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Further intracellular proteins and signaling pathways regulated by angiotensin-(1–7) in human endothelial cells



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ABSTRACT

In 2016, Meinert et al. (doi: [10.1016/j.jprot.2015.09.020](https://doi.org/10.1016/j.jprot.2015.09.020)) published the first 25 proteins in a protein array regulated in Human Umbilical Vein Endothelial Cells (HUVEC) by the heptapeptide angiotensin (Ang)-(1–7) and the first 10 intracellular signaling cascades at different time points. This supporting data article shows further proteins and pathways stimulated by Ang-(1–7) in human endothelial cells at time points of 1 h, 3 h, 6 h, and 9 h. HUVECs were stimulated with Ang-(1–7), and regulated proteins were identified via antibody microarray. Bioinformatics software IPA was used for association of regulated proteins to metabolic pathways.

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Specifications Table

Subject area	<i>Cardiovascular</i>
More specific subject area	<i>Renin-angiotensin system</i>
Type of data	<i>5 tables</i>
How data was acquired	<i>Antibody microarray for regulated proteins using a GenePix 4100A Microarray Scanner (Molecular Devices, Sunnyvale, USA), and the program IPA (Ingenuity Systems, Redwood City, USA) for the identification of potential metabolic pathways.</i>
Data format	<i>analyzed</i>
Experimental factors	<i>Human Umbilical Vein Endothelial Cells were stimulated with angiotensin-(1–7)</i>
Experimental features	<i>Screening of proteins and pathways in angiotensin-(1–7) stimulated Human Umbilical Vein Endothelial Cells</i>
Data source location	<i>Cork, Ireland</i>
Data accessibility	<i>Data within this article</i>

Value of the data

- First screening of 725 proteins potentially regulated by angiotensin (Ang)-(1–7) in endothelial cells via antibody microarray.
- As often slightly regulated proteins have already dramatic biological effects, identification of further proteins altered by Ang-(1–7) might have significant scientific relevance.
- Detailed description of Ang-(1–7) effects on intracellular signaling pathways under non-pathophysiological circumstances can identify further areas of benefit using Ang-(1–7).
- The understanding of intracellular network signaling initiated by Ang-(1–7) might allow conclusions on how the heptapeptide can oppose the effects of the detrimental Ang II.

1. Data

The antibody microarray identified 110 regulated proteins in human umbilical vein endothelial cells (HUVEC) cells after 1-h stimulation with Ang-(1–7), 119 after 3 h, 31 after 6 h, and 86 after 9 h. The first 25 regulated proteins have been published in Meinert et al. [1] in Tables 1–4. Here the name and ranking of the next regulated proteins are shown (Tables 1–4). Additionally, further intracellular pathways affected by Ang-(1–7) are shown in Table 5A–D.

2. Experimental design, materials and methods

2.1. Cell culture and cell stimulation

HUVEC were grown on 100-mm dishes in EBM (Endothelial basal medium)-2 medium under standard conditions of 37 °C in a humidified incubator and 5% CO₂ [2]. Cells were used in passage 6. When they reached 70% confluence, they were washed twice with DPBS (Dulbecco's phosphate-buffered saline) and serum starved for 1 h in supplements-free medium. HUVECs were stimulated with 10⁻⁷ M Ang-(1–7) for 1 h, 3 h, 6 h and 9 h. Control cells were treated only with DPBS (solvent).

Table 1

The proteins ranked 26–100 based on the detected fold change values after 1 h incubation of HUVEC with 10^{-7} M Ang-(1–7). The order of the numbers is oriented on the highest single value. Expression fold change lower than 1.5 is given in hyphen. Data that could not be detected is marked as n.d. Proteins marked in *Italic* show repeatedly identified differentially expressed proteins (RIDEPs). The mentioned dye indicates with which dye the unstimulated sample was labeled with.

	Protein	Antibody id	Cy3	Cy5	Cy5
26.	CIN85	C8116	2.68	–	–
27.	Annexin VII	A4475	–	2.64	–
28.	AOP1	A7674	2.44	2.64	n.d
29.	RALAR	R8529	2.63	2.03	–
30.	PINCH-1	P9371	–	2.61	–
31.	Rab9	R5404	2.6	1.76	–
32.	BOB.1/OBE1	B7810	2.57	–	n.d
33.	GFI1	G6670	–	2.51	–
34.	MAPK14 (NonActivated)	M8432	2.5	2.09	–
35.	Bim	B7929	2.49	–	n.d
36.	PSF	P2860	2.45	1.57	–
37.	ERK2	M7431	2.44	1.69	–
38.	ASPP2	A4480	1.64	2.44	n.d
39.	BACE1	B0806	2.43	2.29	–
40.	MTBP	M3566	2.43	1.79	–
41.	RICK	R9650	2.43	1.66	–
42.	Bmf	B1684	1.53	2.38	–
43.	MADD	M5683	–	2.37	–
44.	c-Raf (pSer621)	R1151	1.95	2.36	n.d
45.	p53R2	P4993	2.35	1.54	–
46.	<i>SLIPR/MAGI-3</i>	S4191	2.35	1.77	–
47.	<i>SMAD4</i>	S3934	2.30	–	–
48.	ASC-2	A5355	1.59	1.61	2.28
49.	Calretinin	C7479	2.25	1.96	n.d
50.	TBP	T1827	n.d	n.d	2.24
51.	PRNP	P5999	2.23	–	n.d
52.	<i>SIAH2</i>	S7945	2.23	–	–
53.	MTA2	M7569	2.18	1.56	1.62
54.	FAK (pTyr397)	F7926	1.73	–	2.17
55.	Nuf2	N5287	2.16	–	–
56.	UCHL1	U5258	2.16	–	–
57.	NBS1	N9287	2.16	–	–
58.	FKHRL1	F2178	1.74	2.15	–
59.	RAIDD	R5275	2.15	–	n.d
60.	Cyclin A	C4710	n.d	2.14	–
61.	BAP1	B9303	–	2.14	n.d
62.	p57kip2	P2735	–	2.13	–
63.	Importin α 1	I9658	2.12	–	–
64.	WAVE	W0392	2.10	–	–
65.	Caldesmon	C6542	2.08	1.64	–
66.	AP1	A5968	2.08	1.60	–
67.	Zip Kinase	Z0134	2.07	1.66	n.d
68.	FLIP γ/δ	F9925	2.07	–	–
69.	ARC	A8344	–	–	2.05
70.	Fas	F4424	2.04	1.54	–
71.	Pan Cytokeratin	C2931	1.92	–	2.03
72.	S100	S2532	2.00	1.68	–
73.	H3 (Ac-Lys9, pSer10)	H0788	–	2.00	–
74.	H3 (Ac-Lys9)	H0913	1.99	1.52	–
75.	Nitrotyrosin	N0409	1.98	1.50	–
76.	PID/MTA2	P5118	1.98	–	n.d
77.	APRIL	A1726	1.91	1.95	–
78.	δ -Catenin/NPRAP	C4864	1.95	–	–
79.	hABH2	A8228	1.94	1.57	–
80.	Desmosomal Protein	D1286	1.94	–	–
81.	Coilin	C1862	1.89	1.94	–
82.	H3 (diMe-Lys9)	D5567	–	–	1.94

Table 1 (continued)

	Protein	Antibody id	Cy3	Cy5	Cy5
83.	TRF1	T1948	1.92	1.52	–
84.	cAbl	A5844	1.91	–	–
85.	Tyrosin Hydrolase	T2928	1.91	1.59	–
86.	β -COP	G6160	1.91	–	n.d
87.	E2F1	E9026	1.77	1.85	–
88.	SUMO1	S5446	–	1.85	–
89.	Parkin	P6248	1.85	–	–
90.	SynCAM	S4945	1.60	1.84	–
91.	Protein Kinase C β 2	P2584	n.d	n.d	1.84
92.	MTA1	M1320	1.84	–	–
93.	BUB1	B0561	1.82	1.64	–
94.	ASPP1	A4355	1.82	–	n.d
95.	Caspase 13	C8854	1.82	–	1.75
96.	FXR2	F1554	1.82	–	–
97.	Caspase 10	C1229	1.81	1.75	–
98.	PKR	P0244	–	–	1.81
99.	hnRNP-C1/C2	R5028	1.80	–	–
100.	Importin α 3	I9783	1.77	1.74	–

Table 2

The proteins ranked 26–100 based on the detected fold change values after 3 h incubation of HUVEC with 10^{-7} M Ang-(1–7). The order of the numbers is oriented on the highest single value. Expression fold change lower than 1.5 is given in hyphen. Data that could not be detected is marked as n.d. Proteins marked in *Italic* show repeatedly identified differentially expressed proteins (RIDEPs). The mentioned dye indicates which dye the unstimulated sample was labeled with.

	Protein	Antibody id	Cy3	Cy5	Cy5
26.	<i>BID</i>	B3183	2.85	–	–
27.	β -Tubulin	T5201	2.47	2.85	2.11
28.	<i>Centrin</i>	C7736	1.98	–	2.75
29.	p21	P1484	2.12	–	2.68
30.	FOXO2	F1054	–	–	2.67
31.	PIAS2	P9498	–	2.64	2.09
32.	Annexin VII	A4475	–	2.64	1.69
33.	Neurofibromin	N3662	1.59	–	2.64
34.	AOP1	A7674	n.d	2.64	–
35.	TRAIL	T9191	–	2.31	2.62
36.	Rab5	R7904	2.05	–	2.57
37.	GFI1	G6670	n.d	2.51	n.d
38.	DRAK1	D1314	2.48	–	1.76
39.	Cdk3	C9987	2.01	2.47	1.57
40.	ASPP2	A4480	1.77	2.44	n.d
41.	S100	S2532	2.40	1.68	2.03
42.	N-Cadherin	C2542	1.83	–	2.40
43.	Nitrotyrosin	N0409	1.74	1.5	2.39
44.	MADD	M5683	n.d	2.37	1.81
45.	hSNF5/INI1	H9912	1.56	–	2.33
46.	<i>IKKα</i>	I6139	1.52	–	2.33
47.	PRMT1	P6871	1.78	–	2.32
48.	DR3	D3563	–	–	2.32
49.	PP2A	P8109	–	2.31	–
50.	Connexin-32	C3470	1.73	–	2.30
51.	Tal	T1075	1.61	–	2.29
52.	BACE 1	B0806	–	2.29	–
53.	Sir2	S5313	–	–	2.27
54.	ARP3	A5979	1.74	–	2.27
55.	Striatin	S0696	–	–	2.26
56.	SMAD4	S3934	1.60	–	2.18
57.	Apaf1	A8469	2.18	–	–

Table 2 (continued)

	Protein	Antibody id	Cy3	Cy5	Cy5
58.	p57kip2	P2735	1.84	2.13	2.16
59.	Sirt1	S5196	1.82	–	2.16
60.	RICK	R9650	2.16	1.66	–
61.	FAK (pTyr577)	F8926	2.15	–	1.56
62.	FKHRL1	F2178	–	2.15	–
63.	Cyclin A	C4710	n.d	2.14	n.d
64.	BAP1	B9303	–	2.14	–
65.	MBD4	M9817	–	–	2.12
66.	MeCP2	M9317	1.66	1.63	2.10
67.	HDAC8	H6412	2.05	–	2.10
68.	MAPK14 (nonActivated)	M8432	–	2.09	–
69.	TOM22	T6319	1.54	1.66	2.08
70.	Annexin V	A8604	1.89	–	2.06
71.	c-Myc	M4439	–	–	2.06
72.	DEDAF	D3316	2.06	–	–
73.	eNOS	N9532	1.64	–	2.05
74.	RALAR	R8529	–	2.03	n.d
75.	H3 (Ac-Lys9, pSer10)	H0788	–	2.00	2.03
76.	TSG101	T5826	2.02	1.95	–
77.	Dystrophin	D8168	1.66	–	2.02
78.	Connexin 43	C8093	–	–	2.01
79.	p63	P3362	1.89	–	1.96
80.	Protein Kinase B α	P2482	–	–	1.96
81.	Calretinin	C7479	–	1.96	–
82.	Coilin	C1862	–	1.94	–
83.	<i>MyD88</i>	<i>M9934</i>	–	–	1.91
84.	ROCK 2	R8653	1.77	–	1.90
85.	I-Afadin	A0349	1.52	–	1.90
86.	Connexin 43	C6219	1.56	–	1.89
87.	α -Actinin	A5044	1.58	–	1.88
88.	E2F1	E9026	1.88	1.85	–
89.	Chk2	C9233	1.88	–	1.84
90.	Importin α 1	I9658	1.87	–	–
91.	F1A α	F3428	–	1.86	–
92.	SUMO1	S5446	–	1.85	–
93.	ASPP1	A4355	1.84	–	–
94.	SynCAM	S4945	–	1.84	–
95.	Chk1	C9358	1.80	1.51	1.70
96.	Sp1	S9809	1.80	–	1.60
97.	Pyk2 (pTyr579)	P7114	n.d	1.80	n.d
98.	RIP	R8274	1.63	–	1.79
99.	Transportin 1	T0825	1.54	–	1.77
100.	GADD153	G6916	1.56	–	1.76

Table 3

The proteins ranked 26–31 based on the detected fold change values after 6 h incubation of HUVEC with 10^{-7} M Ang-(1–7). The order of the numbers is oriented on the highest single value. Expression fold change lower than 1.5 is given in hyphen. Data that could not be detected is marked as n.d. Proteins marked in *Italic* show repeatedly identified differentially expressed proteins (RIDEPs). The mentioned dye indicates which dye the unstimulated sample was labeled with.

	Protein	Antibody id	Cy3	Cy5	Cy5
26.	E2F1	E9026	1.89	–	–
27.	Zip Kinase	Z0134	–	1.87	–
28.	<i>BID</i>	<i>B3183</i>	–	–	1.85
29.	Cyclin D1	C7464	–	1.85	–
30.	Nerve Growth Factor β	N3279	1.81	n.d	–
31.	HDAC7	H2537	1.78	1.57	–

Table 4

The proteins ranked 26–86 based on the detected fold change values after 9 h incubation of HUVEC with 10^{-7} M Ang-(1–7). The order of the numbers is oriented on the highest single value. Expression fold change lower than 1.5 is given in hyphen. Data that could not be detected is marked as n.d. Proteins marked in *Italic* show repeatedly identified differentially expressed proteins (RIDEPs). The mentioned dye indicates which dye the unstimulated sample was labeled with.

	Protein	Antibody id	Cy3	Cy5	Cy5
26.	DR3	D3563	2.67	–	–
27.	DNase I	D0188	2.65	–	–
28.	Nitrotyrosin	N0409	2.61	2.27	–
29.	NGFR	N3908	n.d	2.57	–
30.	MDC1	M2444	2.55	–	–
31.	p120	P1870	2.54	–	–
32.	mTor	T2949	–	2.48	–
33.	<i>BID</i>	<i>B3183</i>	<i>2.43</i>	<i>1.71</i>	<i>2.14</i>
34.	MDM2	M4308	2.42	–	–
35.	WAVE	W0392	2.38	–	–
36.	MAP1	M6783	n.d	2.38	–
37.	c-Raf (pSer621)	R1151	n.d	2.37	n.d
38.	TGF β	T9429	n.d	1.41	2.31
39.	DR4	D3813	2.28	–	–
40.	HDAC6	H2287	2.26	–	–
41.	Desmosomal Protein	D1286	2.24	–	–
42.	Calnexin	C4731	2.21	–	–
43.	FGF9	F1672	2.19	–	–
44.	Coilin	C1862	2.18	1.61	–
45.	Phospholipase Cγ1	P8104	–	2.17	–
46.	APRIL	A1851	2.17	n.d	n.d
47.	TBP	T1827	–	2.08	2.16
48.	DRAK1	D1314	n.d	1.81	2.13
49.	UCHL1	U5258	2.12	–	–
50.	Parkin	P6248	2.09	–	–
51.	PIASγ	P0104	2.09	–	–
52.	GF11	G6670	2.07	–	–
53.	HDAC5	H4538	2.07	–	–
54.	Protein Kinase Cβ2	P3203	1.89	2.05	–
55.	Apaf1	A8469	2.03	–	–
56.	MRP2	M3692	n.d	2.01	–
57.	Neurabin II	N5037	1.99	–	–
58.	AP1	A5968	1.98	–	–
59.	p19	P4354	1.97	–	–
60.	hABH2	A8228	1.96	–	–
61.	E2F1	E9026	1.95	1.87	1.63
62.	E2F6	E1532	n.d	n.d	1.95
63.	PRMT2	P0748	–	–	1.95
64.	TAP	T1076	1.94	–	–
65.	PRMT1	P6871	n.d	–	1.89
66.	ε-Tubulin	T1323	1.89	–	–
67.	MDMX	M0445	1.88	1.52	–
68.	Paxillin	P1093	1.88	–	–
69.	Filamin	F1888	1.88	1.69	–
70.	Caldesmon	C6542	1.88	1.85	–
71.	p34	C3085	1.87	–	–
72.	JNK	J4500	1.86	1.6	–
73.	Survivin	S8191	1.86	–	–
74.	Melanocortin 3	M4937	1.86	–	–
75.	H3 (pSer10)	H6409	1.85	–	1.86
76.	Sir2	S5313	1.50	1.84	–
77.	Ciliated Cell Marker	C5867	1.84	–	–
78.	Collagen Type IV	C1926	1.82	–	–
79.	MAPK14	M8432	1.81	–	–
80.	FANCD2	F0305	1.81	–	–
81.	Syntaxin 8	S8945	1.81	–	–
82.	S6 Kinase	S4047	–	–	1.80

Table 4 (continued)

	Protein	Antibody id	Cy3	Cy5	Cy5
83.	HDAC10	H3413	1.64	1.76	–
84.	Chk1	C9358	1.52	–	1.60
85.	Bcl-x	B9304	1.59	1.53	–
86.	Aly	A9979	1.59	1.57	–

Table 5

Metabolic pathways ranked position 11–25 (bold) using the *p*-values associated by the IPA software to each of the different antibody microarray sets (A: 1 h; B: 3 h; C: 6 h; D: 9 h). For completion, the ranking of the first ten pathways are also listed (in italic). The ratio states the number of proteins detected in the microarray versus the total number of proteins being part of the particular pathway.

A)			
	Pathway	1 h <i>p</i> -Value	Ratio
1.	<i>Molecular Mechanisms of Cancer</i>	3.67E–11	17/379 (4.5%)
2.	<i>p53 Signaling</i>	6.57E–09	9/96 (9.4%)
3.	<i>Glucocorticoid Receptor Signaling</i>	9.70E–09	13/295 (4.4%)
4.	<i>Chemokine Signaling</i>	2.44E–07	7/73 (9.6%)
5.	<i>Cyclins and Cell Cycle regulation</i>	6.24E–07	7/89 (7.9%)
6.	<i>PI3K/AKT Signaling</i>	7.24E–07	8/140 (5.7%)
7.	<i>ATM Signaling</i>	7.59E–07	6/54 (11.1%)
8.	<i>VEGF Signaling</i>	8.91E–07	7/99 (7.1%)
9.	<i>Apoptosis Signaling</i>	1.26E–06	7/96 (7.3%)
10.	<i>Death Receptor Signaling</i>	1.58E–06	6/95 (9.9%)
11.	Chronic Myeloid Leukemia Signaling	2.00E–06	7/105 (6.7%)
12.	ERK/MAPK Signaling	2.94E–06	9/204 (4.4%)
13.	Cholecystokinin/Gastrin-mediated Signaling	3.62E–06	7/106 (6.6%)
14.	Parkinson's Signaling	4.80E–06	4/18 (22.2%)
15.	Pancreatic Adenocarcinoma Signaling	5.01E–06	7/119 (5.9%)
16.	CCR5 Signaling in Macrophages	5.92E–06	6/94 (6.4%)
17.	PTEN Signaling	6.31E–06	7/124 (5.6%)
18.	PDGF Signaling	6.80E–06	6/79 (7.6%)
19.	Renin-Angiotensin Signaling	7.30E–06	7/126 (5.6%)
20.	PI3K Signaling in B Lymphocytes	2.40E–05	7/143 (4.9%)
21.	Protein Kinase A Signaling	2.76E–05	10/328 (3.0%)
22.	Breast Cancer Regulation by Stathmin1	3.17E–05	8/210 (3.8%)
23.	B Cell Receptor Signaling	3.40E–05	7/156 (4.5%)
24.	IGF-1 Signaling	4.50E–05	6/107 (5.6%)
25.	IL-15 Signaling	5.18E–05	5/67 (7.5%)
B)			
	Pathway	3 h <i>p</i> -Value	Ratio
1.	<i>Molecular Mechanisms of Cancer</i>	1.20E–22	32/379 (8.4%)
2.	<i>p53 Signaling</i>	3.00E–20	19/96 (19.7%)
3.	<i>Chronic Myeloid Leukemia Signaling</i>	1.59E–14	15/105 (14.3%)
4.	<i>Cyclins and Cell Cycle regulation</i>	2.70E–14	14/89 (15.7%)
5.	<i>Death Receptor Signaling</i>	3.51E–13	12/65 (18.5%)
6.	<i>Cell Cycle: G1/S Checkpoint regulation</i>	3.98E–12	11/61 (18.0%)
7.	<i>PTEN Signaling</i>	3.16E–11	13/124 (10.5%)
8.	<i>VEGF Signaling</i>	5.01E–11	12/99 (12.1%)
9.	<i>PI3K/AKT Signaling</i>	1.58E–10	13/140 (9.3%)
10.	<i>Huntington's Disease Signaling</i>	7.94E–10	16/238 (6.7%)
11.	TNFR1 Signaling	1.94E–09	9/53 (17.0%)

Table 5 (continued)

B)			
	Pathway	3 h p-Value	Ratio
12.	Aryl Hydrocarbon Receptor Signaling	2.24E−09	13/159 (8.2%)
13.	Apoptosis Signaling	2.51E−09	11/96 (11.5%)
14.	IL-8 Signaling	3.80E−09	14/193 (7.3%)
15.	Small Cell Lung Cancer Signaling	3.98E−09	18/89 (11.2%)
16.	ATM Signaling	5.01E−09	9/54 (16.7%)
17.	Glioma Signaling	6.31E−09	11/112 (9.8%)
18.	Role of PKR in Interferon Induction and Antiviral Response	1.22E−08	8/46 (17.4%)
19.	Pancreatic Adenocarcinoma Signaling	2.00E−08	11/119 (9.2%)
20.	TWEAK Signaling	4.66E−08	7/39 (17.9%)
21.	Glucocorticoid Receptor Signaling	5.01E−08	15/295 (5.1%)
22.	Myc Mediated Apoptosis Signaling	5.08E−08	8/61 (13.1%)
23.	Type I Diabetes Mellitus Signaling	5.15E−08	10/121 (8.3%)
24.	Induction of Apoptosis by HIV1	5.22E−08	8/66 (12.1%)
25.	Hereditary Breast Cancer Signaling	5.25E−08	10/129 (7.8%)
C)			
	Pathway	6 h p-Value	Ratio
1.	Molecular Mechanisms of Cancer	1.33E−09	3/379 (2.4%)
2.	Small Cell Lung Cancer Signaling	7.65E−08	5/89 (5.6%)
3.	Cyclins and Cell Cycle regulation	1.31E−07	5/89 (5.6%)
4.	VEGF Signaling	2.14E−07	5/99 (5.1%)
5.	p53 Signaling	2.99E−07	5/96 (5.2%)
6.	Chronic Myeloid Leukemia Signaling	3.16E−07	5/105 (4.8%)
7.	Glioma Signaling	3.98E−07	5/112 (4.5%)
8.	GM-CSF Signaling	3.16E−06	4/67 (6.0%)
9.	IL-8 Signaling	6.31E−06	5/193 (2.6%)
10.	HGF Signaling	2.00E−05	4/105 (3.8%)
11.	Huntington's Disease Signaling	2.19E−05	5/238 (2.1%)
12.	Pancreatic Adenocarcinoma Signaling	2.29E−05	4/119 (3.4%)
13.	PTEN Signaling	2.69E−05	4/124 (3.2%)
14.	14-3-3-mediated Signaling	3.28E−05	4/120 (3.3%)
15.	PI3K/AKT Signaling	3.31E−05	4/140 (2.9%)
16.	p70S6K Signaling	4.15E−05	4/130 (3.1%)
17.	Melanoma Signaling	4.41E−05	3/46 (6.5%)
18.	Cell Cycle: G1/S Checkpoint regulation	8.91E−05	3/61 (4.9%)
19.	Induction of Apoptosis by HIV1	1.28E−04	3/66 (4.5%)
20.	IL-15 Signaling	1.36E−04	3/67 (4.5%)
21.	Retinoic acid Mediated Apoptosis Signaling	1.44E−04	3/68 (4.4%)
22.	Non-Small Cell Lung Cancer Signaling	1.83E−04	3/79 (3.8%)
23.	Chemokine Signaling	6.31E−04	3/73 (4.1%)
24.	ERK/MAPK Signaling	6.37E−04	4/204 (2.0%)
25.	Integrin Signaling	6.41E−04	4/210 (1.9%)

D)

	Pathway	9 h p-Value	Ratio
1.	p53 Signaling	1.73E-19	15/96 (15.6%)
2.	Molecular Mechanisms of Cancer	1.14E-15	19/379 (5.0%)
3.	Chronic Myeloid Leukemia Signaling	1.71E-14	12/105 (11.4%)
4.	ATM Signaling	3.94E-14	10/54 (18.5%)
5.	Huntington's Disease Signaling	1.48E-12	14/238 (5.9%)
6.	Cyclins and Cell Cycle regulation	2.51E-12	10/89 (11.2%)
7.	Glioma Signaling	3.16E-11	10/112 (8.9%)
8.	Role of NFAT in Cardiac Hypertrophy	6.31E-11	12/208 (5.8%)
9.	Pancreatic Adenocarcinoma Signaling	7.94E-11	10/119 (8.4%)
10.	Hereditary Breast Cancer Signaling	2.00E-10	10/129 (7.8%)
11.	B Cell Receptor Signaling	2.02E-09	10/156 (6.4%)
12.	Glucocorticoid Receptor Signaling	1.26E-08	12/295 (4.1%)
13.	PI3K/AKT Signaling	1.58E-08	9/140 (6.4%)
14.	FGF Signaling	1.69E-08	8/90 (8.9%)
15.	Cell Cycle: G1/S Checkpoint regulation	1.91E-08	7/61 (11.5%)
16.	Neuregulin Signaling	1.92E-08	8/102 (7.8%)
17.	HGF Signaling	2.75E-08	8/105 (7.6%)
18.	IGF-1 Signaling	3.16E-08	8/107 (7.5%)
19.	Erythropoietin Signaling	3.58E-08	7/78 (9.0%)
20.	Glioblastoma Multiforme Signaling	4.60E-08	9/164 (5.5%)
21.	Neurotrophin/TRK Signaling	6.70E-08	7/77 (9.1%)
22.	FLT3 Signaling in Hematopoietic Progenitor Cells	8.61E-08	7/74 (9.5%)
23.	14-3-3-mediated Signaling	9.75E-08	8/120 (6.7%)
24.	Acute Phase Response Signaling	1.11E-07	9/178 (5.1%)
25.	Cardiac Hypertrophy Signaling	1.61E-07	10/245 (4.1%)

2.2. Antibody microarray

After Ang-(1-7) stimulation, 1 mg/ml protein cell extract was labeled with CyTM3 or CyTM5 dye. The antibody microarray was performed as described in the Panorama Antibody Microarray-XPRESS Profiler725 Kit manual (Sigma-Aldrich, St. Louis, USA). After incubation with the labeled samples, washing and air drying images were acquired using GenePix 4100A Microarray Scanner (Molecular Devices, Sunnyvale, USA). Data was imported into Acuity 4.0 software (Molecular Devices, Sunnyvale, USA) and normalized using the nonlinear Lowess normalization method. Association of regulated proteins to metabolic pathways was done by IPA software (Ingenuity Systems, Redwood City, USA). The software calculated a *p*-value using the right tailed Fisher Exact test. The *p*-value gives the probability that the association between regulated detected proteins and the pathways is due to random association. The software considers a *p*-value < 0.05 as statistically significant.

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Appendix A. Transparency document

Transparency data associated with this article can be found in the online version at: <http://dx.doi.org/10.1016/j.dib.2016.12.004>.

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