0.000949
KLF2	0.109	-0.474	0.000957
PSEN2	-0.287	0.809	0.000971
bardoxolone		0	0.00101
CGS 21680		-0.485	0.00101
miR-182-5p (and other miRNAs w/seed UUGGCAA)		-0.515	0.00105
ZBTB17	0.161	1.633	0.00107
phencyclidine		1.763	0.00115
fluoride		0.842	0.00115
PER2	0.596	0	0.00115
hormone			0.00115
Calcineurin protein(s)		1.192	0.00116
indomethacin		1.004	0.00117
CETP		2.17	0.00118
mannitol		0.381	0.00118
STAT4	-0.115	1.909	0.00121
ascorbic acid		0.473	0.00122
PDGFB	-0.164	0.724	0.00125
ADAM10	-0.863		0.0013
NRG1		1.398	0.00136
NEDD9	0.446	1.508	0.00137
R5020		1.238	0.00139
tributyrin		0.477	0.00139
SMAD3	-0.347	0.533	0.00141
FSHR	-0.413	-0.847	0.00143
FOXO3	0.866	3.157	0.00144
geldanamycin		0.329	0.0015
TOX	-0.045		0.00152
HAO1	-0.891		0.00152
mir-183			0.00152
GC	-1.548		0.00152
SLC12A6	0.683		0.00152
NECTIN1	0		0.00152
BB-2116			0.00152
FGF4	-0.366	-0.114	0.00155
HSPA5	0.649	-1.216	0.00155
fluconazole		-1.501	0.00155

SP600125		-1.705	0.00155
omeprazole		-0.609	0.00157
App	-0.406	1.177	0.00157
MBD2	-0.344	-0.277	0.00157
GLI1	-0.459	0.043	0.0016
miR-122-5p (miRNAs w/seed GGAGUGU)		-1.197	0.00167
8-chlorophenylthio-adenosine 3',5'-cyclic monophosphate		2.977	0.00169
TEF	-0.398	1.214	0.0017
AGRP	-0.1		0.0017
S100P			0.0017
tanespimycin		0.032	0.00172
glutamine		-0.272	0.00173
SOD1	0.46	0.152	0.00173
MLXIPL	0.071	0.75	0.00175
RXRG	-0.298		0.00175
H89		0.631	0.00177
TRH	-0.559	1.977	0.00177
IRS2	0.24	-0.383	0.00177
eicosapentenoic acid		1.002	0.00178
thiazolidinedione		0.871	0.00181
glutamyl-Se-methylselenocysteine		-1.134	0.00181
gefitinib		-0.312	0.00183
CD 437		-3.281	0.00184
let-7		0.197	0.00185
trichloroethylene		1.846	0.00189
benzene		1.846	0.00189
ADRB3	-0.37	0.104	0.00193
cyclooxygenase		-0.577	0.00193
mir-221		-0.744	0.00193
TMBIM6	0.345	-1.638	0.00193
CFB	0.632	-2.449	0.00193
sodium arsenite		2.048	0.00194
capsaicin		0.143	0.00194
phenethyl isothiocyanate			0.00202
benzo(a)pyrene		0.847	0.00204
mir-21		0.59	0.00205
CEBPD	1.607	-1.498	0.00206
ERBB3	0.199	-0.073	0.00208
KITLG	0.641	2.347	0.00209
docosahexaenoic acid		-0.789	0.00209
NR4A2	-0.143	1.929	0.00212

BNIP3L	0.538	1.604	0.00213
FANCC	-0.394		0.00213
MAP3K12	0.894	1.154	0.00217
meclizine		1	0.00217
NCK1	0.044	-0.831	0.00217
benfluorex		-1	0.00217
H6PD	0.361	-1	0.00217
ADCY5		-1	0.00217
CYB5R4	0.211	-1.981	0.00217
PTBP1	-0.061		0.00217
TAF10	0.124		0.00217
CSNK2A2	0.567		0.00217
SRD5A1			0.00217
mir-1		0.611	0.00227
Nr1h		-2.016	0.00227
PRKCE	0.197	0.477	0.00236
fluoxetine		-0.335	0.00236
ouabain		3.051	0.00236
metformin		-0.456	0.00237
salicylic acid		0.439	0.00238
Growth hormone		0.885	0.00241
PAX7	-0.226	0.13	0.00241
NFKB1	0.01	1.186	0.00243
ADORA2A	-0.658	0.833	0.00255
MAP3K1	0.184	1.269	0.00258
dimethylnitrosamine		0.788	0.00263
P38 MAPK		0.785	0.00264
Tgf beta		1.446	0.00264
PDGF-AA		0.762	0.00266
PER1	0.744	-0.339	0.00266
BTRC	-0.666	-1.012	0.00266
FOXA3	-0.381		0.00266
E. coli serotype 0127B8 lipopolysaccharide		-1.383	0.00268
calcitriol		2.767	0.00272
MAX	-0.079	0.555	0.00282
NRL	-0.671	0.056	0.00286
5-hydroxytryptamine		1.431	0.00291
clozapine		1.027	0.00291
miR-17-5p (and other miRNAs w/seed AAAGUGC)		-1.268	0.00291
aldosterone		1.645	0.00292
MBD1	0.59		0.00303

isobutylmethylxanthine		-0.491	0.00303
miR-18a-5p (and other miRNAs w/seed AAGGUGC)		0	0.00305
pCPT-cAMP		1.427	0.00307
RANBP9	-0.146	1.4	0.00307
CRY1	0.038	-0.254	0.00307
farglitazar		-0.447	0.00307
miR-30a-3p (and other miRNAs w/seed UUUCAGU)		-1.287	0.00307
2-amino-1-methyl-6-phenylimidazo-4-5-b-pyridine		3.317	0.00325
2-deoxyglucose		2.597	0.00325
Collagen(s)		1	0.00325
SIRT1	0.573	-0.222	0.0033
HDAC1	0.005	-0.088	0.00354
vincristine		0.707	0.00358
ATF1	0.4	-1.309	0.00358
GnRH analog		0.082	0.0037
GNRH		2.416	0.0038
MNT	-0.361	0	0.0038
RHOJ	0.436		0.0038
SOX2	0.002	0.535	0.00382
gemfibrozil		2.386	0.00384
XDH	0.063	-1.32	0.00387
GATA3	-0.003	-0.758	0.00391
AICAR		-0.44	0.00397
SRF	0.148	0.938	0.00398
arsenic trioxide		1.725	0.004
salmonella minnesota R595 lipopolysaccharides		0.229	0.00406
lithocholic acid		0.708	0.00409
pravastatin		1.242	0.00424
epigallocatechin-gallate		0.026	0.00428
IKBKB	-0.746	0.886	0.00429
mir-210		-2.173	0.00433
E2F1	-0.307	-0.26	0.0044
PLN	-0.733		0.0044
SNAI2	-0.031	-0.737	0.00443
LMNB1	-0.164		0.00443
IKBKG	-0.595	2.142	0.00446
CDX2	-0.414	1.203	0.00447
atorvastatin		-0.629	0.00449
vitamin K3		2.176	0.00459
LIN28A	-0.375	0.412	0.00459

miR-103-3p (and other miRNAs w/seed GCAGCAU)		-0.179	0.00459
MST1R	-0.11	-0.618	0.00459
retinol		-0.816	0.00459
SPTLC2	0.003	-2.425	0.00459
2-mercaptoethanol		1.981	0.00459
L-type Calcium Channel		0	0.00459
L-phenylalanine		-0.152	0.00459
miR-320b (and other miRNAs w/seed AAAGCUG)		-1.176	0.00459
PGK1	0.282		0.00459
VDR	0.313	2.85	0.00462
CCND1	0.45	-0.926	0.00467
RAC1	-0.376	1.072	0.0048
CYP1A2	-1.543	2.309	0.00482
VitaminD3-VDR-RXR		0.98	0.00482
25-hydroxycholesterol		-1.071	0.00482
pimagedine		-0.285	0.00487
NR2F1	0.038	-1.016	0.00487
22(R)-hydroxycholesterol		-1.938	0.00487
VEGFA	-0.237	2.782	0.00506
SCD	0.842	-0.337	0.00507
N-Ac-Leu-Leu-norleucinal		0.173	0.0051
FADD	-0.471	0.04	0.0051
CRY2	0.025	0.317	0.0051
estrone		-1.964	0.0051
ATF2	0.402	0.758	0.00519
NR1H2	-0.018	-0.411	0.0052
UPF2	0.878	0.103	0.00523
MBD3	0.138		0.00523
Ro41-5253		0.752	0.00528
MAP2K5	0.093	0.562	0.00528
Rar		0	0.00528
ZMPSTE24	-0.025	-1.672	0.00528
amitriptyline		-2.588	0.00528
paraquat		0	0.00532
KN-62		0.933	0.00541
4-hydroxynonenal		0.657	0.00541
RCE1	-0.02		0.00544
dextran sulfate			0.00546
STAT5A	-0.2	1.589	0.00551
obatoclax			0.00556
RS1	0.02		0.00556

CA4	-0.416		0.00556
HMGN1			0.00556
NCK2	-0.576		0.00556
APAF1	-0.088		0.00556
GCLC	0.42		0.00556
SLIT2	0.215		0.00556
CITED1	0.008		0.00556
PCYT1A	-0.571		0.00556
ibotenic acid			0.00556
apamin			0.00556
ARNT	-0.508	1.067	0.00567
nocodazole		-0.486	0.00567
RELA	0.221	1.277	0.00571
cigarette smoke		-0.135	0.00577
deoxycholate		1.119	0.00581
iron		-1.095	0.00581
NCOA2	-0.333	-1.212	0.00581
AIRE	-0.345	-1.938	0.00581
TNFSF11	-0.298	0.565	0.00585
2,4,5,2',4',5'-hexachlorobiphenyl		0.167	0.00586
MYB	-0.076	-0.242	0.00586
TCF3	-0.16	-0.641	0.00591
brefeldin A		1.363	0.00606
APOA1	-4.404	-0.675	0.00606
KLF6	1.023	-1	0.00606
mir-17		-1.928	0.00606
ATP-gamma-S			0.00609
NRG2			0.00609
HIC1	-0.307	0.137	0.00611
caffeic acid phenethyl ester		-1.462	0.00619
INSIG1		-0.51	0.00631
APOE	-1.25	-0.296	0.00642
RUNX1	-0.514	0.767	0.00646
FOXO4	-0.373	0.832	0.00662
NTRK2	-0.304	-0.378	0.00662
amiodarone		0.707	0.00663
KAT2B	-0.44	-1.016	0.00663
HBEGF	0.953	-1.939	0.00663
PTK2B	0.633	1.246	0.00664
GLP-1-(7-34)-amide		0.364	0.00664
1-methyl-4-phenylpyridinium		0.059	0.00664
MIR124		-0.816	0.00664
Hmga1	0.088	-0.513	0.00666

CNTF	0	1.449	0.00671
plicamycin		-0.675	0.00671
GnRH-A		3.152	0.00692
NCOA1	0.584	0.268	0.00692
FN1	-0.254	-0.181	0.00694
CDK9	0.227	0	0.00704
tetrodotoxin		-0.158	0.00704
PPP3CA	0.399		0.00707
CAR ligand-CAR-Retinoic acid-RXRα		0.57	0.00714
panobinostat		0.478	0.00714
LRP5	-0.19	0.378	0.00714
AZGP1	-1.336	-0.54	0.00714
ADIPOQ	0.079	-0.852	0.00723
CD44	-0.022	0.013	0.00743
SB 216763		1.234	0.00746
ESR2	-0.053	0.957	0.00773
CHRM1	-0.129	1.513	0.00793
ASIP	-0.065	1.213	0.00793
clotrimazole		0.162	0.00793
nimodipine		-0.447	0.00793
hyperforin		-0.447	0.00793
miR-19b-3p (and other miRNAs w/seed GUGCAAA)		-1.252	0.00793
prazosin		-1.342	0.00793
U18666A		-2.236	0.00793
IRAK4	-0.14		0.00793
GHRL	-0.045	1.78	0.00799
N-methyl-D-aspartate		-0.058	0.00799
TCF7	-0.54	-0.728	0.00799
3,3'-diindolylmethane		-0.737	0.00799
Am 580		0.375	0.0083
MSX2	0.063	0.348	0.0083
PRKAA2		-0.104	0.0083
sphingosylphosphocholine		1.067	0.00835
LIMS1	-0.254	1	0.00835
miR-199a-3p (and other miRNAs w/seed CAGUAGU)		0.28	0.00835
8,9-epoxyeicosatrienoic acid		0.152	0.00835
nicardipine		-0.805	0.00835
ARHGDIA	-0.006	-2	0.00835
phosphatidylcholine			0.00835
FGF3	-0.419		0.00835
BCAR1	0.035		0.00835

RP 73401			0.00835
CYP1B1	-0.264	2.496	0.00836
TCF12	0.441	-0.723	0.00836
medroxyprogesterone acetate		2.223	0.00839
rifampin		-0.302	0.00855
LDLR	-0.303	-1.728	0.0087
IL1A	0	-0.651	0.00872
CSF1	-0.355	-0.075	0.00874
BMP2	-0.008	-0.413	0.00883
phorbol 12,13-didecanoate		1.587	0.00902
carbohydrate		1.134	0.00902
PLAT	0.618	0.478	0.00902
GDF9	-0.103	-0.846	0.00902
methyl methanesulfonate		2.573	0.00911
fluocinolone acetonide		0.632	0.00911
caffeine		-1.135	0.00911
HNRNPA2B1	0.89		0.00922
1-(carboxymethylthio)tetradecane		0.647	0.00928
NFIA	0.835	-0.277	0.00928
C5	-1.088	0.274	0.00938
SPDEF	-0.466	-1.585	0.00938
ARNTL	-0.872	0.96	0.00945
SUPT16H	0.045		0.00945
15-deoxy-delta-12,14 -PGJ 2		-0.027	0.00957
PTPN1	1.017	0.547	0.00957
3-methylcholanthrene		-0.315	0.00957
NGF	-0.173	-0.075	0.00958
REL	-0.153	0.187	0.00973
ERK1/2		0.902	0.00976
beta-naphthoflavone		0.64	0.00977
RBPJ	-0.591	0.37	0.0102
GATA1	-0.124	-0.481	0.0102
propranolol		-1.445	0.0103
SUMO2		-2.36	0.0103
LIF	-0.624	1.787	0.0103
tacrolimus		0.961	0.0103
miR-125b-5p (and other miRNAs w/seed CCCUGAG)		-0.658	0.0103
CNR1	-0.097	-0.074	0.0105
GDF2	-0.584	0.092	0.0107
ANXA7	0.552	-0.246	0.0107
STAT6	0.73	-1.332	0.011
ethionine		0.588	0.011

retinoid		0.563	0.011
CD247	-0.236	0.535	0.0111
MEF2C	0.497	0.286	0.0111
EPAS1	-0.067	0.05	0.0111
IL6R	-0.376	-0.878	0.0114
apomorphine		1.579	0.0114
mir-15		0.896	0.0114
MUC1	0.213	0.127	0.0114
ABCB4	-0.589	-1.005	0.0114
glucagon		-0.038	0.0115
hydrocortisone		1.553	0.0115
CD24		3.207	0.0116
CYP27A1	0.202	0.6	0.0117
MLX	0.095	0.418	0.0117
ESRRG	-0.416	0.261	0.0117
mir-205		-0.895	0.0117
TAF1			0.0117
mir-126			0.0117
tert-butyl-hydroquinone		2.318	0.0117
SMARCA4	0.578	-0.209	0.0119
MEF2A	0.849	1.407	0.0123
SPRY2	-0.241	0	0.0123
miR-200b-3p (and other miRNAs w/seed AAUACUG)		-0.41	0.0123
TGM2	0.53	-0.3	0.0123
losartan potassium		-2.175	0.0126
IHH	0.13	1.446	0.0126
finasteride		0.928	0.0126
POSTN	-0.039	-0.44	0.0126
NAB2	0.903	-1.131	0.0126
NFIX	-0.448	-1.671	0.0126
EIF4EBP1	0.309	-1.732	0.0126
MECOM	-0.586		0.0126
cetuximab			0.0127
RNF187	0.273		0.0127
FOXE3	-0.338		0.0127
Gpcr			0.0127
KLB	-0.422		0.0127
CREB3L4	-0.287		0.0127
ghrelin			0.0127
PSMB9	-0.155		0.0127
ERN2	-0.303		0.0127
SMC3	0.372		0.0127

HNF4G	-0.638		0.0127
MAD2L2	-0.066		0.0127
RHOC	0.098		0.0127
catechol			0.0127
PRNP	0.387	1.109	0.0132
MTA1	0.165	-0.696	0.0132
5,6-epoxyeicosatrienoic acid			0.0132
CHD5			0.0132
L3MBTL1			0.0132
potassium channel			0.0132
PACS2	0.342		0.0132
SRA1	0.021		0.0132
GFRA1	-0.259		0.0132
MAPK8IP2	-0.349		0.0132
OAZ1	-0.33		0.0132
ULK1	-0.163		0.0132
RFX4			0.0132
CELA1	0.604		0.0132
PMAIP1			0.0132
NMB	-0.194		0.0132
mir-489			0.0132
PRSS2			0.0132
HCRT	-0.06		0.0132
TCF20	-0.516		0.0132
MXD4	-0.22		0.0132
PCSK6	0.039		0.0132
HNRNPL	0.15		0.0132
GABRG2	-0.184		0.0132
AKAP13			0.0132
IMPACT	0.552		0.0132
GPS1	-0.081		0.0132
FRAT1	-0.125		0.0132
MID1	-0.456		0.0132
BUB1B	-0.325		0.0132
buformin			0.0132
palytoxin			0.0132
marimastat			0.0132
phenformin			0.0132
teleocidins			0.0132
D-lysergic acid diethylamide			0.0132
trans-4-phenylbut-3-en-2-one			0.0132
protamine zinc insulin			0.0132
vigabatrin			0.0132

KB-R7785			0.0132
NOTCH1	-0.191	1.305	0.0132
vitamin E		0.458	0.0134
colchicine		1.778	0.0134
fish oils		-0.728	0.0134
WNT1	-0.417	-0.383	0.0137
PIAS3	-0.425	1.948	0.0137
[D-Ala2,N-Me-Phe4,Gly5-ol]-Enkephalin		1.266	0.0137
TFF3	0.083	0.849	0.0137
tolbutamide		-0.762	0.0137
OSMR	0.737	-0.849	0.0137
DUSP14	-0.021	-1	0.0137
AURKA	-0.529	-1.004	0.0137
NPC1L1		-2	0.0137
TAF5			0.0137
HGS	0.037		0.0137
dichloroacetic acid			0.0137
CHUK	0.127	1.26	0.0138
APC	-0.202	0.431	0.0138
STAT5B	0.573	1.041	0.0139
nitric oxide		-0.557	0.0144
MAPK1	-0.229	2.332	0.0148
ELK1	-0.359	1.16	0.0152
SUMO3	-0.465	-2.36	0.0152
ursodeoxycholic acid		-0.043	0.0155
HRG	-0.866	1.276	0.0156
butylated hydroxyanisol		1.243	0.0156
TRPV4	-0.033	1.011	0.0156
indole-3-carbinol		0.537	0.0156
mir-29		0	0.0156
CTBP1	0.067	-0.218	0.0156
HSD17B4	0.442	-2.63	0.0156
HBD	0.21	-1.89	0.0157
TSC2	-0.276	-1.984	0.0157
SERPINF1	-1.323	-1.969	0.0158
CALCA	-0.303	-0.117	0.0158
BMP6	0.64	-0.594	0.0158
morphine		-0.184	0.0158
EP300		0.825	0.0164
mir-8		1.262	0.0165
1-naphthylisothiocyanate		0.447	0.0165
cobalt		0.391	0.0165

acetaldehyde		0.128	0.0165
aroclor 1254		-0.625	0.0165
spermine nitric oxide complex		-0.737	0.0165
PTPRE	-0.068	-1.342	0.0165
pentobarbital		-1.379	0.0165
HNF4α dimer		-1.387	0.0165
mir-122			0.0165
BAG1	0.871		0.0165
reactive oxygen species		1.057	0.0165
(+)-MK-801		-0.296	0.0166
FBN1	-0.574	1.516	0.0166
Rp-cAMPS		0.928	0.0166
SMARCE1	0.507	0.277	0.0166
SCP2	0.847	-0.392	0.0166
leuprolide		-0.896	0.0166
naloxone		-2.297	0.0166
ETS			0.0166
ACKR1	-0.589		0.0166
mycophenolic acid		1.546	0.0168
EIF4E	0.091	1.431	0.0168
BRCA1	-0.766	1.185	0.0168
Tnf (family)		-0.182	0.0168
REST	0.755	2.388	0.017
sphingosine-1-phosphate		1.015	0.0173
MEN1	0.422	-0.651	0.0174
4-tert-octylphenol		-1	0.0174
IFRD1	0.757	-1.294	0.0174
Focal adhesion kinase		-1.937	0.0174
tetracycline		-1.855	0.0178
di(2-ethylhexyl) phthalate		1.599	0.018
ADCYAP1	-0.251	0.403	0.018
mir-10		1.003	0.0183
IL24	-0.436	0.333	0.0183
SHH	-0.235	0.526	0.0184
let-7a-5p (and other miRNAs w/seed GAGGUAG)		-2.219	0.0184
carboplatin		0.777	0.0184
TCF4	1.012	-0.122	0.0184
phenacetin		1.265	0.0186
LPL	0.106	0.095	0.0186
ETV5	-0.052	-0.152	0.0186
cyclophosphamide		1.351	0.0188
HSF2	-0.095	1.982	0.0196

arginine		1	0.0196
dithiothreitol		0.834	0.0196
cyanocobalamin		-0.447	0.0196
ICMT	0.345		0.0196
CDKN1A	0.241	0.874	0.0203
MXD1	0.032	1.987	0.0207
EPHB1		1.987	0.0207
PDGFRB	0.31	1.236	0.0207
RPTOR		1.131	0.0207
ANKRD17	0.971	1	0.0207
NMNAT1	0.21	0.218	0.0207
14,15-epoxyeicosatrienoic acid		0.152	0.0207
MMP7	-0.1	-0.218	0.0207
bile salt		-0.218	0.0207
HLF	0.485	-0.577	0.0207
mir-199		-0.975	0.0207
miR-375-3p (and other miRNAs w/seed UUGUUCG)		-1.257	0.0207
HIST2H3C (includes others)	-0.423		0.0207
HIST1H4A (includes others)			0.0207
mir-103			0.0207
EIF2AK2	-0.011	1.193	0.021
GSK3B	0.488	-0.992	0.021
SRC	0.155	1.031	0.0211
guanidinopropionic acid		1.354	0.0213
doxycycline		0.166	0.0213
SOX9	-0.252	-1.18	0.0213
glutathione		-2.051	0.0213
VHL	-0.377	0.727	0.0214
NTRK1		1.342	0.0215
MAPK7	-0.14	0.869	0.0215
TFAM	0.316	0.816	0.0215
bufalin		0.447	0.0215
TWIST2	-0.453	0.418	0.0215
COMMD1	0.624	0	0.0215
everolimus		-0.813	0.0215
L-tryptophan		-1.709	0.0215
MEF2			0.0215
CDX1	-0.541		0.0215
NFATC2	-0.17	1.594	0.0216
nitroprusside		1.006	0.0218
miR-483-3p (miRNAs w/seed CACUCCU)		0.157	0.0218

DCN	-0.045	-0.954	0.0218
vitamin D		1.671	0.0218
TXNIP	-0.476	0.18	0.0218
IGFBP2	-0.372	-0.186	0.0218
GATA4	-0.443	-1.221	0.0218
UBE2I	0.301	1.109	0.0224
metyrapone		0.492	0.0224
ESRRB	0.26	0.128	0.0224
PPARα-RXRα		-0.447	0.0224
NDRG1	-0.599	-0.528	0.0224
leupeptin		-0.555	0.0224
SMYD3		-1.411	0.0224
phenytoin		-1.539	0.0224
EHHADH	0.01	-2.219	0.0224
NFAT (complex)			0.0224
SP2	-0.025		0.0224
CHD4	0.507		0.0224
MKL1	0.176	2.155	0.0229
LMNA	0.614		0.023
MAPT	0.148	2	0.023
SERCA			0.0233
Stat5 dimer			0.0233
BCL2L12			0.0233
DAB2	0.633		0.0233
mir-26			0.0233
mir-320			0.0233
ATP2B2	-0.514		0.0233
ERCC1	-0.156		0.0233
PPM1B	0.756		0.0233
LIMS2	-0.008		0.0233
LMO4	0.465		0.0233
AFF1	-0.621		0.0233
PTGDS	-0.227		0.0233
S1PR3	-0.327		0.0233
SAFB	0.412		0.0233
CAMK2A	-0.056		0.0233
ERCC3	0.109		0.0233
6,7-dinitroquinoxaline-2,3-dione			0.0233
fluphenazine			0.0233
volinanserin			0.0233
acetic acid			0.0233
4-aminophenol			0.0233
retinol acetate			0.0233

2-amino-5-phosphonovaleric acid			0.0233
HDAC4		1.387	0.0234
Nfat (family)		1.175	0.0234
cobalt chloride		1.556	0.0236
THRA	-0.35	-0.423	0.0242
levothyroxine		1.046	0.0246
HBB	0.03	-1.89	0.0246
Gsk3		0.026	0.0253
A2M	-0.114	2.121	0.0255
F7	-0.65	1.945	0.0255
Fgf		0.497	0.0255
verapamil		-1.414	0.0255
NR2F2	0.602	-1.741	0.0255
POU2F1	-0.222	-0.149	0.0255
MKL2	-0.101	1.89	0.026
L-glutamic acid		1.199	0.0267
COL18A1	0.216	-1.161	0.0267
sulindac sulfide		0.355	0.0269
AMPK		0.201	0.0269
PD 153035		0	0.0272
mir-132		-1.98	0.0272
NF1	-0.144	-2.236	0.0272
Ap1		-1.679	0.0275
F2R	0.61	3.271	0.0282
enalapril		0.535	0.0282
FLI1	0.339	0.171	0.0282
delta-9-tetrahydrocannabinol		-0.003	0.0282
Jnk		1.476	0.0286
SB203580		-0.618	0.0286
IL15	0.302	0.406	0.0289
CSF3	-0.267	0.486	0.029
PPRC1	0.389	1.265	0.0293
IL1R1	-0.296	0.485	0.0293
ITGA5	-0.33	-1.118	0.0293
HIPK2	0.34	-1.282	0.0293
Pdgf (complex)		0.645	0.0294
KIT	-0.516		0.0294
ASAH1	-0.202	1.026	0.0296
THBS1	1.288	-1.216	0.0296
NCAM1	-0.451	2.216	0.0296
GC-GCR dimer		1.477	0.0296
ammonium chloride		0.447	0.0296
nickel		0.391	0.0296

JUN/JUNB/JUND		0.132	0.0296
vanadate		-0.351	0.0296
C1QA	-0.044		0.0296
DL-fructose		1.131	0.0297
RGS2	1.67	1	0.0297
RASGRF1	-0.352	0.132	0.0297
LXR ligand-LXR-Retinoic acid-RXRα		-0.916	0.0297
quetiapine		-1.114	0.0297
miR-96-5p (and other miRNAs w/seed UUGGCAC)		-1.982	0.0297
Agtr1b			0.0297
mir-22			0.0297
RELN	-0.293		0.0297
ING1	0.578		0.0297
quercetin		-0.289	0.0301
Alpha catenin		-0.213	0.0302
SRC (family)		0.055	0.0303
seocalcitol		1.792	0.0304
silibinin		1.136	0.0304
FOXP3	-0.184	-1	0.0304
Salmonella enterica serotype abortus equi lipopolysaccharide		1.003	0.0323
SUZ12	0.771	-0.625	0.0327
ZNF217		-0.333	0.0335
PTK2	0.893	0.189	0.0337
MED13		1.633	0.0339
PRKG1	0.156	1.387	0.0339
cis-urocanic acid		0.44	0.0339
AREG	0.06	0	0.0339
nicotinic acid		-0.392	0.0339
NFIC	0.624	-1.091	0.0339
TLR4	-0.08	0.232	0.0341
TAZ	-0.02		0.0343
cerivastatin		0.746	0.0344
MAPK9	-0.358	2.202	0.0349
KLF15	0.261	0.138	0.035
N-cor		-0.82	0.035
H-7		-1.349	0.035
PRKCD	-0.124	-0.446	0.0351
CLDN7	0.8	0.559	0.0355
TFEB	-0.353	0.857	0.0356
miR-27a-3p (and other miRNAs w/seed UCACAGU)		0.373	0.0356
ETV4	-0.465	0.147	0.0356

dopamine		0.399	0.0357
sulforafan		-0.183	0.0357
PTGS1	0.464	0	0.0358
MAP2K4	-0.098	0.843	0.0365
SNCA	-0.258	0.842	0.0365
carbon monoxide		-0.213	0.0365
chloride			0.0367
GDP			0.0367
Dynamin			0.0367
palbociclib			0.0367
Dexamethasone-GR			0.0367
PRCP	0.097		0.0367
DROSHA			0.0367
C1QL1	-0.383		0.0367
ERFE			0.0367
CHTOP	0.585		0.0367
Aldosterone-MR dimer			0.0367
DTNBP1	0.035		0.0367
sepantronium			0.0367
DNAJC3	0.738		0.0367
ABL2			0.0367
MYH9	0.895		0.0367
Serpina3k (includes others)	-6.085		0.0367
CLDN1	-0.765		0.0367
TMOD1	0.127		0.0367
mir-204			0.0367
miR-153-3p (miRNAs w/seed UGCAUAG)			0.0367
SNIP1	0.056		0.0367
MAPKAP1	-0.247		0.0367
PPP1R13L			0.0367
EIF2B1	-0.255		0.0367
NCOA4	0.512		0.0367
PTP4A2	1.283		0.0367
F2RL3	-0.136		0.0367
TRAF7	-0.21		0.0367
ADCY6	0.806		0.0367
UBE2L3	0.304		0.0367
GRB10	-0.429		0.0367
PPP1CA	0.137		0.0367
PPP5C	0.066		0.0367
CTH	0.184		0.0367
LOR	-0.513		0.0367

MXD3	-0.183	0.0367
RING1	-0.454	0.0367
EMD	-0.134	0.0367
NTRK3	-0.265	0.0367
singlet oxygen		0.0367
griseofulvin		0.0367
gabapentin		0.0367
dichlorodiphenyl dichloroethylene		0.0367
mecamylamine		0.0367
amantadine		0.0367
mianserin		0.0367
atipamezole		0.0367
p-chloroamphetamine		0.0367
naphthalene		0.0367
N-ethylmaleimide		0.0367
nevirapine		0.0367
trimetazidine		0.0367
cycloserine		0.0367
etodolac		0.0367
actinomycin		0.0367
5R,11R-diethyl-5,6,11,12-tetrahydrochrysene-2,8-diol		0.0367
R-etodolac		0.0367
yohimbine		0.0367
palmitoleic acid		0.0367
stavudine		0.0367
2-amino-3-phosphonopropionic acid		0.0367
N-butyldeoxynojirimycin		0.0367
GSTP1	-0.444	0.0369
L-lysine		0.0373
glucosylceramide		0.0373
PARP		0.0373
SNED1		0.0373
RICTOR	-0.358	0.0373
CTR9	0.366	0.0373
ACACA	-0.151	0.0373
SNTA1	0.278	0.0373
MED14	0.122	0.0373
TTN	-0.682	0.0373
ERCC4	-0.638	0.0373
MIR101		0.0373
mir-193		0.0373
miR-185-5p (and other miRNAs		0.0373

w/seed GGAGAGA)			
NUP107	-0.159		0.0373
WFS1	0.042		0.0373
RBP4	-2.452		0.0373
MCAM	0		0.0373
RAD21	0.671		0.0373
diltiazem			0.0373
raclopride			0.0373
hydroquinone			0.0373
ferric chloride			0.0373
N-methyl-3,4-methylenedioxyamphetamine			0.0373
phytanic acid			0.0373
betaine			0.0373
20alpha-hydroxycholesterol			0.0373
Ras homolog		1.109	0.038
ethoxyquin		0.277	0.038
N(6)-(3-iodobenzyl)-5'-N-methylcarboxamidoadenosine		0.271	0.038
IL11RA	0.114	0	0.038
naringenin		-0.152	0.038
MAPKAPK2	0.053	0.751	0.0386
methamphetamine		0.017	0.0386
RUNX2	-0.376	-0.349	0.0389
TNFRSF1A	-0.145	0.276	0.0389
Akt		0.506	0.039
FGFR1	0.603	-0.508	0.0401
AVP	-0.388	0.598	0.0404
KT5720		-0.152	0.0406
miR-205-5p (and other miRNAs w/seed CCUUCAU)		-0.339	0.0406
27-hydroxycholesterol		-0.655	0.0406
LCAT	-0.898	-1	0.0406
topiramate		-1	0.0406
NPPC	-0.267	-2	0.0406
CDK1	-0.744		0.0406
OGT	0.945		0.0406
GNRH1		1.279	0.0413
ATM	0.422	1.274	0.0413
PTHLH	-0.077	0.798	0.0413
fibric acid derivative		0.334	0.0416
F3	-0.115	0.277	0.0416
exenatide		0	0.0416
ZEB2	0.826	-0.003	0.0416

BMPR2	0.102	-0.391	0.0416
ELF3	-0.037	-0.739	0.0416
CD36	-0.25	-0.44	0.0419
3,4,5,3',4'-pentachlorobiphenyl		1.724	0.0419
haloperidol		0.351	0.0419
SMAD7	0.206	-0.128	0.0419
STK11	-0.206	-0.813	0.0419
phorbol esters		1.273	0.0423
dichlorovinylcysteine		-1.335	0.0424
ELAVL1	0.205	1.091	0.0446
lithium		-0.91	0.0446
vorinostat		0.425	0.0447
INHA	-0.734	1.338	0.0461
Notch		0.433	0.0464
SSTR2	-0.453	-0.152	0.0478
lisinopril		-1.342	0.0478
TF	-1.984	-1.551	0.0478
IDH1	0.088		0.0478
PPP1R15A	0.237		0.0478
ADRB1	0.215		0.0478
HDAC2	0.639	0.378	0.0482
JAG2	-0.52	1.414	0.0486
bromocriptine		0.287	0.0486
CXCR4	0.005	-1.31	0.0486
Immunoglobulin		-0.453	0.0492
PAX6	-0.284	-0.597	0.0494
E. coli B4 lipopolysaccharide		1.402	0.0496
Pro-inflammatory Cytokine		-0.277	0.0497
HDAC3	0.156	-0.9	0.0497
BIRC5	-0.078		0.0497

Table S2. cDNA array gene expression analysis of kidneys. mRNA was extracted from kidneys 48 hour after induction of BP1 and analyzed relative to controls without induction. Gene Set Enrichment Analysis (GSEA [7]; Broad Institute, http://software.broadinstitute.org/gsea/index.jsp) was applied to the data set. Hallmark pathways are shown. The size of the respective data set is shown. NES and ES = (normalized) enrichment scores; Nominal p-values and false discovery corrected p-values, q-values, are included.

NAME	SIZE	ES	NES	NOM p-val	FDR q-val	FWER p-val	RANK AT MA	LEADING EDGE
HALLMARK_COAGULATION	125	0.58361745	2.0375695	0	0	0	1110	tags=23%, list=8%, signal=25%
HALLMARK_MYC_TARGETS_V1	160	0.5052857	2.260066	0	0	0	3265	tags=43%, list=24%, signal=55%
HALLMARK_KRAS_SIGNALING_DN	165	0.53707117	1.8984914	0	2.88E-04	0.001	3724	tags=52%, list=27%, signal=70%
HALLMARK_HYPOXIA	178	0.3918239	1.8286988	0	0.00135135	0.001	2337	tags=30%, list=17%, signal=35%
HALLMARK_PANCREAS_BETA_CELLS	35	0.60931903	1.7752738	0.00405405	0.00143508	0.011	3258	tags=51%, list=24%, signal=67%
HALLMARK_XENOBIOTIC_METABOLISM	184	0.5025341	1.8154243	0	0.00157202	0.009	449	tags=14%, list=3%, signal=14%
HALLMARK_MTORC1_SIGNALING	169	0.4029112	1.8576065	0	0.00168919	0.001	3319	tags=38%, list=24%, signal=50%
HALLMARK_CHOLESTEROL_HOMEOSTASIS	70	0.4716467	1.8866167	0	0.00225225	0.001	1641	tags=27%, list=12%, signal=31%
HALLMARK_UNFOLDED_PROTEIN_RESPONSE	92	0.42484844	1.7931446	0	0.003003	0.003	2390	tags=27%, list=17%, signal=33%
HALLMARK_OXIDATIVE_PHOSPHORYLATION	176	0.42629647	1.9596773	0	0.00337838	0.001	3838	tags=36%, list=28%, signal=50%
HALLMARK_PROTEIN_SECRETION	79	0.42448673	1.7675484	0	0.00371085	0.006	2677	tags=34%, list=19%, signal=42%
HALLMARK_INFLAMMATORY_RESPONSE	174	0.4606851	1.6529925	0	0.00731885	0.065	3498	tags=41%, list=25%, signal=55%
HALLMARK_ALLOGRAFT_REJECTION	172	0.44336256	1.6014868	0	0.01208986	0.126	2802	tags=31%, list=20%, signal=39%
HALLMARK_P53_PATHWAY	167	0.33986056	1.5498704	0	0.01896072	0.037	1967	tags=22%, list=14%, signal=25%
HALLMARK_TNFA_SIGNALING_VIA_NFKB	175	0.34041455	1.531902	0	0.01950792	0.044	1132	tags=18%, list=8%, signal=19%
HALLMARK_TGF_BETA_SIGNALING	43	0.42256013	1.5143765	0.01333333	0.02262265	0.052	2684	tags=37%, list=19%, signal=46%
HALLMARK_UV_RESPONSE_UP	140	0.33770084	1.4950206	0	0.02515644	0.061	2371	tags=26%, list=17%, signal=32%
HALLMARK_ESTROGEN_RESPONSE_EARLY	156	0.31769428	1.4318058	0	0.04228199	0.114	2431	tags=29%, list=18%, signal=35%
HALLMARK_APICAL_SURFACE	36	0.5065839	1.4724264	0.04244032	0.04418378	0.444	1940	tags=33%, list=14%, signal=39%
HALLMARK_MITOTIC_SPINDLE	149	0.31450102	1.3986725	0.01834862	0.04970767	0.141	2174	tags=26%, list=16%, signal=30%

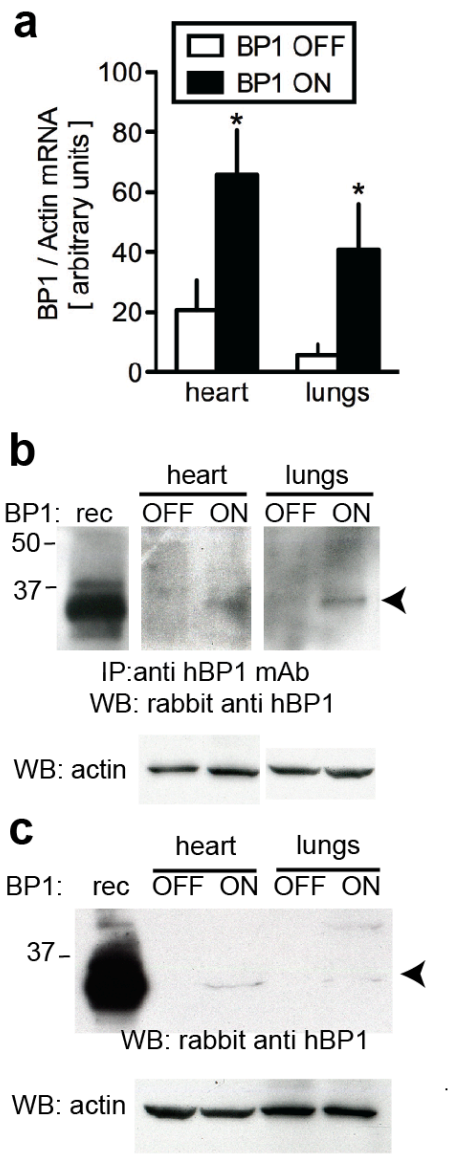

Figure S1. Conditional BP1 transgene expression *in vivo*. **a**, BP1 mRNA expression in hearts and lungs of BP1 OFF and ON animals. mRNA expression was monitored by quantitative RT-PCR. Expression was normalized to endogenous beta-actin mRNA (means ± SEM; n = 4 to 6 animals per group). *, P< 0.05, BP1 ON versus OFF. **b**,**c**, BP1 protein expression in tissue lysates from BP1 OFF and ON animals. Immunoprecipitations (IP) followed by Western Blots (**b**) or direct Western blots of lysates (**c**). 10 mg (**b**) or 0.3 mg (**c**) of lysates were used. To compare loading between BP1 OFF and ON samples, blots for beta-actin were run in parallel. Recombinant human BP1 (20 ng; rec) was used as a positive control and arrowheads indicate the position of BP1 at an apparent molecular mass of 34 kDa. Data are representative of samples from three BP1 OFF and BP1 ON sets of organs run on parallel gels.

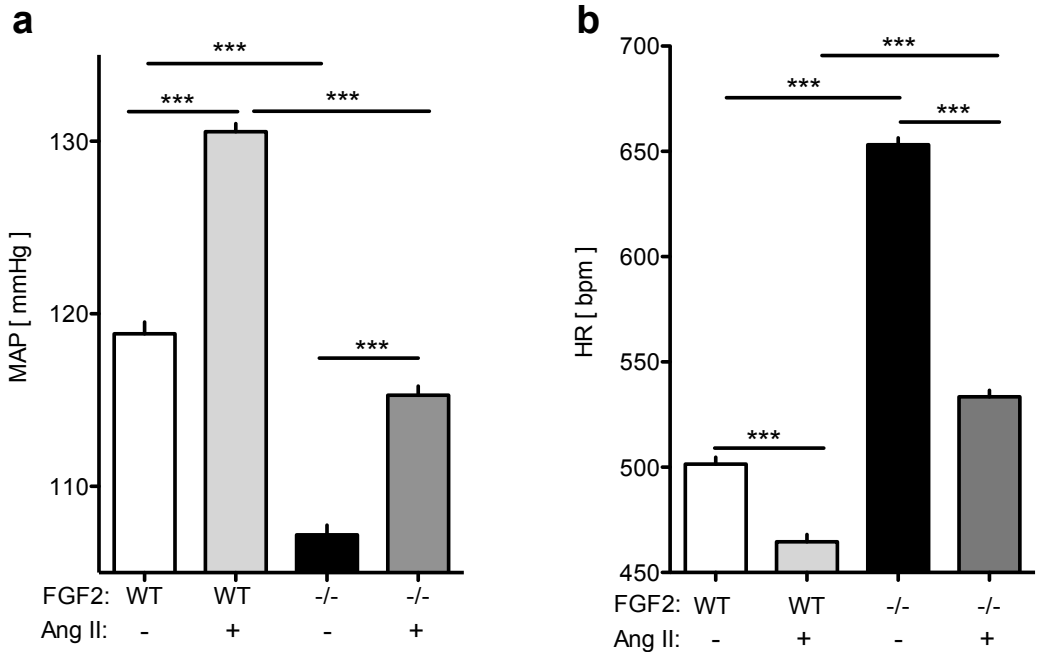

Figure S2. Blood pressure (MAP) and heart rate (HR) after Ang II in FGF2$^{-/-}$ mice. Cardiovascular parameters were obtained by telemetry in wild-type (WT; n=6) and FGF2$^{-/-}$ (n=7) mice. Mean MAP and HR from the peak activity time of the animals are shown. In the FGF2$^{-/-}$ mice baseline MAP is reduced by 15 mm Hg. Ang II treatment (400 mg/kg/day) increased MAP by 11 mm Hg in the WT animals. In the FGF2$^{-/-}$ animals Ang II raised the lowered MAP to the control levels. ***, P<0.001, ANOVA. There was no significant difference between the FGF2 WT and the FGF$^{-/-}$ treated with AngII.

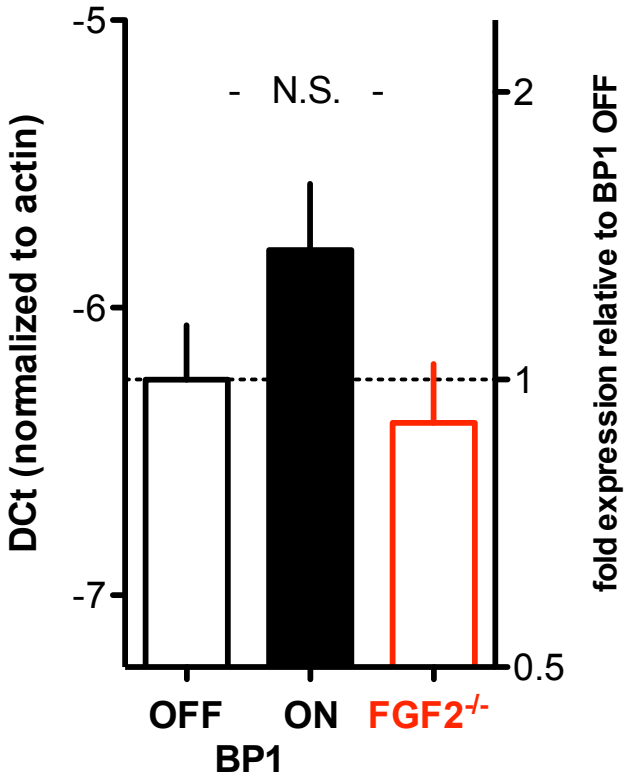

Figure S3. Ang II receptor type 1 (AGTR1 or AT1R) mRNA expression in kidneys from different groups of mice (n=3 per group; mean ± SEM). qRT-PCR cycle threshold relative to actin (DCt) is shown on the left ordinate and fold expression relative to BP1 on the right ordinate. N.S., no significant difference; *P*>0.05.

Protein acronym and full name	Protein ID	Peptides identified	Protein score	BP1 ON/OFF fold
CIT=CTRO; Citron Rho-interacting kinase	P49025	21	41.1	+ 3.6
MKK4=MAP2K4; Dual specificity mitogen-activated protein kinase kinase 4	P47809	9	41.8	+ 3.6
PAK2; p21-activated kinase 2	Q8CIN4	8	42.1	+ 4.2
PTPN12; Protein Tyrosine Phosphatase, Non-Receptor Type 12	P35831	11	41.6	- 2.8

Figure S4. Proteins identified by mass spectrometry analysis of kidney extracts from mice with BP1 ON and OFF. Proteins in lysates from kidneys were immunoprecitipated with an anti-phospho tyrosine antibody and the precipitated complexes separated by 2D gel electrophoresis. After a Coomassie stain peaks were quantitated and cut from the gel for identification by mass spectrometry. The number of peptides identified for the respective protein, the score and the fold change based on the a comparison with the scan of control group are provided.

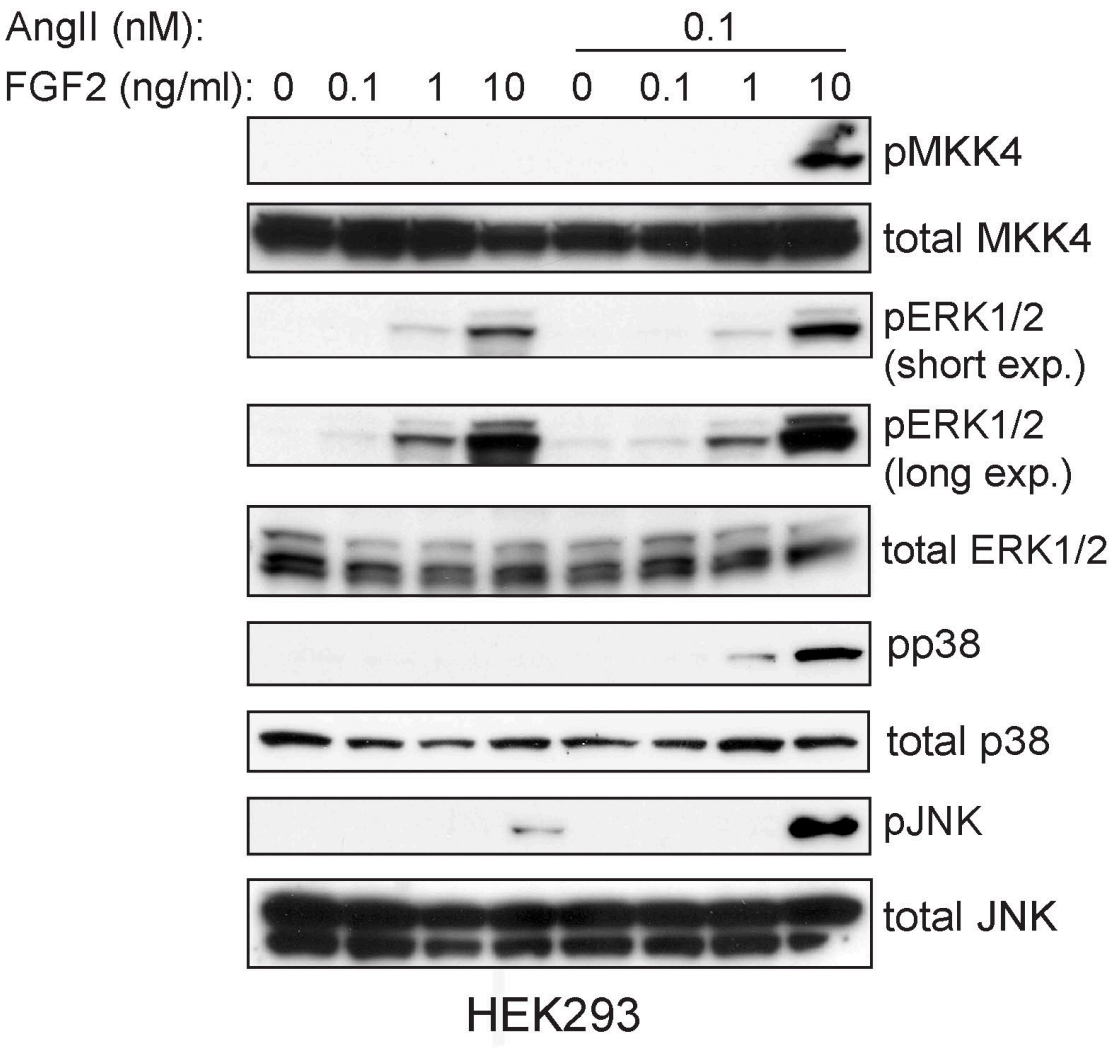

Figure S5. Signal transduction crosstalk between Ang II and FGF2. Serum-deprived primary HEK293 cells were treated for 10 minutes with different concentrations of FGF2 ± Ang II, as indicated. Western blot analysis for phospho- and total MKK4, ERK1/2, p38 and JNK of cell extracts is shown. Data are representative of three independent experiments. Note the synergism for pp38 induction, when both stimuli are applied.

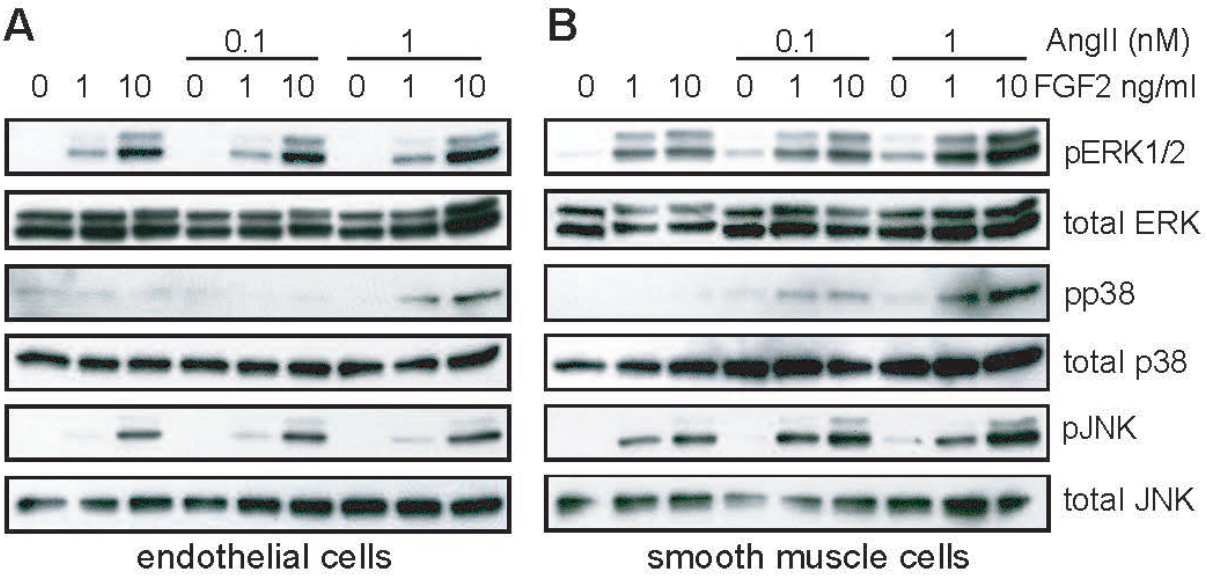

Figure S6. Signaling crosstalk between Ang II and FGF2. Serum-deprived primary endothelial cells (HMVEC-L) or smooth muscle cells (PASMC) were treated for 10 minutes with different concentrations of FGF2 + Ang II, as indicated. Western blot analysis for phospho- and total ERK1/2, p38 and JNK of cell extracts is shown. Data are representative of three independent experiments. Serum-deprived primary endothelial cells (HUVEC) or smooth muscle cells were treated for 10 minutes with different concentrations of FGF2 $\pm$ Ang II, as indicated. Western blot analysis for phospho- and total ERK1/2, p38 and JNK of cell extracts is shown. Note the synergism for pp38 induction, when both stimuli are applied in contrast to FGF2 alone or AngII alone.