

SUPPORTING INFORMATION

QUERCETIN-3-O-GLUCURONIDE AFFECTS GENE EXPRESSION PROFILE OF M1 AND M2a MACROPHAGES EXHIBITING ANTI-INFLAMMATORY EFFECTS

Eleonora Derlindati¹, Margherita Dall'Asta², Diego Ardigò¹, Furio Brighenti², Ivana Zavaroni¹, Alan Crozier³, Daniele Del Rio^{2*}

¹Department of Internal Medicine and Biomedical Science, University of Parma

²The φ2 laboratory of Phytochemicals in Physiology, Human Nutrition Unit, Department of Public Health, University of Parma.

³School of Medicine, College of Medical, Veterinary and Life Sciences. University of Glasgow, Glasgow G12 888, UK

*Corresponding author: Tel.: +39-0521-903830; fax: +39-0521-903832.

E-mail address: daniele.delrio@unipr.it (Daniele Del Rio)

Table S1: Gene Ontology (GO) terms resulted up-regulated in classical activated macrophages (M1) and M1 exposed to quercetin-3-O-glucuronide (M1+Q3GA). The gene expression values of M1 and M1+Q3GA were normalised to the Resting Macrophages (RM) gene expression values. P-value is calculated based on the mean of the gene expression values for the three points of the time course (6, 12 and 24 hours).

GO Term	Description	P-value M1	Enrich ^{a)}	P-value M1+Q3GA	Enrich ^{a)}
GO:0019221	cytokine-mediated signaling pathway	6,48E-36	6,01	8,16E-19	3,84
GO:0034097	response to cytokine stimulus	1,30E-35	4,36	8,32E-25	3,51
GO:0002376	immune system process	2,23E-35	2,63	1,42E-28	2,10
GO:0071345	cellular response to cytokine stimulus	2,26E-35	5,68	2,25E-20	3,78
GO:0034340	response to type I interferon	2,48E-32	8,47	1,71E-12	6,40
GO:0071357	cellular response to type I interferon	2,12E-31	8,43	9,57E-13	4,83
GO:0060337	type I interferon-mediated signaling pathway	2,12E-31	8,43	9,57E-13	4,83
GO:0002682	regulation of immune system process	5,87E-30	2,84	3,55E-21	2,19
GO:0006955	immune response	7,36E-30	3,00	2,92E-28	2,50
GO:0006952	defense response	2,85E-27	2,87	3,77E-26	2,52
GO:0007165	signal transduction	1,71E-26	1,61	2,08E-14	1,42
GO:0050776	regulation of immune response	4,45E-26	3,22	3,82E-19	3,03
GO:0009615	response to virus	2,20E-25	6,28	1,47E-15	4,00
GO:0009607	response to biotic stimulus	3,80E-24	4,73	4,68E-21	3,22
GO:0048583	regulation of response to stimulus	5,63E-24	1,81	2,69E-20	1,69
GO:0051707	response to other organism	1,00E-22	7,78	1,22E-17	3,43
GO:0050896	response to stimulus	7,12E-22	1,38	6,40E-17	1,31
GO:0034341	response to interferon-gamma	2,13E-21	6,01	9,62E-16	5,67
GO:0048518	positive regulation of biological process	9,49E-21	1,69	3,15E-14	1,53
GO:0031347	regulation of defense response	2,11E-20	4,31	2,16E-17	3,50
GO:0050789	regulation of biological process	4,06E-20	1,33	2,59E-12	1,23
GO:0002684	positive regulation of immune system process	2,47E-19	2,88	3,18E-17	2,78
GO:0060333	interferon-gamma-mediated signaling pathway	4,20E-19	6,50	1,00E-11	5,72
GO:0010033	response to organic substance	6,72E-19	2,74	7,73E-14	1,89
GO:0051716	cellular response to stimulus	7,75E-19	1,45	3,61E-13	1,44
GO:0071346	cellular response to interferon-gamma	1,03E-18	6,19	2,93E-14	5,81
GO:0071310	cellular response to organic substance	9,58E-18	2,69	3,35E-11	2,33
GO:0048584	positive regulation of response to stimulus	2,08E-17	2,11	4,84E-17	1,98
GO:0065007	biological regulation	3,29E-17	1,29	5,84E-12	1,18
GO:0051704	multi-organism process	6,16E-17	5,14	1,38E-13	2,33
GO:0050794	regulation of cellular process	1,42E-16	1,32	3,00E-08	1,16
GO:0048522	positive regulation of cellular process	1,61E-16	1,66	6,46E-13	1,50
GO:0070887	cellular response to chemical stimulus	2,40E-16	2,43	2,34E-12	2,23
GO:0042981	regulation of apoptosis	4,70E-16	2,07	1,14E-15	3,67
GO:0043067	regulation of programmed cell death	5,78E-16	2,06	1,29E-15	1,92
GO:0080134	regulation of response to stress	1,95E-15	3,00	5,63E-13	2,46
GO:0042127	regulation of cell proliferation	2,13E-15	2,12	1,94E-12	1,99
GO:0001817	regulation of cytokine production	2,40E-15	3,17	2,35E-15	2,73

GO:0010941	regulation of cell death	2,43E-15	2,03	6,34E-15	1,89
GO:0002697	regulation of immune effector process	4,44E-15	5,25	5,40E-14	4,05
GO:0042221	response to chemical stimulus	4,52E-15	1,69	2,40E-13	1,48
GO:0050865	regulation of cell activation	1,64E-14	3,28	2,07E-12	2,57
GO:0051239	regulation of multicellular organismal process	2,59E-14	1,79	3,45E-15	1,70
GO:0032101	regulation of response to external stimulus	3,23E-14	4,40	1,16E-10	2,61
GO:0050778	positive regulation of immune response	3,82E-14	2,92	7,51E-13	2,47
GO:0001819	positive regulation of cytokine production	5,40E-14	3,95	6,61E-12	3,14
GO:0006950	response to stress	5,43E-14	2,16	6,11E-14	1,60
GO:0045088	regulation of innate immune response	6,63E-14	4,57	1,51E-12	3,02
GO:0009611	response to wounding	7,24E-14	2,77	2,41E-14	2,45
GO:0051249	regulation of lymphocyte activation	9,71E-14	3,27	2,19E-10	2,58
GO:0043065	positive regulation of apoptosis	1,25E-13	2,37	6,80E-10	3,89
GO:0010647	positive regulation of cell communication	1,42E-13	2,19	1,01E-11	1,92
GO:0002694	regulation of leukocyte activation	1,47E-13	3,25	7,53E-12	2,59
GO:0051240	positive regulation of multicellular organismal process	1,52E-13	2,91	3,59E-12	2,38
GO:0009966	regulation of signal transduction	2,00E-13	1,70	5,12E-12	1,58
GO:0043068	positive regulation of programmed cell death	2,05E-13	2,35	2,40E-10	2,08
GO:0070663	regulation of leukocyte proliferation	2,18E-13	4,48	4,03E-10	3,27
GO:0023056	positive regulation of signaling	2,30E-13	2,17	7,83E-12	1,92
GO:0009967	positive regulation of signal transduction	2,53E-13	2,20	4,33E-11	1,91
GO:0010740	positive regulation of intracellular protein kinase cascade	3,64E-13	3,18	5,44E-08	2,08
GO:0048519	negative regulation of biological process	4,40E-13	1,60	1,35E-13	1,44
GO:0010942	positive regulation of cell death	4,74E-13	2,32	1,25E-10	2,09
GO:0051094	positive regulation of developmental process	6,24E-13	2,28	1,78E-06	1,96
GO:0031349	positive regulation of defense response	1,52E-12	3,45	2,01E-14	3,20
GO:0023051	regulation of signaling	1,58E-12	1,62	6,12E-12	1,54
GO:0050670	regulation of lymphocyte proliferation	2,21E-12	4,40	4,45E-10	3,32
GO:0008285	negative regulation of cell proliferation	2,25E-12	2,46	3,46E-07	3,46
GO:0032944	regulation of mononuclear cell proliferation	3,15E-12	4,35	6,12E-10	3,29
GO:0045597	positive regulation of cell differentiation	4,57E-12	2,42	4,08E-05	1,98
GO:0045087	innate immune response	6,46E-12	4,99	1,16E-12	3,18
GO:0050867	positive regulation of cell activation	7,60E-12	3,12	1,27E-11	3,13
GO:0006954	inflammatory response	7,92E-12	4,65	1,63E-14	2,86
GO:0008284	positive regulation of cell proliferation	8,63E-12	2,31	1,02E-12	2,43
GO:0048523	negative regulation of cellular process	1,37E-11	1,56	1,75E-08	1,36
GO:0002696	positive regulation of leukocyte activation	1,53E-11	3,10	1,45E-11	3,16
GO:0050863	regulation of T cell activation	2,02E-11	3,30	1,61E-07	2,75
GO:0050727	regulation of inflammatory response	2,80E-11	7,05	1,88E-10	3,42
GO:0010646	regulation of cell communication	3,07E-11	1,72	4,19E-11	1,62
GO:0042531	positive regulation of tyrosine phosphorylation of STAT protein	3,74E-11	9,92	5,91E-07	14,37
GO:0001775	cell activation	5,37E-11	2,06	9,23E-11	2,01
GO:0050793	regulation of developmental process	9,01E-11	1,77	2,73E-08	1,67
GO:0070665	positive regulation of leukocyte proliferation	1,36E-10	4,70	8,04E-10	4,45
GO:0002819	regulation of adaptive immune response	1,54E-10	4,98	3,01E-10	4,04
GO:0051251	positive regulation of lymphocyte activation	1,65E-10	3,22	4,09E-10	3,11
GO:2000026	regulation of multicellular organismal development	2,04E-10	1,84	8,02E-09	1,81
GO:0012501	programmed cell death	2,04E-10	2,05	1,03E-08	2,01

GO:0032103	positive regulation of response to external stimulus	2,36E-10	5,81	9,78E-11	4,46
GO:0042509	regulation of tyrosine phosphorylation of STAT protein	2,36E-10	8,35	1,08E-08	14,81
GO:0002237	response to molecule of bacterial origin	2,39E-10	4,49	6,06E-10	3,22
GO:0045321	leukocyte activation	2,81E-10	2,81	3,61E-10	2,33
GO:0002699	positive regulation of immune effector process	3,25E-10	4,33	1,49E-08	4,43
GO:0050671	positive regulation of lymphocyte proliferation	4,42E-10	4,64	3,27E-10	4,07
GO:0046427	positive regulation of JAK-STAT cascade	4,84E-10	8,73	1,39E-06	82,47
GO:0051222	positive regulation of protein transport	4,98E-10	3,60	2,77E-08	3,23
GO:0032946	positive regulation of mononuclear cell proliferation	6,12E-10	4,58	4,46E-10	4,02
GO:0006915	apoptosis	6,14E-10	2,03	7,22E-09	1,73
GO:0002822	regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	7,11E-10	4,85	4,11E-10	4,11
GO:0051223	regulation of protein transport	8,13E-10	2,71	1,19E-09	2,57
GO:0051091	positive regulation of sequence-specific DNA binding transcription factor activity	8,66E-10	3,65	2,58E-06	2,47
GO:0042129	regulation of T cell proliferation	8,81E-10	4,69	2,89E-08	4,25
GO:0050729	positive regulation of inflammatory response	1,06E-09	11,08	4,20E-09	5,68
GO:0046425	regulation of JAK-STAT cascade	1,18E-09	7,12	5,35E-08	9,22
GO:0010627	regulation of intracellular protein kinase cascade	1,23E-09	2,46	5,39E-08	1,87
GO:0019220	regulation of phosphate metabolic process	1,26E-09	2,06	1,25E-06	2,03
GO:0051174	regulation of phosphorus metabolic process	1,26E-09	2,06	1,25E-06	2,03
GO:0006917	induction of apoptosis	1,36E-09	2,35	3,99E-05	1,94
GO:0042325	regulation of phosphorylation	1,41E-09	2,07	1,25E-07	1,79
GO:0012502	induction of programmed cell death	1,85E-09	2,34	2,99E-05	1,91
GO:0001932	regulation of protein phosphorylation	2,06E-09	2,10	5,58E-07	1,84
GO:0032496	response to lipopolysaccharide	2,24E-09	4,61	1,12E-09	3,28
GO:0007259	JAK-STAT cascade	2,46E-09	10,61	4,20E-09	5,16
GO:0070201	regulation of establishment of protein localization	2,84E-09	2,56	2,81E-08	2,36
GO:0032880	regulation of protein localization	3,81E-09	2,45	1,30E-07	2,19
GO:0031341	regulation of cell killing	4,11E-09	7,10	3,90E-07	6,37
GO:0045595	regulation of cell differentiation	4,21E-09	1,81	1,02E-06	1,86
GO:0050870	positive regulation of T cell activation	4,87E-09	3,28	1,59E-08	3,16
GO:0031399	regulation of protein modification process	4,99E-09	1,91	4,48E-06	1,94
GO:0009893	positive regulation of metabolic process	5,53E-09	1,69	2,48E-07	1,57
GO:0042035	regulation of cytokine biosynthetic process	6,26E-09	5,75	1,33E-12	5,60
GO:0002252	immune effector process	7,09E-09	3,27	9,36E-10	3,38
GO:0048660	regulation of smooth muscle cell proliferation	7,73E-09	5,61	5,82E-08	5,99
GO:0001910	regulation of leukocyte mediated cytotoxicity	8,98E-09	7,31	4,47E-06	6,29
GO:0065009	regulation of molecular function	9,61E-09	1,66	1,38E-06	1,37
GO:0051246	regulation of protein metabolic process	9,90E-09	1,76	1,17E-07	1,50
GO:0042327	positive regulation of phosphorylation	1,47E-08	3,10	8,69E-06	2,78
GO:0010604	positive regulation of macromolecule metabolic process	1,58E-08	1,71	2,74E-07	1,60
GO:0002706	regulation of lymphocyte mediated immunity	1,62E-08	3,92	4,29E-07	4,61
GO:0051092	positive regulation of NF-kappaB transcription factor activity	1,77E-08	4,04	2,11E-04	2,62
GO:0045089	positive regulation of innate immune response	2,23E-08	3,33	3,53E-09	3,10
GO:0001959	regulation of cytokine-mediated signaling pathway	2,53E-08	5,71	2,78E-08	6,43
GO:0051090	regulation of sequence-specific DNA binding transcription factor activity	2,69E-08	2,54	1,53E-05	1,88
GO:0042108	positive regulation of cytokine biosynthetic process	2,72E-08	4,63	5,54E-10	4,31
GO:0010562	positive regulation of phosphorus metabolic process	2,98E-08	3,03	1,89E-05	2,66

GO:0045937	positive regulation of phosphate metabolic process	2,98E-08	3,03	1,89E-05	2,66
GO:0031343	positive regulation of cell killing	3,23E-08	6,45	1,21E-05	6,35
GO:0050731	positive regulation of peptidyl-tyrosine phosphorylation	3,67E-08	4,92	3,33E-05	39,18
GO:0001934	positive regulation of protein phosphorylation	3,71E-08	3,27	5,24E-06	2,92
GO:0043900	regulation of multi-organism process	4,37E-08	3,62	4,40E-06	3,83
GO:0031325	positive regulation of cellular metabolic process	5,02E-08	1,67	6,56E-07	1,60
GO:0060759	regulation of response to cytokine stimulus	5,13E-08	5,49	1,48E-08	6,24
GO:0001912	positive regulation of leukocyte mediated cytotoxicity	5,90E-08	6,74	2,34E-05	6,71
GO:0002821	positive regulation of adaptive immune response	6,28E-08	6,02	4,22E-06	4,14
GO:0046634	regulation of alpha-beta T cell activation	7,79E-08	5,38	3,85E-06	6,15
GO:0032755	positive regulation of interleukin-6 production	8,58E-08	6,52	7,23E-05	5,25
GO:0032879	regulation of localization	1,04E-07	2,05	1,08E-07	1,53
GO:0043122	regulation of I-kappaB kinase/NF-kappaB cascade	1,06E-07	2,65	2,40E-08	2,65
GO:0002703	regulation of leukocyte mediated immunity	1,06E-07	4,03	1,92E-05	3,63
GO:0043123	positive regulation of I-kappaB kinase/NF-kappaB cascade	1,16E-07	2,78	3,71E-07	2,62
GO:0002683	negative regulation of immune system process	1,17E-07	3,41	5,73E-05	2,31
GO:0008219	cell death	1,24E-07	1,78	4,82E-07	1,79
GO:0016265	death	1,24E-07	1,63	7,23E-07	1,77
GO:0002705	positive regulation of leukocyte mediated immunity	1,26E-07	4,49	1,17E-05	4,07
GO:0002708	positive regulation of lymphocyte mediated immunity	1,26E-07	4,49	1,17E-05	4,07
GO:0032649	regulation of interferon-gamma production	1,35E-07	9,67	9,12E-06	3,58
GO:0050864	regulation of B cell activation	1,38E-07	4,32	1,00E-05	3,26
GO:0032268	regulation of cellular protein metabolic process	1,38E-07	1,72	1,10E-04	1,65
GO:0030335	positive regulation of cell migration	1,54E-07	3,96	1,20E-04	5,18
GO:2000147	positive regulation of cell motility	1,54E-07	3,96	1,35E-04	5,09
GO:0050691	regulation of defense response to virus by host	1,54E-07	30,00	1,72E-04	6,99
GO:0046649	lymphocyte activation	1,57E-07	3,49	3,72E-06	2,09
GO:2000242	negative regulation of reproductive process	1,72E-07	11,87	2,79E-05	4,82
GO:0009605	response to external stimulus	1,74E-07	1,61	6,49E-09	1,63
GO:0002253	activation of immune response	2,02E-07	2,47	5,25E-05	1,94
GO:0051272	positive regulation of cellular component movement	2,06E-07	3,77	1,93E-04	4,89
GO:0052548	regulation of endopeptidase activity	2,20E-07	3,79	1,29E-04	5,80
GO:0051241	negative regulation of multicellular organismal process	2,24E-07	2,23	3,41E-07	2,10
GO:0001914	regulation of T cell mediated cytotoxicity	2,41E-07	9,74	3,43E-04	7,59
GO:0031401	positive regulation of protein modification process	2,81E-07	2,60	1,57E-05	2,34
GO:0009891	positive regulation of biosynthetic process	2,84E-07	1,64	6,75E-07	1,70
GO:0042102	positive regulation of T cell proliferation	3,06E-07	4,78	5,81E-09	5,20
GO:0040017	positive regulation of locomotion	3,08E-07	3,84	1,65E-04	4,95
GO:0048661	positive regulation of smooth muscle cell proliferation	3,14E-07	6,85	2,15E-05	4,08
GO:0002824	positive regulation of adaptive immune response based on somatic recombination of immune receptors built from immunoglobulin superfamily domains	3,25E-07	4,83	1,17E-05	4,07
GO:0050730	regulation of peptidyl-tyrosine phosphorylation	3,62E-07	4,01	1,30E-05	13,26
GO:0050714	positive regulation of protein secretion	4,02E-07	5,03	1,31E-09	7,98
GO:0045071	negative regulation of viral genome replication	4,17E-07	29,02	8,52E-06	6,63
GO:0048525	negative regulation of viral reproduction	4,17E-07	29,02	8,52E-06	6,63
GO:0010557	positive regulation of macromolecule biosynthetic process	4,25E-07	1,67	2,72E-07	1,78
GO:0045580	regulation of T cell differentiation	4,50E-07	4,39	2,82E-06	4,09
GO:0052547	regulation of peptidase activity	4,78E-07	3,63	1,86E-04	5,60
GO:0060338	regulation of type I interferon-mediated signaling pathway	5,07E-07	10,10	9,33E-05	7,94

GO:0050708	regulation of protein secretion	5,60E-07	3,45	4,79E-09	6,41
GO:0032655	regulation of interleukin-12 production	5,60E-07	5,10	8,46E-05	4,63
GO:0070482	response to oxygen levels	5,88E-07	2,47	9,22E-05	3,46
GO:0031328	positive regulation of cellular biosynthetic process	6,47E-07	1,62	2,01E-06	1,67
GO:0002831	regulation of response to biotic stimulus	7,31E-07	4,38	3,52E-06	4,24
GO:0048545	response to steroid hormone stimulus	7,35E-07	3,28	9,18E-06	4,80
GO:0045429	positive regulation of nitric oxide biosynthetic process	7,47E-07	8,42	1,46E-05	23,98
GO:0002675	positive regulation of acute inflammatory response	7,76E-07	16,14	1,16E-06	81,40
GO:0050790	regulation of catalytic activity	7,90E-07	1,64	2,05E-05	1,47
GO:0051270	regulation of cellular component movement	7,91E-07	2,07	6,07E-04	3,48
GO:0006959	humoral immune response	8,23E-07	3,11	2,76E-06	5,04
GO:0030334	regulation of cell migration	8,57E-07	3,07	1,41E-04	1,93
GO:0001916	positive regulation of T cell mediated cytotoxicity	8,65E-07	10,10	4,81E-04	8,86
GO:0042110	T cell activation	1,01E-06	4,08	5,11E-05	2,33
GO:0060341	regulation of cellular localization	1,03E-06	1,88	7,29E-07	1,78
GO:2000145	regulation of cell motility	1,11E-06	3,03	2,99E-04	1,86
GO:0045622	regulation of T-helper cell differentiation	1,12E-06	20,22	2,35E-05	13,85
GO:0007243	intracellular protein kinase cascade	1,15E-06	2,90	3,87E-08	2,09
GO:0033157	regulation of intracellular protein transport	1,18E-06	2,87	4,73E-04	2,30
GO:0044093	positive regulation of molecular function	1,19E-06	1,61	3,73E-08	1,60
GO:0051607	defense response to virus	1,24E-06	6,59	3,32E-05	4,02
GO:0032642	regulation of chemokine production	1,35E-06	8,27	3,81E-04	4,54
GO:0032270	positive regulation of cellular protein metabolic process	1,39E-06	2,34	3,22E-05	2,16
GO:0043069	negative regulation of programmed cell death	1,41E-06	1,85	3,49E-08	1,81
GO:0045619	regulation of lymphocyte differentiation	1,49E-06	3,94	1,97E-07	4,03
GO:0070431	nucleotide-binding oligomerization domain containing 2 signaling pathway	1,52E-06	35,90	5,35E-05	15,21
GO:0070423	nucleotide-binding oligomerization domain containing signaling pathway	1,52E-06	35,90	6,74E-04	3,90
GO:0042306	regulation of protein import into nucleus	1,75E-06	3,01	1,75E-04	2,53
GO:0051247	positive regulation of protein metabolic process	1,96E-06	2,28	6,30E-08	2,39
GO:0035556	intracellular signal transduction	2,16E-06	1,64	2,81E-06	1,48
GO:0060548	negative regulation of cell death	2,36E-06	1,82	2,03E-07	1,75
GO:0040012	regulation of locomotion	2,65E-06	2,84	6,78E-04	3,43
GO:0032675	regulation of interleukin-6 production	2,76E-06	3,79	5,90E-04	3,47
GO:0045428	regulation of nitric oxide biosynthetic process	2,79E-06	6,74	3,13E-05	5,34
GO:0048585	negative regulation of response to stimulus	3,05E-06	1,77	2,15E-05	1,60
GO:0050707	regulation of cytokine secretion	3,51E-06	5,25	1,44E-07	7,53
GO:0002673	regulation of acute inflammatory response	5,79E-06	10,23	2,16E-07	5,43
GO:0042517	positive regulation of tyrosine phosphorylation of Stat3 protein	5,79E-06	10,15	2,85E-04	8,44
GO:0071219	cellular response to molecule of bacterial origin	5,86E-06	3,80	8,09E-05	3,75
GO:0006916	anti-apoptosis	5,90E-06	2,39	2,31E-08	2,48
GO:0031622	positive regulation of fever generation	6,73E-06	21,77	1,45E-04	44,77
GO:0031620	regulation of fever generation	6,73E-06	21,77	1,45E-04	44,77
GO:0050715	positive regulation of cytokine secretion	7,86E-06	4,56	5,85E-06	7,54
GO:0001666	response to hypoxia	8,30E-06	2,35	2,75E-04	3,46
GO:0032729	positive regulation of interferon-gamma production	8,32E-06	5,02	4,52E-04	4,73
GO:0046635	positive regulation of alpha-beta T cell activation	8,66E-06	5,15	1,27E-04	5,92
GO:0043549	regulation of kinase activity	9,07E-06	1,72	3,50E-05	1,73
GO:0050871	positive regulation of B cell activation	9,42E-06	6,17	7,63E-05	3,39

GO:0051173	positive regulation of nitrogen compound metabolic process	9,83E-06	1,57	2,45E-05	1,62
GO:0009617	response to bacterium	1,02E-05	2,83	1,17E-06	3,41
GO:0042345	regulation of NF-kappaB import into nucleus	1,07E-05	4,98	8,94E-04	3,55
GO:0045859	regulation of protein kinase activity	1,22E-05	1,73	9,12E-05	1,71
GO:0050688	regulation of defense response to virus	1,27E-05	4,53	4,33E-04	3,84
GO:0043370	regulation of CD4-positive, alpha-beta T cell differentiation	1,33E-05	6,59	2,95E-06	8,88
GO:2000514	regulation of CD4-positive, alpha-beta T cell activation	1,33E-05	6,59	5,99E-06	8,24
GO:0042516	regulation of tyrosine phosphorylation of Stat3 protein	1,33E-05	7,98	1,03E-04	10,68
GO:0051046	regulation of secretion	1,37E-05	2,16	4,43E-06	3,68
GO:0051047	positive regulation of secretion	1,43E-05	2,92	2,81E-07	2,43
GO:0051049	regulation of transport	1,50E-05	2,03	1,43E-06	1,59
GO:0034762	regulation of transmembrane transport	1,57E-05	2,42	4,72E-05	2,10
GO:0046637	regulation of alpha-beta T cell differentiation	1,69E-05	5,26	5,52E-06	10,77
GO:0022603	regulation of anatomical structure morphogenesis	1,81E-05	1,98	1,68E-04	1,60
GO:0008283	cell proliferation	1,85E-05	8,81	4,37E-04	2,69
GO:0051338	regulation of transferase activity	2,00E-05	1,68	5,64E-05	1,70
GO:0045621	positive regulation of lymphocyte differentiation	2,10E-05	4,61	6,38E-05	4,00
GO:0045944	positive regulation of transcription from RNA polymerase II promoter	2,15E-05	1,76	2,38E-04	1,78
GO:0045069	regulation of viral genome replication	2,15E-05	13,06	7,31E-04	4,95
GO:0023052	signaling	2,37E-05	1,87	9,68E-06	2,07
GO:0032386	regulation of intracellular transport	2,39E-05	2,47	1,89E-04	2,08
GO:0031650	regulation of heat generation	2,44E-05	17,82	3,05E-04	36,63
GO:0031652	positive regulation of heat generation	2,44E-05	17,82	3,05E-04	36,63
GO:0042742	defense response to bacterium	2,50E-05	3,11	1,24E-04	7,50
GO:0071222	cellular response to lipopolysaccharide	2,57E-05	3,79	3,81E-05	3,98
GO:0010628	positive regulation of gene expression	2,66E-05	1,60	8,30E-05	1,63
GO:0046822	regulation of nucleocytoplasmic transport	2,86E-05	2,58	6,43E-04	2,26
GO:0042493	response to drug	2,97E-05	1,92	4,94E-08	4,62
GO:0030155	regulation of cell adhesion	3,41E-05	2,21	2,32E-05	2,72
GO:0032355	response to estradiol stimulus	3,47E-05	5,11	1,42E-04	2,85
GO:0032770	positive regulation of monooxygenase activity	3,52E-05	8,26	9,14E-04	5,06
GO:0007154	cell communication	3,70E-05	1,73	4,95E-06	1,95
GO:0045582	positive regulation of T cell differentiation	3,71E-05	4,70	2,13E-04	4,08
GO:0007267	cell-cell signaling	4,30E-05	3,59	3,59E-05	2,01
GO:0009653	anatomical structure morphogenesis	4,47E-05	1,51	5,20E-04	2,83
GO:0006935	chemotaxis	4,91E-05	1,67	9,61E-05	1,61
GO:0042330	taxis	4,91E-05	1,67	9,61E-05	1,61
GO:0051050	positive regulation of transport	4,95E-05	1,86	9,71E-06	1,93
GO:0051353	positive regulation of oxidoreductase activity	5,20E-05	6,00	5,12E-06	5,21
GO:0032735	positive regulation of interleukin-12 production	5,39E-05	6,42	2,60E-04	195,88
GO:0003013	circulatory system process	5,44E-05	4,97	5,06E-05	3,01
GO:0002274	myeloid leukocyte activation	5,78E-05	3,89	3,12E-05	3,16
GO:0048513	organ development	6,17E-05	1,53	2,19E-04	1,45
GO:0032844	regulation of homeostatic process	6,21E-05	3,03	4,77E-06	2,18
GO:0060664	epithelial cell proliferation involved in salivary gland morphogenesis	6,35E-05	20,13	1,50E-05	80,59
GO:0032494	response to peptidoglycan	6,35E-05	14,96	3,68E-05	8,19
GO:0045672	positive regulation of osteoclast differentiation	7,85E-05	8,91	5,37E-04	31,00
GO:0045893	positive regulation of transcription, DNA-dependent	7,90E-05	1,58	7,77E-05	1,65

GO:0040011	locomotion	8,31E-05	1,50	4,42E-05	1,48
GO:0050866	negative regulation of cell activation	8,40E-05	3,30	9,77E-05	6,64
GO:0002690	positive regulation of leukocyte chemotaxis	8,44E-05	16,53	5,61E-07	9,83
GO:0002695	negative regulation of leukocyte activation	8,77E-05	3,43	2,32E-04	8,26
GO:0071260	cellular response to mechanical stimulus	8,98E-05	6,26	3,84E-04	3,12
GO:0032760	positive regulation of tumor necrosis factor production	9,30E-05	5,42	3,50E-04	4,89
GO:0042307	positive regulation of protein import into nucleus	9,36E-05	3,61	4,60E-04	3,44
GO:0023057	negative regulation of signaling	9,76E-05	1,70	1,44E-04	1,58
GO:0002685	regulation of leukocyte migration	1,03E-04	5,44	2,40E-07	8,24
GO:0010648	negative regulation of cell communication	1,05E-04	1,70	1,53E-04	1,58
GO:0032663	regulation of interleukin-2 production	1,09E-04	4,58	1,04E-04	11,40
GO:0050830	defense response to Gram-positive bacterium	1,17E-04	3,95	4,92E-04	4,66
GO:0071496	cellular response to external stimulus	1,18E-04	3,01	7,28E-04	1,89
GO:0006956	complement activation	1,27E-04	3,49	3,68E-04	5,07
GO:0045073	regulation of chemokine biosynthetic process	1,32E-04	11,99	1,68E-04	8,51
GO:0009725	response to hormone stimulus	1,35E-04	2,10	7,54E-04	3,28
GO:0060334	regulation of interferon-gamma-mediated signaling pathway	1,50E-04	7,32	4,52E-05	12,50
GO:0060330	regulation of response to interferon-gamma	1,50E-04	7,32	5,85E-05	12,00
GO:0002688	regulation of leukocyte chemotaxis	1,59E-04	24,77	1,61E-06	8,83
GO:0043627	response to estrogen stimulus	1,63E-04	3,68	7,02E-04	2,13
GO:0032647	regulation of interferon-alpha production	1,88E-04	18,51	5,92E-04	6,27
GO:0009719	response to endogenous stimulus	2,06E-04	2,02	6,57E-04	2,24
GO:0060021	palate development	2,10E-04	7,60	5,02E-05	5,85
GO:0045926	negative regulation of growth	2,14E-04	2,20	4,39E-08	5,70
GO:0002700	regulation of production of molecular mediator of immune response	2,17E-04	3,23	2,21E-04	6,66
GO:0044419	interspecies interaction between organisms	2,28E-04	2,10	1,17E-04	1,99
GO:0060559	positive regulation of calcidiol 1-monooxygenase activity	2,33E-04	20,22	6,45E-05	31,06
GO:0009612	response to mechanical stimulus	2,48E-04	2,46	2,09E-06	2,78
GO:0002687	positive regulation of leukocyte migration	2,51E-04	22,02	1,76E-07	9,52
GO:0050921	positive regulation of chemotaxis	2,65E-04	5,38	8,68E-06	7,46
GO:0033674	positive regulation of kinase activity	2,67E-04	1,75	1,10E-04	1,84
GO:0050920	regulation of chemotaxis	2,76E-04	4,46	2,66E-05	5,95
GO:0051250	negative regulation of lymphocyte activation	2,99E-04	3,42	9,07E-04	8,16
GO:0034612	response to tumor necrosis factor	3,07E-04	4,76	2,27E-07	4,86
GO:0008633	activation of pro-apoptotic gene products	3,19E-04	5,84	6,19E-06	4,44
GO:0010661	positive regulation of muscle cell apoptosis	3,42E-04	17,81	2,90E-04	119,52
GO:0034393	positive regulation of smooth muscle cell apoptosis	3,42E-04	17,81	2,90E-04	119,52
GO:0045080	positive regulation of chemokine biosynthetic process	3,46E-04	13,70	4,03E-04	9,22
GO:0051336	regulation of hydrolase activity	3,50E-04	1,96	2,21E-04	2,77
GO:0009968	negative regulation of signal transduction	3,63E-04	1,67	9,02E-04	1,53
GO:0014070	response to organic cyclic compound	3,85E-04	2,10	2,21E-05	2,13
GO:0009991	response to extracellular stimulus	3,92E-04	1,77	2,97E-06	1,91
GO:0030595	leukocyte chemotaxis	4,07E-04	19,82	2,66E-06	36,69
GO:0045625	regulation of T-helper 1 cell differentiation	4,15E-04	24,26	3,28E-05	15,64
GO:0045860	positive regulation of protein kinase activity	4,30E-04	1,74	2,38E-04	1,82
GO:0031324	negative regulation of cellular metabolic process	4,54E-04	1,50	5,66E-05	1,72
GO:0046883	regulation of hormone secretion	4,85E-04	4,05	8,46E-06	7,01
GO:0032731	positive regulation of interleukin-1 beta production	5,34E-04	9,29	5,04E-04	5,92

GO:0032502	developmental process	5,47E-04	1,21	1,50E-04	1,23
GO:0009892	negative regulation of metabolic process	5,51E-04	1,47	9,51E-05	1,67
GO:0006968	cellular defense response	5,60E-04	2,90	1,46E-04	3,26
GO:0010940	positive regulation of necrotic cell death	5,75E-04	21,65	1,91E-04	15,12
GO:0071216	cellular response to biotic stimulus	5,79E-04	2,64	5,06E-04	3,23
GO:0032495	response to muramyl dipeptide	5,80E-04	21,54	9,47E-05	10,87
GO:0051347	positive regulation of transferase activity	6,29E-04	1,69	2,09E-04	1,80
GO:0060558	regulation of calcidiol 1-monoxygenase activity	6,58E-04	11,55	1,34E-04	17,75
GO:0042269	regulation of natural killer cell mediated cytotoxicity	6,93E-04	4,58	2,30E-05	7,63
GO:0002715	regulation of natural killer cell mediated immunity	6,93E-04	4,58	4,00E-05	7,22
GO:0006928	cellular component movement	7,02E-04	1,54	6,85E-04	3,46
GO:0032727	positive regulation of interferon-alpha production	7,17E-04	78,17	7,18E-04	10,29
GO:0048520	positive regulation of behavior	7,55E-04	16,87	2,53E-05	6,66
GO:0002676	regulation of chronic inflammatory response	8,13E-04	6,76	4,14E-04	29,55
GO:0031663	lipopolysaccharide-mediated signaling pathway	8,42E-04	5,27	1,17E-05	6,39
GO:0051023	regulation of immunoglobulin secretion	8,53E-04	7,47	2,44E-05	29,63
GO:0051254	positive regulation of RNA metabolic process	8,56E-04	1,48	1,27E-04	1,62
GO:0050795	regulation of behavior	8,61E-04	3,68	2,42E-04	24,05
GO:0048856	anatomical structure development	9,72E-04	1,27	3,46E-04	1,28

a) Enrich: Enrichment Value

Table S2: Gene Ontology (GO) terms up-regulated in classical activated macrophages (M1) compared to M1 exposed to quercetin-3-O-glucuronide (M1+Q3GA) macrophages after 6, 12 and 24 hours of incubation. The gene expression values of M1 and M1+Q3GA were normalised to the Resting Macrophages (RM) gene expression values. P-value is calculated based on the differences of gene expression value between M1 and M1+Q3GA for the three points of the time course (6, 12 and 24 hours).

GO Term	Description	P-value 6h	Enrich 6h ^{a)}	P-value12h	Enrich 12h ^{a)}	P-value24h	Enrich 24h ^{a)}
GO:0002688	regulation of leukocyte chemotaxis	3,00E-06	3,83	2,56E-05	41,12	2,79E-05	3,46
GO:0009611	response to wounding	1,03E-12	2,73	8,87E-09	6,96	6,00E-09	2,21
GO:0050691	regulation of defense response to virus by host	1,04E-07	21,91	7,61E-05	10,59	6,41E-04	30,73
GO:0043065	positive regulation of apoptotic process	1,05E-05	1,67	-	-	2,36E-04	1,66
GO:0050793	regulation of developmental process	1,05E-07	1,91	2,29E-04	1,59	8,81E-11	1,79
GO:0002696	positive regulation of leukocyte activation	1,07E-05	2,02	4,40E-04	2,41	-	-
GO:0002684	positive regulation of immune system process	1,11E-07	1,86	5,94E-07	2,92	4,77E-04	1,65
GO:0009991	response to extracellular stimulus	1,14E-04	2,44	-	-	3,33E-05	2,50
GO:0043410	positive regulation of MAPK cascade	1,19E-05	2,80	-	-	8,88E-04	4,37
GO:0032502	developmental process	1,22E-11	1,42	2,42E-06	1,25	9,22E-09	1,48
GO:0042516	regulation of tyrosine phosphorylation of Stat3 protein	1,24E-04	7,83	-	-	5,64E-04	5,05
GO:0050795	regulation of behavior	1,20E-05	4,04	3,32E-04	13,83	3,20E-06	2,93
GO:0050867	positive regulation of cell activation	1,20E-05	2,00	6,83E-04	3,03	-	-
GO:0050896	response to stimulus	1,31E-13	1,35	3,00E-09	1,38	3,26E-12	1,30
GO:0050794	regulation of cellular process	1,31E-08	1,20	2,19E-06	1,29	1,72E-05	1,13
GO:0050792	regulation of viral reproduction	1,32E-04	5,00	4,75E-04	41,97	-	-
GO:0002697	regulation of immune effector process	1,33E-05	3,64	1,30E-08	4,91	5,65E-04	10,00
GO:0010638	positive regulation of organelle organization	1,34E-04	2,13	1,00E-04	3,37	-	-
GO:0071346	cellular response to interferon-gamma	1,30E-08	5,91	2,56E-08	3,69	-	-
GO:0052547	regulation of peptidase activity	1,44E-04	2,19	-	-	3,80E-05	2,37
GO:0051091	positive regulation of sequence-specific DNA binding transcription factor activity	1,45E-06	2,44	7,64E-05	2,64	1,94E-04	4,02
GO:0048585	negative regulation of response to stimulus	1,46E-05	1,64	-	-	9,37E-05	1,72
GO:0046425	regulation of JAK-STAT cascade	1,51E-04	3,94	9,73E-04	4,63	1,01E-06	4,17
GO:0001819	positive regulation of cytokine production	1,51E-06	2,39	1,27E-08	4,08	1,53E-08	2,79
GO:0050920	regulation of chemotaxis	1,52E-04	2,74	1,93E-04	25,18	2,11E-04	2,77
GO:0007154	cell communication	1,59E-08	2,26	1,29E-07	2,65	1,76E-04	1,57
GO:0045428	regulation of nitric oxide biosynthetic process	1,61E-05	6,56	4,51E-05	5,81	-	-
GO:0009967	positive regulation of signal transduction	1,61E-07	1,99	1,00E-09	2,18	1,08E-07	1,93
GO:0002237	response to molecule of bacterial origin	1,61E-09	2,65	7,47E-06	3,97	-	-
GO:0048870	cell motility	1,62E-04	1,87	-	-	3,36E-04	1,57
GO:0032496	response to lipopolysaccharide	1,63E-08	2,57	1,41E-05	4,01	-	-
GO:0065009	regulation of molecular function	1,68E-04	1,39	-	-	2,52E-05	1,54

GO:0043068	positive regulation of programmed cell death	1,69E-05	1,65	-	-	3,16E-04	1,65
GO:0034097	response to cytokine stimulus	1,71E-16	3,68	1,13E-10	2,25	4,68E-07	1,83
GO:0051707	response to other organism	1,73E-17	7,91	1,20E-13	2,92	1,78E-11	7,52
GO:0051241	negative regulation of multicellular organismal process	1,73E-04	2,42	3,36E-04	4,26	3,63E-08	3,23
GO:2000145	regulation of cell motility	1,75E-04	2,30	1,07E-04	2,47	1,69E-05	1,93
GO:0040011	locomotion	1,76E-07	2,23	2,99E-06	6,08	4,34E-06	1,63
GO:2000026	regulation of multicellular organismal development	1,77E-07	1,98	5,52E-04	1,65	1,72E-08	1,80
GO:0051272	positive regulation of cellular component movement	1,79E-06	3,27	3,03E-04	17,61	7,92E-05	2,14
GO:0031347	regulation of defense response	1,82E-08	3,53	3,13E-08	2,75	4,17E-04	1,72
GO:0071850	mitotic cell cycle arrest	1,84E-05	11,52	-	-	1,80E-05	25,41
GO:0002694	regulation of leukocyte activation	1,84E-06	1,97	1,98E-05	3,21	-	-
GO:0048523	negative regulation of cellular process	1,86E-06	1,33	5,96E-06	1,70	3,03E-07	1,33
GO:0002682	regulation of immune system process	1,80E-10	1,79	8,44E-08	2,56	3,15E-05	1,50
GO:0052548	regulation of endopeptidase activity	1,95E-04	2,20	-	-	1,09E-04	1,91
GO:0007165	signal transduction	1,96E-13	1,51	9,74E-11	1,34	2,69E-09	1,34
GO:0009891	positive regulation of biosynthetic process	1,90E-04	1,43	4,27E-04	2,13	-	-
GO:0002690	positive regulation of leukocyte chemotaxis	2,01E-05	4,27	1,98E-04	53,42	5,41E-04	3,17
GO:0032879	regulation of localization	2,11E-04	1,43	2,39E-05	1,81	2,04E-04	1,98
GO:0035457	cellular response to interferon-alpha	2,11E-05	440,72	2,25E-04	135,61	-	-
GO:0043066	negative regulation of apoptotic process	2,14E-04	1,60	-	-	9,40E-04	1,83
GO:0060333	interferon-gamma-mediated signaling pathway	2,14E-06	8,81	1,74E-06	3,55	-	-
GO:0051094	positive regulation of developmental process	2,16E-06	1,81	3,94E-05	1,78	9,77E-08	2,01
GO:0048856	anatomical structure development	2,24E-06	1,57	3,02E-04	1,35	1,17E-06	1,58
GO:0030154	cell differentiation	2,24E-08	1,56	-	-	5,99E-05	1,48
GO:0042531	positive regulation of tyrosine phosphorylation of STAT protein	2,26E-04	7,59	2,03E-04	6,35	7,07E-07	5,36
GO:0010562	positive regulation of phosphorus metabolic process	2,31E-06	3,01	1,63E-05	2,76	3,09E-06	2,28
GO:0045937	positive regulation of phosphate metabolic process	2,31E-06	3,01	1,63E-05	2,76	3,09E-06	2,28
GO:0090287	regulation of cellular response to growth factor stimulus	2,33E-04	9,25	-	-	6,89E-04	3,82
GO:0045087	innate immune response	2,35E-06	1,97	8,23E-07	2,63	9,63E-05	2,10
GO:0050789	regulation of biological process	2,37E-08	1,19	3,31E-06	1,13	2,17E-07	1,14
GO:0023052	signaling	2,38E-08	2,47	6,71E-06	2,66	-	-
GO:0006955	immune response	2,45E-12	2,49	7,01E-10	2,29	1,88E-08	1,78
GO:0016477	cell migration	2,45E-04	2,29	-	-	1,01E-04	1,74
GO:0031667	response to nutrient levels	2,45E-04	2,42	-	-	1,99E-05	4,49
GO:0048520	positive regulation of behavior	2,45E-05	5,89	8,26E-05	31,00	-	-
GO:0007267	cell-cell signaling	2,46E-08	4,57	5,41E-06	2,69	-	-
GO:0030335	positive regulation of cell migration	2,47E-06	3,32	2,36E-04	18,65	5,78E-05	2,21
GO:0006952	defense response	2,51E-17	2,19	7,55E-14	2,58	4,18E-10	1,94
GO:0048519	negative regulation of biological process	2,57E-08	1,36	2,67E-07	1,74	4,06E-09	1,36
GO:0071310	cellular response to organic substance	2,66E-10	2,22	2,38E-05	1,93	1,09E-05	2,70
GO:0048583	regulation of response to stimulus	2,68E-12	1,51	2,23E-10	1,50	3,51E-12	1,49
GO:0071345	cellular response to cytokine stimulus	2,60E-17	4,23	8,78E-11	2,46	1,12E-05	3,60
GO:0042221	response to chemical stimulus	2,78E-13	1,80	1,28E-07	1,73	4,33E-09	1,47
GO:0002252	immune effector process	2,82E-06	4,05	1,09E-04	4,73	1,17E-06	2,72

GO:0042509	regulation of tyrosine phosphorylation of STAT protein	2,96E-05	6,15	8,52E-04	5,24	1,77E-06	4,74
GO:0010941	regulation of cell death	2,99E-06	1,45	-	-	4,93E-05	1,49
GO:0051704	multi-organism process	2,90E-13	3,67	1,08E-10	1,98	1,52E-06	2,70
GO:0050727	regulation of inflammatory response	3,02E-06	2,49	5,18E-05	2,62	1,32E-04	2,36
GO:0010575	positive regulation vascular endothelial growth factor production	3,12E-04	17,99	9,05E-04	8,66	9,45E-04	8,55
GO:0007584	response to nutrient	3,13E-04	2,66	-	-	1,87E-05	5,28
GO:0010647	positive regulation of cell communication	3,13E-07	1,94	2,53E-09	2,13	1,19E-07	1,91
GO:0007186	G-protein coupled receptor signaling pathway	3,16E-04	1,63	6,92E-04	7,69	6,77E-05	3,47
GO:0042517	positive regulation of tyrosine phosphorylation of Stat3 protein	3,24E-04	8,20	-	-	1,06E-04	6,18
GO:0032103	positive regulation of response to external stimulus	3,29E-07	5,29	2,51E-04	3,75	1,38E-04	2,54
GO:2000147	positive regulation of cell motility	3,20E-06	3,26	2,51E-04	18,33	3,14E-05	2,23
GO:0045840	positive regulation of mitosis	3,37E-04	4,29	6,95E-06	9,88	-	-
GO:0051785	positive regulation of nuclear division	3,37E-04	4,29	6,95E-06	9,88	-	-
GO:0061041	regulation of wound healing	3,42E-04	2,96	-	-	9,15E-04	3,60
GO:0070887	cellular response to chemical stimulus	3,46E-11	2,12	3,73E-05	1,80	5,61E-07	2,69
GO:0048731	system development	3,51E-04	1,51	7,26E-05	1,59	2,09E-05	1,94
GO:1900047	negative regulation of hemostasis	3,55E-04	4,33	-	-	6,21E-04	7,91
GO:0030195	negative regulation of blood coagulation	3,55E-04	4,33	-	-	6,21E-04	7,91
GO:0010740	positive regulation of intracellular protein kinase cascade	3,63E-05	2,10	1,56E-05	2,22	8,18E-06	2,09
GO:0043331	response to dsRNA	3,60E-04	18,32	2,47E-04	4,73	-	-
GO:0070482	response to oxygen levels	3,71E-04	1,90	-	-	8,51E-04	3,47
GO:0002230	positive regulation of defense response to virus by host	3,78E-05	26,61	6,51E-05	22,89	-	-
GO:0051093	negative regulation of developmental process	3,79E-04	2,14	-	-	5,48E-05	1,91
GO:0009653	anatomical structure morphogenesis	3,82E-09	1,63	2,29E-04	1,40	-	-
GO:0006954	inflammatory response	3,84E-11	2,45	3,13E-09	7,51	9,84E-07	2,05
GO:0009615	response to virus	3,84E-23	12,42	1,41E-14	3,64	3,55E-13	10,97
GO:0032147	activation of protein kinase activity	3,85E-04	2,13	-	-	6,24E-04	3,64
GO:2000242	negative regulation of reproductive process	3,89E-08	7,87	-	-	1,77E-04	254,11
GO:0080134	regulation of response to stress	3,94E-09	2,36	1,16E-06	1,89	1,41E-06	1,83
GO:0009607	response to biotic stimulus	4,04E-19	3,81	1,43E-13	2,57	1,10E-11	2,27
GO:0019220	regulation of phosphate metabolic process	4,17E-04	1,56	8,52E-04	1,59	8,62E-05	1,55
GO:0051174	regulation of phosphorus metabolic process	4,17E-04	1,56	8,52E-04	1,59	8,62E-05	1,55
GO:0032725	positive regulation of granulocyte macrophage colony-stimulating factor production	4,31E-04	97,94	4,16E-05	16,19	-	-
GO:0010528	regulation of transposition	4,32E-04	26,61	4,82E-04	25,37	-	-
GO:0010529	negative regulation of transposition	4,32E-04	26,61	4,82E-04	25,37	-	-
GO:0050730	regulation of peptidyl-tyrosine phosphorylation	4,33E-05	3,86	7,68E-04	2,44	2,20E-04	2,65
GO:0051050	positive regulation of transport	4,34E-04	2,16	-	-	4,88E-05	3,40
GO:0031325	positive regulation of cellular metabolic process	4,37E-04	1,35	6,58E-04	1,55	-	-
GO:0009605	response to external stimulus	4,39E-09	2,13	2,56E-06	1,72	1,70E-07	3,12
GO:0023051	regulation of signaling	4,39E-09	1,49	1,26E-08	1,45	4,64E-09	1,53
GO:0045595	regulation of cell differentiation	4,51E-07	2,07	-	-	6,61E-09	1,87
GO:0023056	positive regulation of signaling	4,53E-07	1,93	3,41E-09	2,11	1,71E-07	1,89
GO:0034341	response to interferon-gamma	4,53E-08	5,20	2,32E-08	3,43	-	-

GO:0051049	regulation of transport	4,58E-04	1,99	8,58E-05	2,01	-	-
GO:0045091	regulation of retroviral genome replication	4,50E-04	23,50	2,19E-04	30,44	-	-
GO:0032479	regulation of type I interferon production	4,66E-04	19,27	4,76E-04	3,24	4,46E-04	12,35
GO:0070665	positive regulation of leukocyte proliferation	4,72E-06	5,29	5,38E-05	81,99	-	-
GO:0001912	positive regulation of leukocyte mediated cytotoxicity	4,73E-04	153,29	7,54E-06	12,23	-	-
GO:0009719	response to endogenous stimulus	4,79E-05	1,51	-	-	6,35E-04	2,49
GO:0032101	regulation of response to external stimulus	4,85E-11	2,42	3,18E-07	2,33	2,83E-09	2,42
GO:0051607	defense response to virus	4,85E-08	10,51	3,41E-07	5,41	4,02E-05	10,24
GO:0042981	regulation of apoptotic process	5,04E-06	1,47	7,46E-04	1,96	9,57E-06	1,54
GO:0045071	negative regulation of viral genome replication	5,05E-06	11,63	3,91E-04	156,70	2,18E-05	626,80
GO:0048525	negative regulation of viral reproduction	5,05E-06	11,63	3,91E-04	156,70	2,18E-05	626,80
GO:0044419	interspecies interaction between organisms	5,07E-04	2,44	3,98E-05	1,89	-	-
GO:0010627	regulation of intracellular protein kinase cascade	5,16E-05	1,66	1,69E-04	1,82	1,46E-04	1,75
GO:0030334	regulation of cell migration	5,17E-05	2,45	9,94E-05	2,52	1,31E-05	1,97
GO:0001932	regulation of protein phosphorylation	5,19E-04	1,58	2,87E-04	1,70	3,19E-06	1,73
GO:0007223	Wnt receptor signaling pathway, calcium modulating pathway	5,23E-04	13,93	-	-	5,65E-04	6,10
GO:0048522	positive regulation of cellular process	5,25E-07	1,34	3,08E-06	1,52	1,16E-06	1,33
GO:0002831	regulation of response to biotic stimulus	5,27E-05	7,04	9,72E-05	4,24	-	-
GO:0048584	positive regulation of response to stimulus	5,31E-09	1,86	2,57E-09	1,90	1,36E-07	1,68
GO:0002687	positive regulation of leukocyte migration	5,33E-05	3,73	2,91E-04	47,01	-	-
GO:0050921	positive regulation of chemotaxis	5,34E-05	6,00	5,10E-05	34,74	9,60E-04	2,94
GO:0050729	positive regulation of inflammatory response	5,34E-05	6,00	1,99E-04	5,17	-	-
GO:0043067	regulation of programmed cell death	5,41E-06	1,47	9,35E-04	1,94	1,58E-05	1,52
GO:0002376	immune system process	5,51E-14	2,16	8,88E-10	1,93	8,68E-09	1,58
GO:0035456	response to interferon-beta	5,56E-04	21,87	-	-	2,63E-04	28,49
GO:0071357	cellular response to type I interferon	5,50E-19	23,95	2,24E-18	6,43	1,31E-05	3,95
GO:0060337	type I interferon-mediated signaling pathway	5,50E-19	23,95	2,24E-18	6,43	1,31E-05	3,95
GO:0040017	positive regulation of locomotion	5,50E-06	3,17	1,17E-04	14,31	2,43E-05	2,23
GO:0010646	regulation of cell communication	5,61E-06	1,45	2,84E-07	1,67	3,86E-08	1,66
GO:0010942	positive regulation of cell death	5,67E-06	1,68	-	-	5,77E-04	1,70
GO:0009893	positive regulation of metabolic process	5,71E-05	1,38	3,67E-04	1,57	8,87E-04	1,35
GO:0006928	cellular component movement	5,76E-05	2,09	7,02E-04	1,45	-	-
GO:0042127	regulation of cell proliferation	5,86E-10	1,67	5,02E-07	2,32	3,00E-08	1,59
GO:0046427	positive regulation of JAK-STAT cascade	5,96E-04	6,59	8,79E-05	6,21	2,75E-07	4,97
GO:0031349	positive regulation of defense response	6,01E-05	2,08	4,49E-07	3,81	-	-
GO:0051716	cellular response to stimulus	6,02E-11	1,37	1,44E-06	1,40	3,15E-07	1,26
GO:0033273	response to vitamin	6,10E-05	4,05	-	-	4,13E-06	3,80
GO:0043900	regulation of multi-organism process	6,22E-06	6,97	2,18E-04	14,99	-	-
GO:0000902	cell morphogenesis	6,35E-04	2,30	-	-	2,86E-04	2,31
GO:0050688	regulation of defense response to virus	6,46E-06	9,04	4,96E-04	4,55	-	-
GO:0051046	regulation of secretion	6,54E-05	1,78	7,03E-05	2,64	6,26E-04	7,73
GO:0048518	positive regulation of biological process	6,59E-08	1,34	1,63E-06	1,50	1,28E-06	1,34
GO:0040012	regulation of locomotion	6,64E-04	2,13	4,05E-04	2,28	4,17E-05	1,85

GO:0001934	positive regulation of protein phosphorylation	6,68E-06	3,04	1,49E-04	2,66	1,21E-05	2,28
GO:0007166	cell surface receptor signaling pathway	6,73E-11	2,88	3,04E-08	1,69	1,20E-06	1,42
GO:0031343	positive regulation of cell killing	6,82E-04	130,58	2,51E-05	10,42	-	-
GO:0008285	negative regulation of cell proliferation	6,86E-05	1,67	8,89E-04	2,11	3,86E-06	1,75
GO:0035455	response to interferon-alpha	6,90E-05	293,81	6,16E-04	90,40	-	-
GO:0048869	cellular developmental process	7,16E-09	1,49	-	-	1,92E-07	1,54
GO:0031328	positive regulation of cellular biosynthetic process	7,20E-04	1,39	6,64E-04	2,02	-	-
GO:0070663	regulation of leukocyte proliferation	7,43E-05	3,96	1,63E-04	57,33	5,19E-04	2,25
GO:0050865	regulation of cell activation	7,40E-07	1,97	1,56E-05	3,15	1,93E-04	1,97
GO:0032816	positive regulation of natural killer cell activation	7,51E-04	26,71	7,92E-04	6,13	-	-
GO:0045429	positive regulation of nitric oxide biosynthetic process	7,51E-05	7,12	1,86E-04	6,31	-	-
GO:0051239	regulation of multicellular organismal process	7,55E-08	1,47	6,86E-07	1,68	1,91E-12	1,74
GO:0045597	positive regulation of cell differentiation	7,64E-06	1,89	-	-	3,87E-06	2,03
GO:0051249	regulation of lymphocyte activation	7,67E-05	1,87	4,19E-04	4,14	-	-
GO:0032501	multicellular organismal process	7,75E-11	1,41	3,53E-05	1,56	2,87E-06	1,47
GO:0042325	regulation of phosphorylation	7,79E-05	1,65	1,22E-04	1,50	1,44E-05	1,63
GO:0008284	positive regulation of cell proliferation	7,81E-11	2,02	3,70E-07	2,48	1,02E-04	1,66
GO:0071496	cellular response to external stimulus	7,91E-04	2,64	2,63E-05	2,29	1,08E-05	3,26
GO:0010033	response to organic substance	7,95E-13	1,97	5,24E-07	1,91	1,48E-06	1,50
GO:0002685	regulation of leukocyte migration	8,03E-07	3,54	3,07E-05	22,39	2,88E-04	2,99
GO:0006950	response to stress	8,17E-08	1,66	4,88E-06	2,63	2,54E-06	1,45
GO:0034340	response to type I interferon	8,31E-19	23,50	3,43E-19	6,51	1,69E-05	3,88
GO:0009966	regulation of signal transduction	8,30E-09	1,52	9,14E-09	1,49	1,14E-08	1,49
GO:0001910	regulation of leukocyte mediated cytotoxicity	8,48E-04	117,52	5,78E-05	9,38	-	-
GO:0050731	positive regulation of peptidyl-tyrosine phosphorylation	8,52E-04	3,69	9,89E-04	117,52	1,80E-04	2,92
GO:0051240	positive regulation of multicellular organismal process	8,75E-09	2,08	2,25E-09	2,72	4,88E-08	2,11
GO:0006926	virus-infected cell apoptosis	8,86E-04	61,05	-	-	7,90E-04	66,21
GO:0050776	regulation of immune response	8,86E-07	1,77	3,78E-07	2,98	-	-
GO:0001817	regulation of cytokine production	8,96E-06	1,89	9,11E-09	2,83	1,14E-07	2,16
GO:0065007	biological regulation	8,90E-11	1,20	8,80E-07	1,13	6,00E-08	1,14
GO:0019221	cytokine-mediated signaling pathway	9,08E-14	5,93	2,12E-08	2,41	1,96E-04	1,79
GO:0042327	positive regulation of phosphorylation	9,11E-07	3,13	7,30E-06	2,88	9,19E-07	2,38
GO:0045069	regulation of viral genome replication	9,22E-07	12,74	7,35E-06	146,91	6,50E-05	391,75
GO:0003008	system process	9,34E-04	1,49	4,86E-04	2,11	-	-
GO:0006935	chemotaxis	9,50E-06	2,37	1,15E-04	6,98	-	-
GO:0042330	taxis	9,50E-06	2,37	1,15E-04	6,98	-	-
GO:0050671	positive regulation of lymphocyte proliferation	9,64E-05	4,70	9,64E-04	4,84	-	-
GO:0048878	chemical homeostasis	9,72E-04	2,25	-	-	8,28E-05	1,98
GO:0032989	cellular component morphogenesis	9,77E-04	1,70	-	-	1,49E-04	2,03
GO:0051270	regulation of cellular component movement	9,70E-05	2,31	1,66E-05	2,57	2,50E-05	1,88
GO:1900046	regulation of hemostasis	9,92E-05	3,55	-	-	5,75E-04	5,77
GO:0030193	regulation of blood coagulation	9,92E-05	3,55	-	-	5,75E-04	5,77
GO:0022610	biological adhesion	9,95E-05	1,64	4,94E-06	2,32	2,51E-06	2,18
GO:0007155	cell adhesion	9,95E-05	1,64	4,94E-06	2,32	2,51E-06	2,18

GO:0070201	regulation of establishment of protein localization	-	-	8,55E-04	2,73	1,02E-04	3,47
GO:0042993	positive regulation of transcription factor import into nucleus	-	-	1,89E-04	9,74	1,41E-05	15,57
GO:0046824	positive regulation of nucleocytoplasmic transport	-	-	6,77E-05	6,69	1,84E-05	7,90
GO:0042345	regulation of NF-kappaB import into nucleus	-	-	9,65E-05	5,17	2,12E-04	9,83
GO:0042307	positive regulation of protein import into nucleus	-	-	1,20E-05	8,18	3,07E-06	9,66
GO:0051222	positive regulation of protein transport	-	-	1,48E-05	4,55	3,51E-07	6,14
GO:0009608	response to symbiont	-	-	5,44E-05	32,80	3,71E-04	17,33
GO:0009602	detection of symbiont	-	-	5,44E-05	32,80	3,71E-04	17,33
GO:0009597	detection of virus	-	-	5,44E-05	32,80	3,71E-04	17,33
GO:0052564	response to immune response of other organism involved in symbiotic interaction	-	-	6,09E-04	21,15	3,70E-05	59,59
GO:0052572	response to host immune response	-	-	6,09E-04	21,15	3,70E-05	59,59
GO:1900048	positive regulation of hemostasis	-	-	7,54E-04	28,94	3,95E-04	36,60
GO:0030194	positive regulation of blood coagulation	-	-	7,54E-04	28,94	3,95E-04	36,60
GO:0032647	regulation of interferon-alpha production	-	-	5,41E-05	14,91	4,19E-04	32,32
GO:0090316	positive regulation of intracellular protein transport	-	-	1,37E-04	6,13	4,61E-06	8,05
GO:0060341	regulation of cellular localization	-	-	1,30E-05	2,34	5,77E-04	2,44
GO:0042346	positive regulation of NF-kappaB import into nucleus	-	-	5,01E-04	10,56	6,13E-05	16,87
GO:0042306	regulation of protein import into nucleus	-	-	3,08E-04	4,59	6,99E-05	5,42
GO:0034764	positive regulation of transmembrane transport	-	-	3,50E-05	7,21	9,56E-06	8,52
GO:0032388	positive regulation of intracellular transport	-	-	2,84E-04	5,66	9,70E-06	7,43

a) Enrich: Enrichment Value

Table S3: Gene Ontology (GO) terms down-regulated in alternative activated macrophages (M2a) compared to M2a exposed to quercetin-3-O-glucuronide (M2a+Q3GA). The gene expression values of M2a and M2a+Q3GA were normalised to the Resting Macrophages (RM) gene expression values. P-value is calculated based on the mean of the gene expression values for the three points of the time course (6, 12 and 24 hours). Values are missing when P > 1.00E-4.

GO Term	Description	P-value M2a	Enrich ^{a)}	P-value M2a+Q3GA	Enrich ^{a)}
GO:0009607	response to biotic stimulus	1,64E-05	4,29	5,32E-21	4,75
GO:0051707	response to other organism	-	-	1,08E-17	5,48
GO:0071357	cellular response to type I interferon	-	-	1,66E-17	17,43
GO:0034340	response to type I interferon	-	-	2,56E-17	17,11
GO:0009615	response to virus	-	-	1,15E-16	6,66
GO:0034097	response to cytokine stimulus	8,33E-04	9,65	8,71E-16	3,52
GO:0071345	cellular response to cytokine stimulus	9,17E-04	13,61	4,29E-15	7,91
GO:0071294	cellular response to zinc ion	-	-	2,43E-13	108,48
GO:0019221	cytokine-mediated signaling pathway	-	-	3,77E-13	5,42
GO:0006952	defense response	1,84E-08	5,33	5,27E-13	2,04
GO:0006955	immune response	7,58E-08	4,92	5,58E-12	2,89
GO:0032101	regulation of response to external stimulus	1,10E-04	4,84	2,48E-11	2,35
GO:0002376	immune system process	7,13E-06	3,17	3,40E-11	2,31
GO:0009611	response to wounding	7,15E-10	4,19	4,04E-11	2,26
GO:0001817	regulation of cytokine production	-	-	6,10E-11	3,15
GO:0050896	response to stimulus	3,69E-05	1,19	6,21E-11	1,37
GO:0071276	cellular response to cadmium ion	-	-	7,88E-11	92,99
GO:0070887	cellular response to chemical stimulus	4,89E-04	5,51	2,17E-10	1,98
GO:0051704	multi-organism process	-	-	2,17E-10	6,02
GO:0001819	positive regulation of cytokine production	-	-	3,28E-10	4,03
GO:0007165	signal transduction	-	-	8,23E-10	1,32
GO:0006954	inflammatory response	2,65E-11	9,31	1,06E-09	2,45
GO:0010033	response to organic substance	-	-	1,99E-09	2,06
GO:0032501	multicellular organismal process	1,77E-05	1,27	3,24E-09	1,36
GO:0007166	cell surface receptor signaling pathway	-	-	3,36E-09	2,13
GO:0071346	cellular response to interferon-gamma	-	-	4,24E-09	9,24
GO:0032103	positive regulation of response to external stimulus	5,31E-05	8,64	5,07E-09	8,43
GO:0034341	response to interferon-gamma	-	-	5,52E-09	8,25
GO:0042221	response to chemical stimulus	6,22E-05	4,09	7,84E-09	1,77
GO:0051716	cellular response to stimulus	7,22E-06	2,60	9,44E-09	1,41
GO:0002237	response to molecule of bacterial origin	1,42E-05	6,74	1,36E-08	3,23
GO:0051050	positive regulation of transport	4,90E-04	1,73	2,04E-08	2,02
GO:0009605	response to external stimulus	3,42E-07	3,91	5,27E-08	1,85
GO:0045765	regulation of angiogenesis	5,93E-04	7,24	6,38E-08	2,78
GO:0010574	regulation of vascular endothelial growth factor production	2,04E-06	33,60	8,60E-08	12,56
GO:0050727	regulation of inflammatory response	-	-	1,17E-07	2,58

GO:0031349	positive regulation of defense response	-	-	1,56E-07	4,47
GO:0051607	defense response to virus	6,32E-04	3,28	1,69E-07	9,26
GO:0032722	positive regulation of chemokine production	6,51E-05	29,79	2,07E-07	21,70
GO:0050729	positive regulation of inflammatory response	-	-	2,12E-07	3,59
GO:0045926	negative regulation of growth	-	-	2,99E-07	10,13
GO:0050715	positive regulation of cytokine secretion	-	-	4,85E-07	6,53
GO:0031347	regulation of defense response	-	-	5,20E-07	2,98
GO:0032755	positive regulation of interleukin-6 production	1,47E-04	24,83	5,98E-07	13,99
GO:0045087	innate immune response	-	-	6,50E-07	2,30
GO:0032502	developmental process	1,57E-04	1,21	7,54E-07	1,26
GO:0032642	regulation of chemokine production	4,52E-04	19,10	1,96E-06	12,47
GO:0045428	regulation of nitric oxide biosynthetic process	1,24E-04	15,92	7,92E-06	6,19
GO:0032757	positive regulation of interleukin-8 production	5,31E-04	32,86	9,84E-06	24,22
GO:0003013	circulatory system process	5,76E-04	2,72	1,23E-05	2,79
GO:0040011	locomotion	8,56E-06	10,96	3,58E-05	1,48
GO:0006935	chemotaxis	2,77E-07	5,52	4,63E-05	1,64
GO:0042330	taxis	2,77E-07	5,52	4,63E-05	1,64
GO:0042307	positive regulation of protein import into nucleus	8,91E-04	16,19	5,80E-05	9,79
GO:0006950	response to stress	3,38E-04	2,08	6,63E-05	1,60
GO:0007154	cell communication	3,34E-06	7,62	7,55E-05	3,44
GO:0007267	cell-cell signaling	2,20E-05	1,74	8,04E-05	5,60
GO:0042346	positive regulation of NF-kappaB import into nucleus	9,33E-04	27,93	8,71E-05	15,74
GO:0023052	signaling	3,37E-05	1,72	8,95E-05	5,53
GO:0045429	positive regulation of nitric oxide biosynthetic process	2,40E-05	21,60	2,43E-04	9,39
GO:0010635	regulation of mitochondrial fusion	5,60E-04	3538,00	2,81E-04	7051,50
GO:0030595	leukocyte chemotaxis	2,79E-04	7,91	7,92E-04	2,63
GO:0006270	DNA-dependent DNA replication initiation	1,40E-06	15,69	-	-
GO:0022610	biological adhesion	1,97E-06	1,64	-	-
GO:0007155	cell adhesion	1,97E-06	1,64	-	-
GO:0006271	DNA strand elongation involved in DNA replication	3,80E-06	6,44	-	-
GO:0030593	neutrophil chemotaxis	3,82E-06	19,11	-	-
GO:0022616	DNA strand elongation	7,79E-06	6,05	-	-
GO:0006260	DNA replication	3,15E-05	2,40	-	-

a) Enrich: Enrichment Value

Table S4: Gene Ontology (GO) terms down-regulated in alternative activated macrophages (M2a) compared to M2a exposed to quercetin-3-O-glucuronide (M2a+Q3GA). The gene expression values of M2a and M2a+Q3GA were normalised to the RM gene expression values. P-value is calculated based on the differences of gene expression value between M2a and M2a+Q3GA for the three point of the time course (6, 12 and 24 hours). Values are missing when P > 1.00E-4.

GO Term	Description	P-value 6h	Enrich 6h ^{a)}	P-value 12h	Enrich 12h ^{a)}	P-value 24h	Enrich 24h ^{a)}
GO:0071357	cellular response to type I interferon	4,47E-20	46,38	3,21E-14	9,02	-	-
GO:0060337	type I interferon-mediated signaling pathway	4,47E-20	46,38	3,21E-14	9,02	-	-
GO:0034340	response to type I interferon	6,28E-20	45,52	5,75E-14	8,85	-	-
GO:0009615	response to virus	7,61E-18	12,75	3,12E-10	2,72	-	-
GO:0071345	cellular response to cytokine stimulus	3,52E-15	5,96	6,87E-10	4,18	-	-
GO:0009607	response to biotic stimulus	1,65E-14	6,08	1,53E-08	1,95	-	-
GO:0051707	response to other organism	5,87E-14	8,88	4,53E-09	2,25	-	-
GO:0019221	cytokine-mediated signaling pathway	1,18E-13	14,24	2,06E-10	5,09	-	-
GO:0034097	response to cytokine stimulus	1,76E-13	5,85	2,79E-09	3,83	-	-
GO:0071294	cellular response to zinc ion	5,77E-10	37,06	3,64E-07	14,51	4,69E-11	52,95
GO:0034341	response to interferon-gamma	1,58E-09	11,49	2,42E-06	3,11	-	-
GO:0071346	cellular response to interferon-gamma	1,58E-09	19,18	5,16E-06	3,25	-	-
GO:0035455	response to interferon-alpha	3,90E-09	223,84	7,92E-05	269,92	-	-
GO:0035457	cellular response to interferon-alpha	2,11E-07	271,7	2,51E-05	404,88	-	-
GO:0010043	response to zinc ion	1,39E-06	12,84	1,17E-04	6,87	5,23E-09	19,76
GO:0048869	cellular developmental process	2,05E-06	1,4	2,35E-04	1,32	6,30E-06	1,49
GO:0071276	cellular response to cadmium ion	3,36E-06	26,47	1,19E-05	12,44	6,01E-09	45,38
GO:0032101	regulation of response to external stimulus	4,68E-06	2,11	2,79E-04	4,35	2,74E-05	2,48
GO:0051239	regulation of multicellular organismal process	6,92E-06	1,4	6,10E-06	1,39	-	-
GO:0007154	cell communication	6,98E-06	1,66	2,27E-05	1,83	1,19E-04	1,64
GO:2000242	negative regulation of reproductive process	1,52E-05	11,77	8,43E-05	3,61	-	-
GO:0002685	regulation of leukocyte migration	1,55E-05	3,21	2,44E-06	3,45	-	-
GO:0009605	response to external stimulus	1,80E-05	1,49	1,56E-04	1,45	-	-
GO:0032502	developmental process	2,76E-05	1,23	1,11E-05	1,24	2,46E-06	1,31
GO:0023052	signaling	3,53E-05	1,79	1,76E-05	1,99	8,13E-05	1,59
GO:0050795	regulation of behavior	4,47E-05	2,48	4,51E-05	2,61	-	-
GO:0007267	cell-cell signaling	4,51E-05	1,79	1,14E-05	2,02	5,00E-05	1,61
GO:0030154	cell differentiation	6,53E-05	1,44	9,16E-04	1,34	4,53E-04	1,46
GO:0040011	locomotion	7,11E-05	1,47	4,96E-05	1,59	9,38E-05	1,70
GO:0045926	negative regulation of growth	1,57E-04	4,15	2,14E-04	2,71	1,15E-08	9,07
GO:0072503	cellular divalent inorganic cation homeostasis	9,71E-04	3,23	1,46E-04	2,06	3,03E-04	4,61

a) Enrich: Enrichment Value