GOATOOLS: A Python library for Gene Ontology analysesSupplemental Material

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Supplemental Tables

Immune Summary in the Consistent Increase Gjoneska cluster with DAVID version 6.7 released Jan 2010

dent	info	D	GO GO	Description GOATOOL DAVID 6.7			/125	/113
1796	6.4	1	GO:0002376	immune system process	5.28e-07	7.96e-20	64	95
1128	6.6	3	GO:0002570 GO:0002682	regulation of immune system process * 3.28e-07 regulation of immune system process		3.03e-08	0	41
835	6.9	2	GO:0002082 GO:0006955			2.12e-17	18	62
596	7.2	4	GO:0050776	regulation of immune response	*	1.19e-07	0	29
523	7.0	4	GO:0002684	1		7.65e-07	0	29
502	7.6	2	GO:0002084 GO:0002252			6.12e-05	0	29
495	12.2	4	GO:0002232 GO:0002520	immune system development	*	1.20e-02	0	28
464	7.4	4	GO:0002320 GO:0001817	regulation of cytokine production	7.84e-04	1.71e-03	8	19
443	7.4	3	GO:0001817 GO:0045321	leukocyte activation	/.0 1 C-0 1	1.71c-03 1.02e-02	0	23
352	8.5	4	GO:0048534	hematopoietic or lymphoid organ devel.	*	1.02c-02 1.10e-02	0	27
334	7.5	5	GO:0048334 GO:0050778	+ reg. of immune response	*	2.47e-07	0	24
333	8.0	4	GO:0030778 GO:0002697	regulation of immune effector process	*	2.47c-07 2.05e-03	0	14
333	9.1	5	GO:0002097 GO:0030097	hemopoiesis	*	3.44e-02	0	24
288	7.5	4	GO:0030097 GO:0045087	innate immune response	3.50e-07	4.73e-02	51	13
256	9.3	3	GO:0043087 GO:0002443	leukocyte mediated immunity	3.300-07	2.28e-03	0	14
247	7.4	5	GO:0002443 GO:0002694	regulation of leukocyte activation		1.33e-02	0	16
226	8.5	3	GO:0002094 GO:0002250	adaptive immune response	4.36e-03	9.48e-03	13	13
211	9.4	4	GO:0002230 GO:0002460	adaptive immune response adaptive immune rsp. based on somatic re-	*		0	13
211	7.4	4	00.0002400	combin. of immune rx. built w/Ig domains		9.48e-03	U	13
205	7.6	6	GO:0051249	regulation of lymphocyte activation		4.28e-02	0	14
189	7.9	4	GO:0031249 GO:0006954		5.09e-07	7.58e-07	41	27
	9.6	4	GO:0000934 GO:0002449	inflammatory response	3.096-07	3.42e-02	0	11
183 179	7.9		GO:0002449 GO:0002253	lymphocyte mediated immunity	-		0	13
		6 5		activation of immune response	*	2.90e-03	0	13
175	8.6 7.9	5	GO:0002703 GO:0001819	regulation of leukocyte mediated immunity	*	5.02e-04	0	15
162 159	8.1	5	GO:0001819 GO:0002764	+ reg. of cytokine production immune response-regulating signaling pw.	1	7.36e-05	0	10
149	8.9	3	GO:0002764 GO:0002263	cell activation in immune response		8.90e-03 1.74e-02	0	8
149	8.8	5	GO:0002203 GO:0002819	regulation of adaptive immune response	 *	6.60e-05	0	13
144	8.9	4	GO:0002819 GO:0002366	leukocyte activation in immune response		1.74e-02	0	8
144	8.1	7	GO:0002300 GO:0002757	immune rsp-activating signal transduction		8.90e-03	0	10
136	8.8	6	GO:0002737 GO:0002822	reg. of adaptive immune rsp. based on	*	6.60e-05	0	13
130	0.0	U	GO.0002822	somatic recombin. of immune rx. built		0.006-03	U	13
				w/Ig superfamily domains				
134	8.2	7	GO:0050863	regulation of T cell activation		3.21e-02	0	12
128	9.7	2	GO:0030803 GO:0019882	antigen processing and presentation	*	2.61e-08	0	20
125	8.8	6	GO:0002706	reg. of lymphocyte mediated immunity	*	8.72e-04	0	12
120	8.5	5	GO:0002700 GO:0002699	positive reg. of immune effector process	*	8.72e-04 8.36e-04	0	11
68	9.2	4	GO:0002099 GO:0002274	myeloid leukocyte activation		1.51e-02	0	9
61	9.2	6	GO:0002274 GO:0002705	pos. reg. of leukocyte mediated immunity	*	6.13e-04	0	10
58	10.3	3	GO:0002703 GO:0048002	antigen processing/present of peptide Ag	*	4.17e-06	0	14
51	9.2	6	GO:0002821	pos. reg. of adaptive immune response	*	4.17c-00 4.03e-04	0	10
48	9.2	7	GO:0002824	+reg. of adaptive immune response	*	4.03e-04 4.03e-04	0	10
70). <u>~</u>	′	30.0002024	somatic recombin. of immune rx. built		4.050-04		10
				w/Ig superfamily domains				
44	9.2	7	GO:0002708	+reg. of lymphocyte mediated immunity	*	6.13e-04	0	10
40	8.3	6	GO:0002768	immune rspreg. cell surface rx. sig. pw.		4.18e-02	0	8
37	9.7	7	GO:0002708 GO:0002709	regulation of T cell mediated immunity	*	2.94e-03	0	8
28	8.3	8	GO:0002709 GO:0002429	immune rspactivate cell surface rx sig. pw.		4.18e-02	0	8
17	11.1	4	GO:0002429 GO:0002474	a.p.p. of peptide antigen via MHC class I	*	4.95e-04	0	9
16	9.9	5	GO:0002474 GO:0001912	+reg. of leukocyte mediated cytotoxicity	*	2.23e-02	0	7
10	7.7	J	30.0001712	1105. Of reakony to inequated cytotoxicity		2.230-02	1	'

13	10.2	8	GO:0002711	pos. reg. of T cell mediated immunity	*	9.07e-04	0	8
11	11.8	4	GO:0032611	interleukin-1 β production	2.06e-03)3		0
10	10.3	6	GO:0030316	osteoclast differentiation	3.51e-02		8	0
9	10.5	3	GO:0019884	a.p.p. of exogenous antigen	4.39e-02	6.77e-05	3	12
9	10.6	8	GO:0001914	regulation of T cell mediated cytotoxicity	*	6.27e-03	0	7
8	8.9	6	GO:0032680	regulation of TNF production	*	6.27e-03	0	8
8	9.1	5	GO:0034341	response to interferon- γ	1.56e-02		6	0
8	10.0	5	GO:0032653	regulation of interleukin-10 production		3.53e-02	0	4
7	9.0	5	GO:0032675	regulation of interleukin-6 production	*	4.93e-02	0	7
7	10.8	4	GO:0002478	a.p.p. of exogenous peptide antigen	*	9.06e-04	0	9
3	10.8	9	GO:0001916	+ reg. of cytotoxicity via T cell	5.40e-03	3.16e-03	6	7
2	9.4	6	GO:0032755	+ reg. of interleukin-6 production	3.81e-04	7.26e-03	12	7
2	9.4	7	GO:0032760	+ reg. of TNF production	7.91e-05	4.80e-03	14	7
2	9.6	6	GO:0032729	+ reg. of interferon- γ production	4.00e-02		7	0
2	11.2	9	GO:0002726	+ reg. of T cell cytokine production	3.87e-02		4	0
2	11.9	5	GO:0042590	a.p.p. of peptide antigen w/MHC class I	1.67e-02		4	0
1	11.3	9	GO:0045651	+ reg. of macrophage differentiation	3.44e-02		5	0
0	10.6	11	GO:0050718	+ reg. of interleukin-1 β secretion	1.94e-04		9	0
0	11.2	5	GO:0019886	a.p.p. of peptide antigen w/MHC class II	4.74e-02		5	0
0	12.8	7	GO:0002485	a.p.p. of endogenous peptide antigen	4.39e-02		3	0
				w/MHC-I w/ER pathway, TAP-dependent				

Table 1. GOATOOLS compared to the older DAVID6.7 for the Gjoneska *Consistent Increase* cluster for immune GO terms. GOATOOLS finds more specific GO terms than the older version of DAVID. Specific GO terms are at the bottom of the table. Broad GO terms are at the top of the table. An asterisk ("*") in the GOATOOL P-value column means that although the GO term was not found statistically significant by GOATOOLS, a more specific descendant term was found statistically significant by GOATOOLS. The numbers in the dent column are descendant counts as counted using both the *is_a* attribute and relationships like *part_of* and *regulates*. The info column contains *information content* using the MGI annotations. The numbers under the column "/125" are counts of Gjoneska genes associated with GO terms found significant by GOATOOLS. The numbers under the "/113" column are counts of Gjoneska genes associated with GO terms found significant by DAVID6.7. The total amount of genes related to significant immune GO terms in the Gjoneska *Consistent Increase* is 125 for GOATOOLS and 113 for DAVID6.7.

Immune Summary in the Consistent Increase Gjoneska cluster with DAVID version 6.8 released Oct 2016

dent	info	D	GO	Description	GOATOOL	DAVID6.8	/125	/119
1796	6.4	1	GO:0002376	immune system process	5.28e-07	2.40e-18	64	61
835	6.9	2	GO:0006955	immune response	7.84e-04	4.75e-04	18	21
464	7.4	4	GO:0001817	regulation of cytokine production 7.84e-04 *		8	0	
288	7.5	4	GO:0045087	innate immune response	3.50e-07	2.83e-12	51	49
226	8.5	3	GO:0002250	adaptive immune response 4.36e-03 3.90e-03		13	14	
189	7.9	4	GO:0006954	inflammatory response	5.09e-07	2.95e-09	41	39
17	11.1	4	GO:0002474	a.p.p. of peptide antigen via MHC class I	*	5.16e-04	0	9
11	11.8	4	GO:0032611	interleukin-1 β production	2.06e-03	2.20e-02	5	5
10	10.3	6	GO:0030316	osteoclast differentiation	3.51e-02		8	0
9	10.5	3	GO:0019884	a.p.p. of exogenous antigen	4.39e-02		3	0
8	9.1	5	GO:0034341	response to interferon- γ	1.56e-02	2.01e-02	6	7
4	9.3	6	GO:0071346	cellular response to interferon- γ		1.81e-03	0	11
3	10.8	9	GO:0001916	+ reg. of cytotoxicity via T cell	5.40e-03	3.70e-03	6	7
2	9.4	6	GO:0032755	+ reg. of interleukin-6 production	3.81e-04	6.86e-04	12	12
2	9.4	7	GO:0032760	+ reg. of TNF production	7.91e-05	1.73e-04	14	14
2	9.6	6	GO:0032729	+ reg. of interferon- γ production	4.00e-02		7	0
2	11.2	9	GO:0002726	+ reg. of T cell cytokine production	3.87e-02		4	0
2	11.9	5	GO:0042590	a.p.p. of peptide antigen w/MHC class I	1.67e-02		4	0
1	11.3	9	GO:0045651	+ reg. of macrophage differentiation	3.44e-02		5	0
0	10.6	11	GO:0050718	+ reg. of interleukin-1 β secretion	1.94e-04	9.09e-03	9	7
0	11.2	5	GO:0019886	a.p.p. of peptide antigen w/MHC class II	4.74e-02		5	0
0	12.8	7	GO:0002485	a.p.p. of endogenous peptide antigen	4.39e-02		3	0
				w/MHC class I w/ER pathway, TAP-				
				dependent				

Table 2. GOATOOLS compared to the current DAVID6.8 for the Gjoneska *Consistent Increase* cluster for immune GO terms. GOATOOLS finds more specific GO terms than DAVID6.8. Specific GO terms are at the bottom of the table. Broad GO terms are at the top of the table. An asterisk ("*") in the GOATOOL or DAVID6.8 P-value columns means that although the GO term was not found statistically significant, a more specific descendant term was found statistically significant. The numbers in the dcnt column are descendant counts as counted using both the *is_a* attribute and relationships like *part_of* and *regulates*. The info column contains *information content* using the MGI annotations. The numbers under the column "/125" are counts of Gjoneska genes associated with GO terms found significant by GOATOOLS. The numbers under the "/119" column are counts of Gjoneska genes associated with GO terms found significant by DAVID6.8. The total amount of genes related to significant immune GO terms in the Gjoneska *Consistent Increase* is 125 for GOATOOLS and 119 for DAVID6.8

Immune Summary in the Consistent Increase Gjoneska cluster with GOstats from Sep 2016

1796 6.4	dent	info	D	GO	Description Description	GOATOOL	GOstats	/125	/212
835 6.9 2 GO:0006955 immune response 7.84e-04 2.49e-02 18 446 7.4 GO:0001817 regulation of cytokine production 7.84e-04 8.84e-06 0 448 7.8 3 GO:0045321 leukocyte activation 3.50e-07 3.15e-08 51 247 7.4 5 GO:0002694 clustory response 3.50e-07 3.26e-06 51 3.86e-02 0 adaptive immune response 4.36e-03 5.68e-05 13 3.87e-02 0 3.60e-007 3.20e-06 41 3.88e-02 0 adaptive immune response 4.36e-03 5.68e-05 13 3.89e-07 5 GO:0002253 inflammatory response 7.9e-07 3.20e-06 41 3.89e-07 5 GO:0002263 clacivation in immune response 8.8 3.60e-03 0 3.89e-07 5 GO:0002263 clacivation of immune response 8.8 3.60e-03 0 3.89e-07 2 GO:000264 decivation of immune response 8.8 3.60e-03 0 3.89e-07 3.20e-06 41 41 41 41 41 41 41 4									0
495 12.2 4 GO:0002520 immune system development * 1.84e-06 0 0 464 7.4 4 GO:0001817 regulation of cytokine production 7.84e-04 * 8 8 443 7.8 3 GO:0045321 leukocyte activation 4.68e-03 0 3.50e-07 3.15e-08 51 247 7.4 5 GO:0002694 regulation of leukocyte activation 3.86e-02 0 3.86e-02 0 3.86e-02 0 3.86e-02 0 3.86e-02 0 3.86e-02 0 3.86e-03 3.88e-03 3.					* *		2.49e-02		126
464 7.4 4 GO:0001817 regulation of cytokine production 7.84e-04 * 8					-				75
443 7.8 3 GO:0045321 leukocyte activation 3.50e-07 3.15e-08 51	1 1					7 84e-04		1	0
288 7.5 4 GO:0045087 innate immune response 3.50e-07 3.15e-08 51 247 7.4 5 GO:0002594 regulation of leukocyte activation 3.86e-02 0 226 8.5 3 GO:0002253 adaptive immune response 4.36e-03 5.68e-05 13 189 7.9 4 GO:0002253 activation of immune response 5.09e-07 3.20e-06 41 179 7.9 6 GO:0002764 immune response 1.14e-03 0 159 8.1 5 GO:0002764 immune response 2.25e-03 0 128 9.7 2 GO:001982 cell activation in immune response 2.25e-03 0 82 10.9 4 GO:0002844 myeloid leukocyte mediated immunity 3.71e-02 0 82 10.9 4 GO:0007663 regulation of leukocyte mediated immunity 3.24e-02 0 48 9.2 7 GO:0007663 regulation of leukocyte mediated immunity 1.58e-0						7.046 04	4 68e-03		72
247 7.4 5 GO:0002250 adaptive immune response 4.36e-03 5.86e-02 0					•	3.50e-07			72
226 8.5 3 GO:0002250 adaptive immune response 4.36e-03 5.68e-05 13 189 7.9 4 GO:0006954 inflammatory response 5.09e-07 3.20e-06 41 41 41 41 41 41 41 4						3.300 07			43
189 7.9 4 GO:0006954 inflammatory response 5.09e-07 3.20e-06 41 179 7.9 6 GO:0002253 activation of immune response 1.14e-03 0 0 1.14e-03 0 1.14e-03	I I					4 36e-03			45
179 7.9 6 GO:0002253 activation of immune response 1.14e-03 0 166 7.9 5 GO:1903706 regulation of hemopoiesis * 3.60e-03 0 159 8.1 5 GO:0002764 immune respregulating signaling pathway 1.16e-04 0 149 8.9 3 GO:0002842 cell activation in immune response 2.25e-03 0 128 9.7 2 GO:0002842 resplaintion of leukocyte mediated immunity 3.71e-02 0 76 8.7 6 GO:0002682 regulation of leukocyte mediated immunity 3.71e-02 0 75 10.6 5 GO:0070663 regulation of leukocyte proliferation 2.79e-02 0 48 9.2 7 GO:0002824 reg. of somatic recomb. of Ig immune rx. * 1.58e-06 0 447 9.6 4 GO:0002708 reg. of leukocyte mediated cytotoxicity * 1.58e-06 0 41 8.8 7 GO:0002010 reg. of leuk					-				60
166 7.9 5 GO:1903706 regulation of hemopoiesis * 3.60e-03 0 159 8.1 5 GO:0002764 immune rsp-regulating signaling pathway 1.16e-04 0 149 8.9 3 GO:0002263 cell activation in immune response 2.25e-03 0 128 9.7 2 GO:0002444 3.86e-02 0 76 8.7 6 GO:0002788 antigen processing and presentation * 3.86e-02 0 75 10.6 5 GO:0071887 leukocyte mediated immunity 3.71e-02 0 48 9.2 7 GO:000788 regulation of leukocyte proliferation 2.79e-02 0 48 9.2 7 GO:0002708 reg. of leukocyte proliferation 2.79e-02 0 44 9.2 7 GO:0002708 reg. of leukocyte mediated cytotoxicity * 1.16e-02 0 41 8.8 7 GO:1902107 reg. of leukocyte mediated immunity * 1.84e-06			- 1			3.050 07			35
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149 8.9 3 GO:0002263 cell activation in immune response 2.25e-03 0 128 9.7 2 GO:0019882 antigen processing and presentation * 3.86e-02 0 82 10.9 4 GO:0002444 myeloid leukocyte mediated immunity 3.71e-02 0 76 8.7 6 GO:0002695 negative regulation of leukocyte activation 4.19e-02 0 75 10.6 5 GO:0071887 leukocyte apoptotic process 3.24e-02 0 75 10.6 5 GO:0070663 regulation of leukocyte proliferation 2.79e-02 0 48 9.2 7 GO:0002824 +reg. of somatic recomb. of Ig immune rx. * 1.58e-06 0 47 9.6 4 GO:0001910 reg. of leukocyte mediated cytotoxicity * 1.16e-02 0 44 9.2 7 GO:0002708 +reg. of lymphocyte mediated cytotoxicity * 1.16e-02 0 41 8.8 7 GO:1902107 +reg. of leukocyte differentiation * 9.69e-05 0 38 9.9 9 GO:2000514 regulation of CD4+, α-β T cell activation * 5.73e-03 0 37 9.7 7 GO:0002709 regulation of T cell mediated immunity * 5.68e-05 0 28 8.3 8 GO:0002429 immune rspactiv. cell surface rx. sig. pw. 1.69e-02 0 26 8.9 5 GO:1903555 reg. of TNF superfamily cytokine prod. * 2.55e-04 0 17 11.1 4 GO:0002474 a.p.p. of peptide antigen via MHC class I * 7.88e-04 0 15 11.4 3 GO:001361 a.p.p. of endogenous antigen * 2.25e-03 0 10 10.3 6 GO:003361 osteoclast differentiation 3.51e-02 8 8 9.1 5 GO:0034341 response to interferon-γ 1.56e-02 * 6 10 10.3 6 GO:0034341 response to interferon-γ 1.56e-02 * 6 10 10.3 6 GO:001346 a.p.p. of endoge peptide antigen via MHC-1 * 5.14e-03 0 10 10.3 6 GO:003760 regulation of interleukin-1 sceretion * 2.25e-03 0 10 10 10 10 10 10 1	, ,								29
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76 8.7 6 GO:0002695 negative regulation of leukocyte activation 4.19e-02 0 75 10.6 5 GO:0071887 leukocyte apoptotic process 3.24e-02 0 56 8.4 5 GO:0070663 regulation of leukocyte proliferation 2.79e-02 0 48 9.2 7 GO:0002824 +reg. of somatic recomb. of Ig immune rx. * 1.58e-06 0 47 9.6 4 GO:0002708 +reg. of leukocyte mediated cytotoxicity * 1.16e-02 0 44 9.2 7 GO:0002708 +reg. of lymphocyte mediated immunity * 1.84e-06 0 41 8.8 7 GO:1902107 +reg. of leukocyte differentiation * 9.69e-05 0 38 9.9 9 GO:2000514 regulation of CD4+, α-β T cell activation 5.73e-03 0 37 9.7 7 GO:0002709 regulation of T cell mediated immunity * 5.68e-05 0 28 8.3 8 <t< td=""><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td></td><td>11</td></t<>									11
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Table 3. GOATOOLS compared to GOstats. Specific GO terms found by both GOATOOLS and GOstats had similar number of associated genes. Broad GO terms found by both showed GOstats was associated with more genes than GOATOOLS, indicating that the original annotations were augmented by propagating counts. See captions in S1 or S2 for table column descriptions.

Method	Category	GOATOOLS	DAV6.8	GD	G	D	Gjoneska Cluster
fdr_bh	GOTERM_BP_DIRECT	124	100	100	24	0	Transient Inc.
fdr_bh	GOTERM_BP_DIRECT	48	29	29	19	0	Consistent Inc.
fdr_bh	GOTERM_BP_DIRECT	135	53	53	82	0	Late Inc.
fdr_bh	GOTERM_BP_DIRECT	21	14	14	7	0	Consistent Dec.
fdr_bh	GOTERM_BP_DIRECT	69	54	54	15	0	Late Dec.
fdr_bh	GOTERM_BP_ALL	598	399	399	199	0	Transient Inc.
fdr_bh	GOTERM_BP_ALL	515	334	334	181	0	Consistent Inc.
fdr_bh	GOTERM_BP_ALL	1274	760	758	516	2	Late Inc.
fdr_bh	GOTERM_BP_ALL	215	178	167	48	11	Consistent Dec.
fdr_bh	GOTERM_BP_ALL	560	449	448	112	1	Late Dec.
bonferroni	GOTERM_BP_DIRECT	67	44	44	23	0	Transient Inc.
bonferroni	GOTERM_BP_DIRECT	25	16	16	9	0	Consistent Inc.
bonferroni	GOTERM_BP_DIRECT	29	14	14	15	0	Late Inc.
bonferroni	GOTERM_BP_DIRECT	5	5	5	0	0	Consistent Dec.
bonferroni	GOTERM_BP_DIRECT	31	22	22	9	0	Late Dec.
bonferroni	GOTERM_BP_ALL	270	227	227	43	0	Transient Inc.
bonferroni	GOTERM_BP_ALL	169	121	121	48	0	Consistent Inc.
bonferroni	GOTERM_BP_ALL	403	268	267	136	1	Late Inc.
bonferroni	GOTERM_BP_ALL	114	103	99	15	4	Consistent Dec.
bonferroni	GOTERM_BP_ALL	252	216	216	36	0	Late Dec.

Table 4. GOATOOLS found more statistically significant GO terms than found by DAVID6.8 when using the same annotations. The annotations used in the GOATOOLS GOEAs shown here were downloaded from DAVID6.8. GOATOOLS ran *Fisher's exact test* and both the *Bonferroni* and *Benjamini-Hochberg* multiple test corrections. Annotation sets downloaded from DAVID6.8 include GOTERM_BP_DIRECT and GOTERM_BP_ALL. GOTERM_BP_DIRECT is new in DAVID6.8 and provides GO mappings directly annotated by the source database. GOTERM_BP_ALL augments the original annotations by propagating parent GO terms up the hierarchy. GOATOOLS' Benjamini-Hochberg scores are compared against DAVID6.8's Benjamini scores. GOATOOLS' Bonferroni scores are compared against DAVID6.8's Bonferroni scores. The number of GO terms found statistically enriched (alpha=0.05) for GOATOOLS and DAVID6.8 is under column headers *GOATOOLS* and *DAV6.8*. The number of GO terms found enriched by both GOATOOLS and DAVID6.8 is listed in the *GD* column. The number of GO terms found only by GOATOOLS is listed in the *G* column. The number of GO terms found only by DAVID6.8 is listed in the *D* column. The last column contains Gjoneska clusters of genes found up-regulated (Inc. for Increase) or down-regulated (Dec. for Decrease) across three different time periods (Transient, Consistent, or Late).

Supplemental Figures

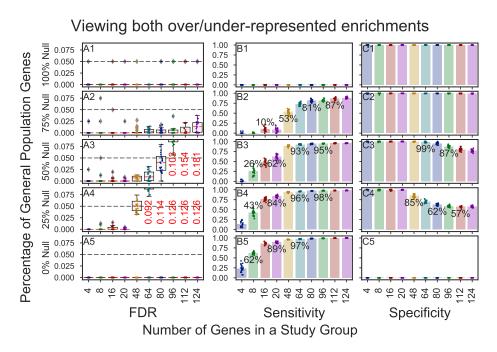


Figure 1. The first GOATOOLS GOEA simulations fail in panels A3 and A4 with FDR values exceeding the alpha of 0.05 set by the researcher. The values of failing FDRs are shown using red text. The source of the failures were false positives for GO terms annotated with large numbers of gene products. For mouse annotations in the *biological_process* branch, GO terms annotated with 1,000 or more genes were the source of failures.

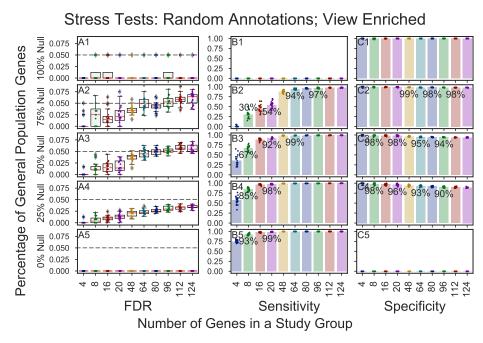


Figure 2. GOATOOLS GOEAs stress tests with randomly shuffled associations nearly pass if only enriched GO terms are viewed. The associations are randomly shuffled while still maintaining the distribution number of GO terms per gene. The failing FDRs (above 0.05) are seen in panels A2 and A3 for gene groups having 96, 112, or 124 genes.

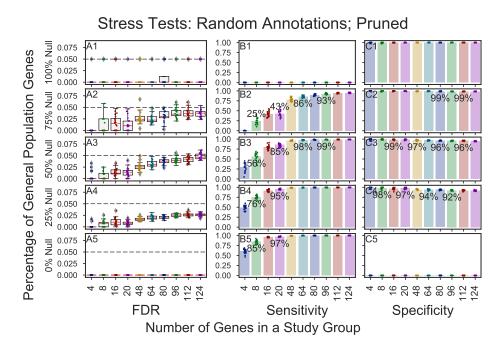


Figure 3. GOATOOLS GOEAs stress tests with randomly shuffled associations pass for all cases if only 30 out of over 17k+ GO terms associated with more than 1000 genes are removed. The median number of genes per GO term in the mouse associations is 3 genes/GO. Genes per GO term ranges from 1 gene to 7k genes per GO term. (mean=16 genes/GO, SD=128).

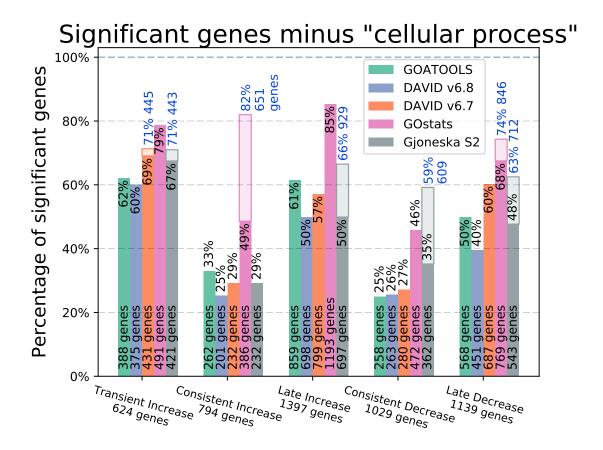


Figure 4. Removing just one broad GO term can dramatically reduce the percentages of genes associated with statistically significant GO terms. The GOEA analyses from four different tools plus the Gjoneska DAVID6.7 GOEA results stored in Gjoneska's Supplemental Table 2 found significant GO IDs for five of the six Gjoneska gene clusters using the Gjoneska population background of 13,838 genes. The x-axis shows the five Gjoneska clusters and the total count of genes found to be up or down regulated in the Gjoneska experiments. The solid bars and their black text show the percentage and number of significant genes in the GOEA analyses if *cellular process* is excluded. The faded bars above the solid bars and the associated blue text show the percentage and number of significant genes in the original analyses if *cellular process* is included. The difference in the solid and faded bars shows the affect of removing just one extremely broad GO term, *cellular process*. The color of each bar represents a GOEA tool as specified in the legend. The height of each bar is the percentage of genes in each cluster that are found to be associated with significant GO IDs. It may be desirable to remove GO terms from GEOA analyses that are both broad and are associated with large numbers of genes.