Supporting Online Materials for

Molecular Network Analysis of Endometriosis Reveals a Novel Role for c-Jun Regulated Macrophage Activation

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Supplemental Materials and Methods

Sample Size Calculations

Sample size estimates were determined using previously reported effect sizes from case-control studies investigating peritoneal fluid cytokine associations with endometriosis. Twenty publications in which parametric statistical findings were reported indicated a broad range of effect sizes achieving significance ($P<0.05$). Shown in Fig. S1, published effect sizes - reported as Standardized Mean Differences (SMD) following log-normalization – ranged between 0.54-4.32 with a median of 0.83. Statistical power for two-tailed Mann-Whitney U-tests tests of association between cytokine concentrations and clinical variables was calculated using G*Power3. Maintaining a 2:1 case:control allocation ratio, approximately 60 samples are required to obtain 0.8 power for moderate effect sizes corresponding to SMD = 0.8.

Gene Set Enrichment Analysis

Gene set enrichment analysis was performed as originally described (Subramanian 2005) using gene profiles derived from the Immune Response in silico (IRIS) expression compendia and Human Immune Cell Transcriptome (GEO Accession GSE22886 and GSE3982, respectively) (Abbas 2005, Jeffrey 2006).

For all analyses, 22,283 U133A probe sets were first mapped to 14,339 unique genes and expressed sequence tags by taking the maximum intensity value across all probes. Expression values for all genes were then median-centered across all profiles in the compendia, and enrichment scores for each profile calculated using a weighting exponent of one. Finally, empirical *P* values for each enrichment score were determined by generating null distributions of scores from 1000 random cytokine signatures of equivalent size selected from the 47 detected cytokines or 79 corresponding receptors.

Pair-wise Enrichment and Reconstruction of Hierarchical Immune Cell Networks

To quantify the degree to which a set of differentially regulated cytokines contribute to specific routes of intercellular communication, we introduce a pair-wise enrichment statistic that captures the coordinate expression of signature cytokines by secreting cell populations and their cognate receptors by responding cell populations. Specifically, we define the pair-wise enrichment score, ES_{ij} between secreting population *i* and responding population *j* as a two-dimensional generalization of the Kolmogorov-Smirnov statistic (Ni 2012):

$$ES_{ij} = \max |F(x_i,y_j) - G(x_0,y_0)|$$

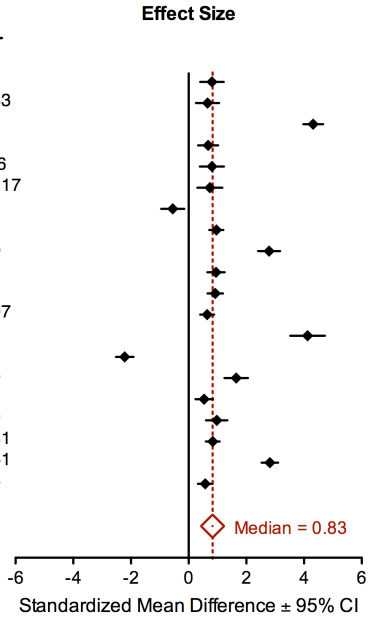
where $F(x_i,y_j)$ is the two-dimensional empirical cumulative distribution function (ECDF) for signature cytokine and receptor expression levels, x_j and y_j, respectively, and $G(x_0,y_0)$ is the reference ECDF for all extracellular gene products and their receptors across all lineages. The reference distribution may be constructed explicitly or approximated; here we use the median cytokine and receptor expression levels of the forty-seven assayed proteins across all cell lineages to approximate $G(x_0,y_0)$.

For *n* distinct cell lineages, the 2D-KS enrichment score ES_{ij} is calculated over all n^2 possible pairwise combinations of secreting and responding populations. Null distributions of ES_{ij} for

each n^2 interactions are similarly constructed from randomly generated cytokine/receptor signatures to obtain the corresponding significance levels. Finally, we rearrange the edge-directed network of significant (P<0.05) interactions according to decreasing out-degree to evaluate the hierarchy of cell-cell interactions.

a

Study			Controls			Endometriosis		
Year	Author	Analyte	N	Mean	SD	N	Mean	SD
1994	Fukaya	M-CSF	17	1352	316	14	1816	449
1994	Oosterlynck	TGFb	10	3.6	4.43	26	11.44	16.83
1996	Arici	IL-8	28	4.8	2.65	21	262	204
1996	McLaren	VEGF	19	13.25	7.2	24	24.05	15
1996	Punnonen	IL-6	12	133	132	15	797	1576
1996	Punnonen	IL-10	12	128	72.75	15	241	147.17
1997	McLaren	IL-13	16	115	30	16	95	9.8
1998	Mazzeo	IL-12p40	40	32.9	34.2	33	59.1	9.8
1998	Iwabe	IL-8	16	33.2	12.7	24	131.4	40.6
2002	Khan	HGF	20	655.4	193	30	1199.3	545
2003	Arici	IL-15	18	2.1	0.3	55	2.7	0.5
2003	Arici	IL-18	18	59.4	8.49	38	91.1	40.07
2003	Mueller	Ena78	9	2	1.77	18	46	16
2004	Gallinelli	IL-13	20	119.8	10.1	43	89.5	7.9
2004	Mahutte	MIF	16	3	2.80	38	10.8	5.55
2004	Oku	IL-18	19	260.5	244	39	592.57	676
2009	Dziunycz	Ghrelin	20	1.74	1.25	46	3.05	1.19
2009	Dziunycz	IL-6	20	21.27	8.98	46	64.96	60.31
2009	Fairbanks	IL-12	33	29.2	10.21	72	82.37	16.61
2011	Andreoli	IL-23	40	9.96	6.31	40	13.89	5.48



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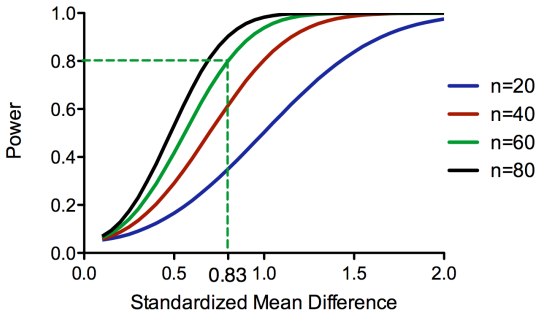


Figure S1. Sample size estimation and power calculations. (a) Published associations between peritoneal fluid cytokines and endometriosis were evaluated to estimate the range of anticipated effect sizes. Standardized mean differences ± 95% confidence intervals are shown to the right (Range = 0.54-4.32; Median = 0.83). (b) Power curves for two-tailed Mann-Whitney U-tests determined at the α=0.05 significance level for the indicated effect sizes and total sample size, assuming a 2:1 case:control allocation.

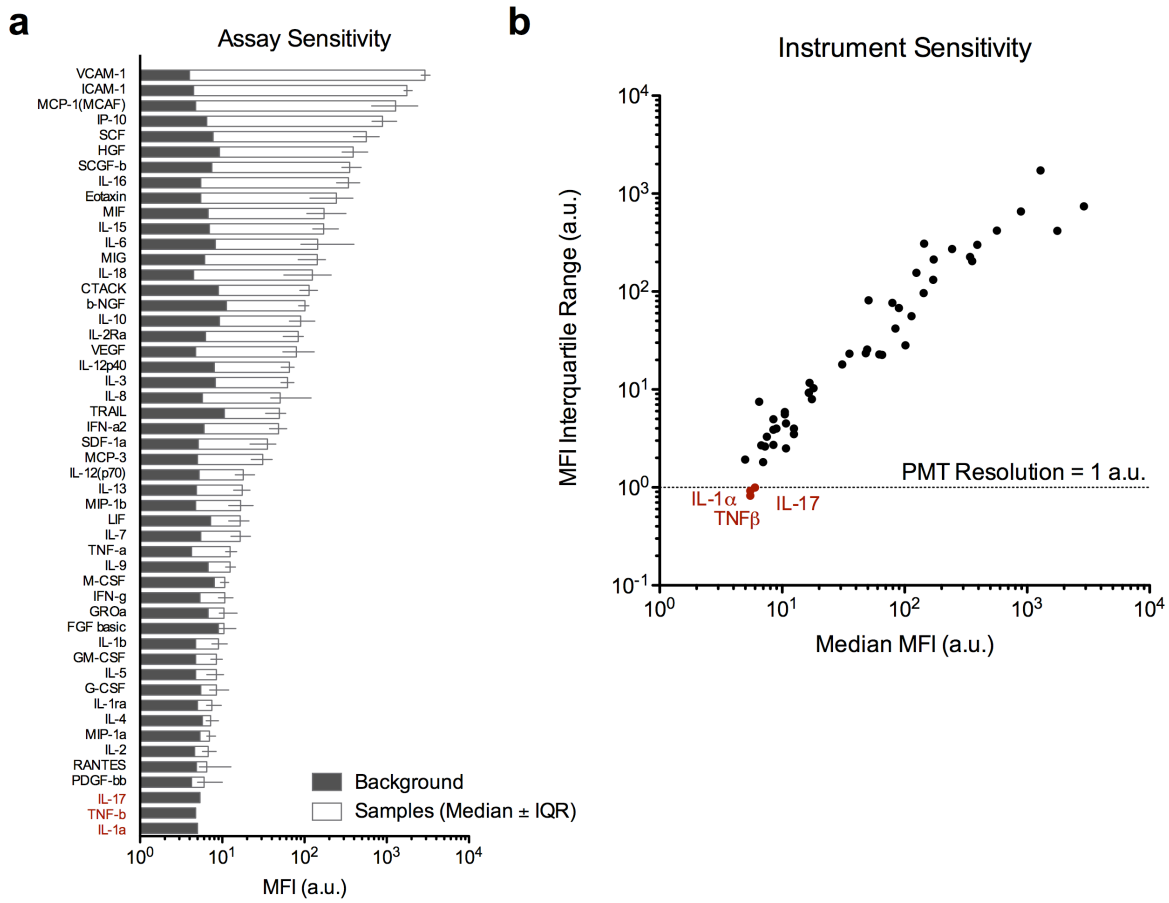


Figure S2. Multiplex immunoassay performance

Prior to analysis, raw fluorescent intensities were evaluated for relative variation above background levels (a) and total sample variation above instrument resolution (b). In (a), bars represent median ± interquartile range. A majority of concentrations for three peritoneal analytes (IL-1α, TNFβ, and IL-17) fall below the lower detection limits for the immunoassay.

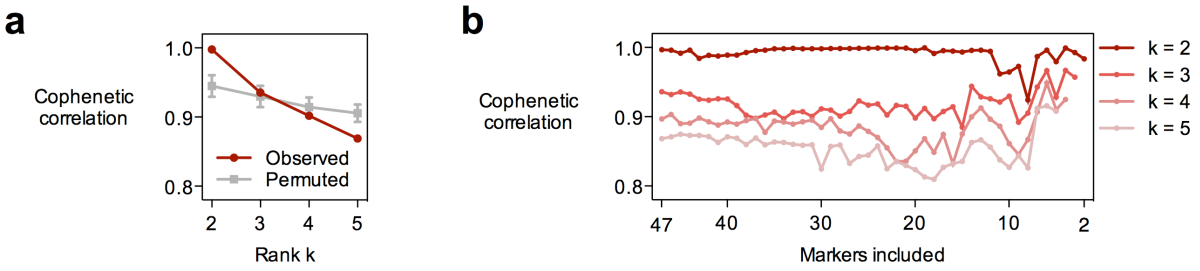


Figure S3. Non-negative matrix factorization of randomized and reduced data sets
(a) Cophenetic correlation of 1000 rank *k* factorizations in the observed (red) and permuted (shaded) data sets. Error bars indicate 95% confidence intervals. (b) Optimal factorization into two subsets is conserved across reduced data sets comprising markers exhibiting maximal variation.

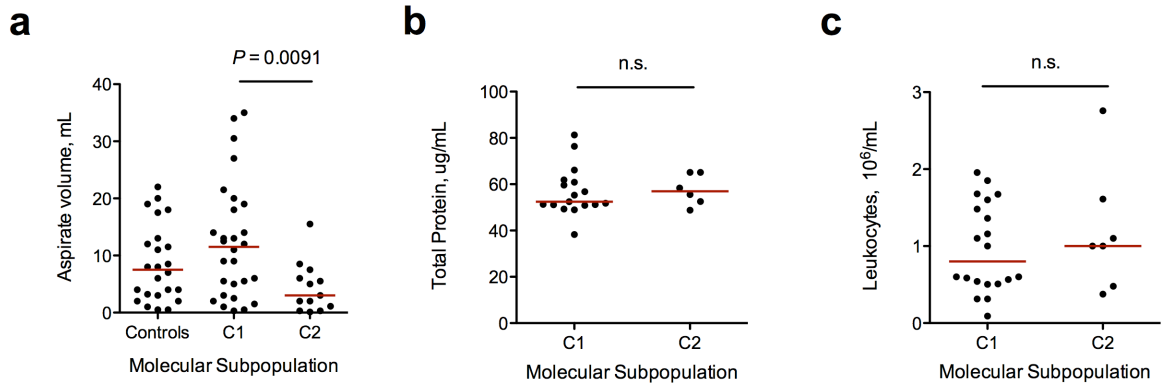


Figure S4. **Peritoneal aspirate characteristics across molecular subpopulations**
Patient subpopulations defined by low (C1) and elevated (C2) peritoneal fluid cytokine concentrations show markedly reduced median aspirate volumes (a), but equivalent total protein and leukocyte levels (b and c).

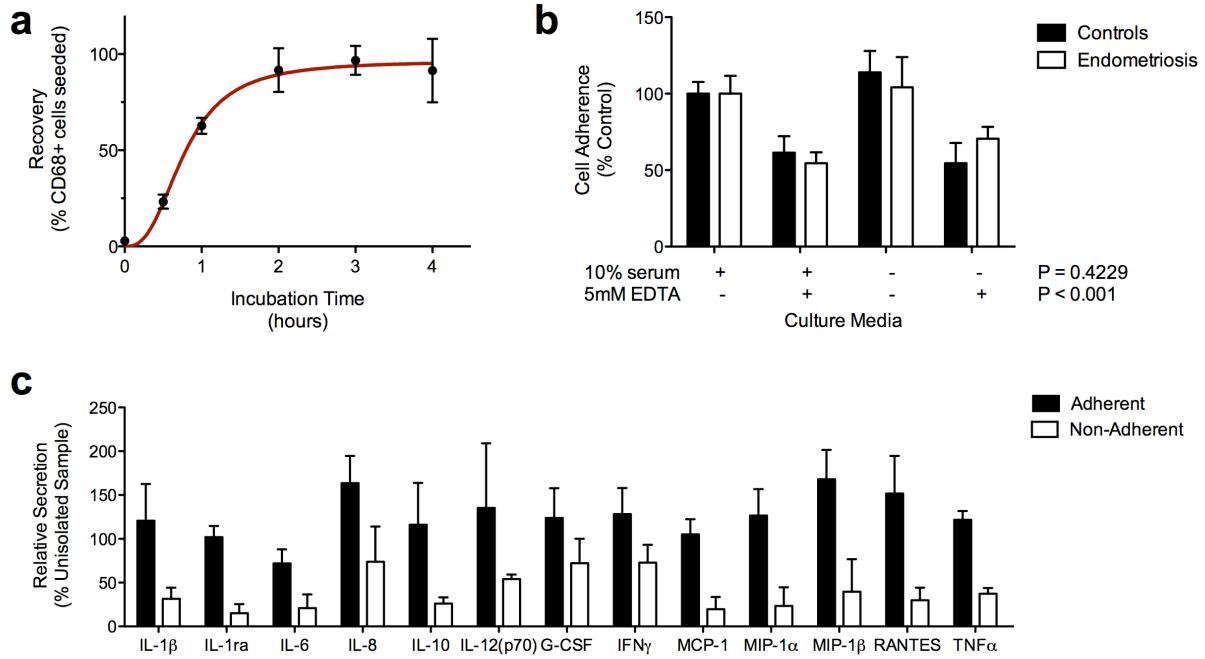
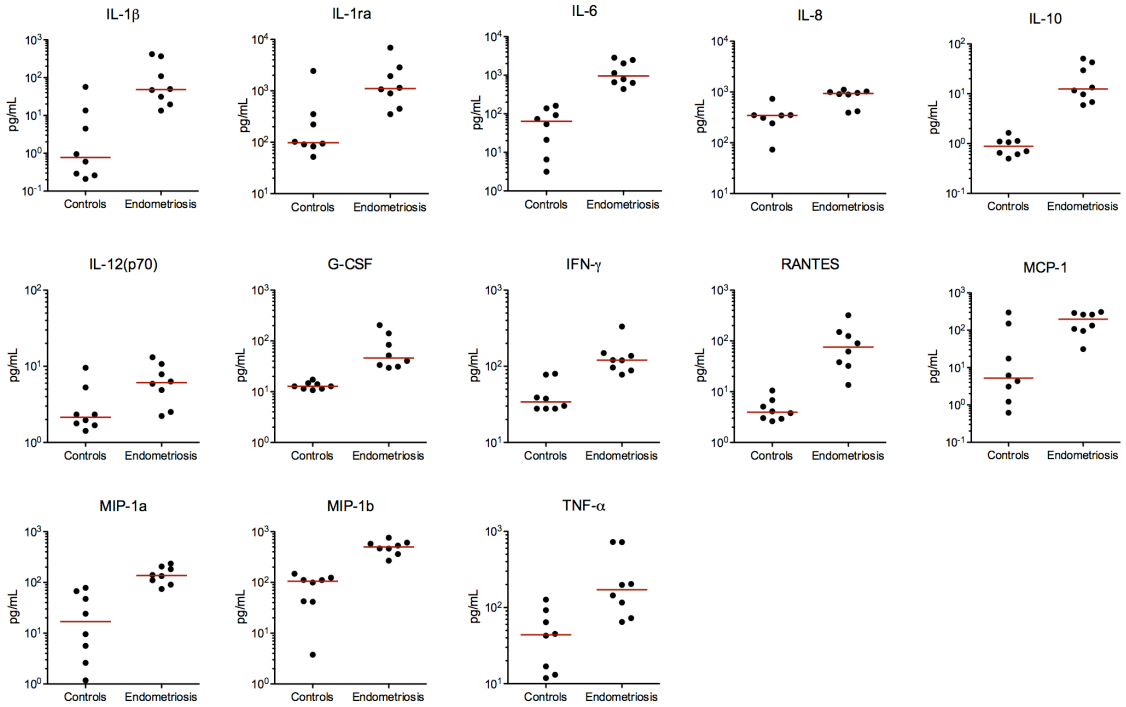


Figure S5. Isolation and relative cytokine secretion of adherent peritoneal macrophages. (A) Recovery of adherent CD68+ macrophages as a function of static incubation period with tissue culture treated polystyrene plates. (B) After two hours of incubation, macrophage adherence is sensitive to the presence of divalent cations, but not substrate deposition of serum components among both control and endometriosis samples. P values indicate significance by two-way ANOVA. (C) Cytokine secretion among adherent and non-adherent peritoneal leukocytes (relative to unisolated, sample-matched controls). For all panels, data are mean ± s.e.m. of three donor samples.

a



b

Cytokine	Rank-sum *P*-value	Fold Change
IL-1β	0.0047	62.5
IL-1ra	0.0086	11.28
IL-6	0.0002	15.1
IL-8	0.0012	2.71
IL-10	0.0002	14.13
IL-12(p70)	0.0312	2.85
G-CSF	0.0009	3.62
IFN-γ	0.0016	3.54
MCP-1	0.0281	37.7
MIP-1α	0.0003	8.09
MIP-1β	0.0002	4.73
RANTES	0.0002	19.2
TNF-α	0.0003	3.90

Figure S6. Differential cytokine secretion by peritoneal macrophages

(a) Thirteen of fifty cytokines assayed in media conditioned by isolated peritoneal macrophages demonstrated significant increases (Wilcoxon rank sum test $P < 0.05$ and minimum two-fold change) in endometriosis samples versus controls. (b) Statistical summary for differentially secreted cytokines in (a).

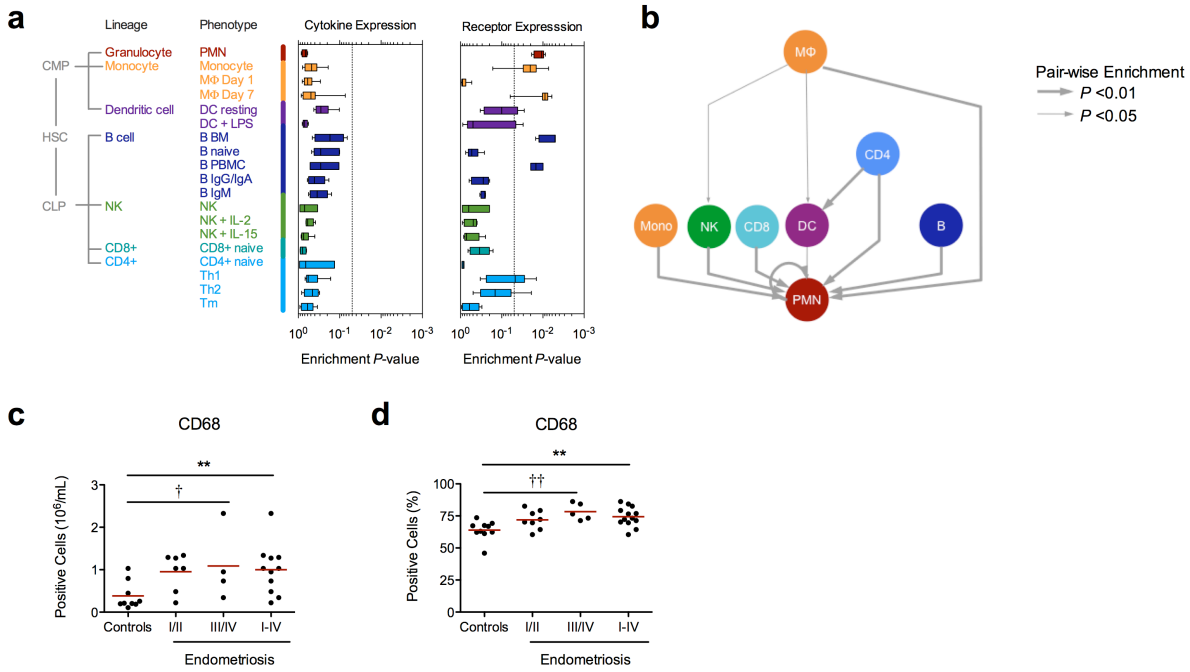


Figure S7. Enrichment analysis of ASRM III/IV cytokines

(A) Significance of lineage-specific enrichment scores for ASRM III/IV cytokine expression obtained by GSEA among Immune Response *in silico* (IRIS) transcriptional profiles. (B) Hierarchy of enriched intercellular cytokine-receptor interactions. Flow cytometric confirmation of increased (C) absolute and (D) relative CD68+ macrophage abundance among endometriosis patient populations. Increasing CD68+ counts among patient subpopulations grouped by ASRM stage are shown for comparison. ***P*<0.01 Wilcoxon rank-sum test; †*P*<0.05, ††*P*<0.01, linear trend test.

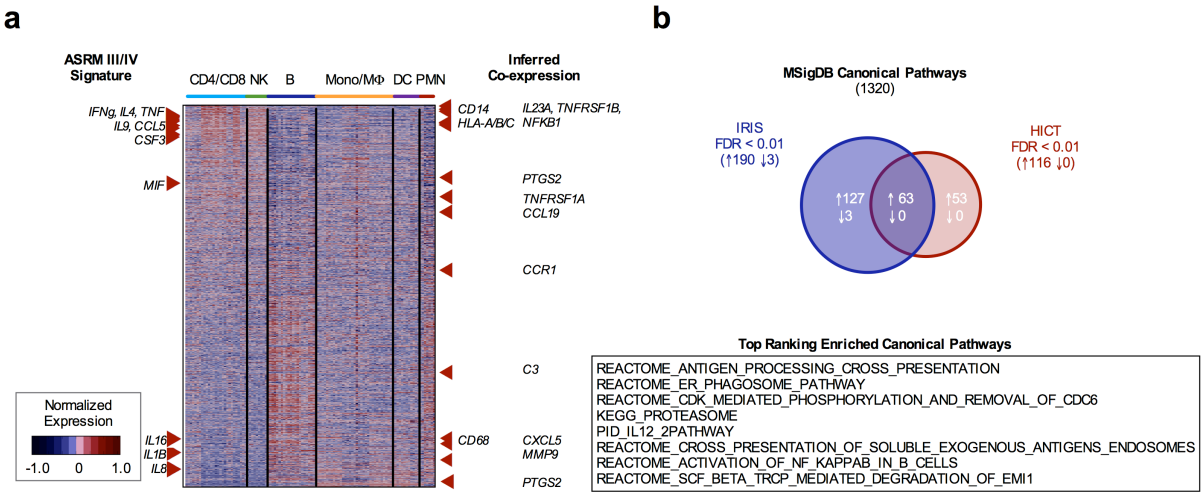


Figure S8. Inferred co-expression of ASRM III/IV cytokines

(A) Transcripts from the IRIS compendia rank-ordered according to median correlation distance to cytokines differentially associated with ASRM stage III/IV endometriosis (left). In contrast to co-expression analysis using the multivariate consensus signature, inferred co-expression of macrophage surface markers and reported disease markers were broad and incoherent (right). (B) Gene set enrichment of IRIS and HICT co-expression profiles derived from the ASRM III/IV signature cytokines likewise demonstrate incoherent enrichment of unrelated canonical pathways.

Table S1. Pair-wise Wilcoxon rank-sum tests – Treatment Status

	Median Concentration (pg/mL)			Untreated vs. Controls		Treated vs. Controls		Treated vs. Untreated	
Cytokine	**Controls**	**Untreated**	**Treated**	**Unadjusted**	**BH**	**Unadjusted**	**BH**	**Unadjusted**	**BH**
PDGF-bb	2.50	2.50	2.35	0.5274	0.1148	0.9617	0.9414	0.4870	0.45478
IL-1b	0.23	0.26	0.24	0.0131	***0.0307***	0.3586	0.8719	0.1906	0.39612
IP-10	667.11	707.89	826.82	0.5908	0.1153	0.8113	0.9006	0.8870	0.59928
IL-1ra	12.27	13.06	11.30	0.3851	0.1081	0.4163	0.8719	0.1309	0.39230
IL-2	0.15	0.15	0.13	0.6834	0.1153	0.6782	0.9006	0.4498	0.44631
IL-4	0.32	0.35	0.33	0.0193	***0.0307***	0.3069	0.8719	0.2548	0.39612
IL-5	0.52	0.52	0.56	0.7176	0.1162	0.0939	0.8719	0.1301	0.39230
IL-6	10.22	10.97	10.70	0.5039	0.1132	0.6906	0.9006	0.3651	0.44351
IL-7	4.93	5.06	5.19	0.4655	0.1081	0.4445	0.8719	0.8730	0.59928
IL-8	2.72	3.48	3.29	0.0221	***0.0307***	0.1150	0.8719	0.4190	0.44351
IL-9	2.81	3.27	2.94	0.0068	***0.0307***	0.6437	0.9006	0.0929	0.39230
IL-10	2.08	2.23	2.32	0.4608	0.1081	0.3988	0.8719	0.8660	0.59928
IL-12(p70)	2.45	2.66	2.79	0.4154	0.1081	0.4353	0.8719	0.8870	0.59928
IL-13	0.64	0.72	0.71	0.2187	0.0881	0.3310	0.8719	0.8800	0.59928
IL-15	1.26	1.32	1.35	0.7470	0.1162	0.6906	0.9006	0.8381	0.59928
IL-17	0.70	0.76	0.68	0.0192	0.0307	0.7236	0.9006	0.1467	0.39230
Eotaxin	70.03	89.44	109.51	0.3606	0.1081	0.1474	0.8719	0.3842	0.44351
FGFb	0.90	0.94	0.90	0.1115	0.0777	0.8483	0.9006	0.1308	0.39230
G-CSF	1.69	2.03	1.76	0.0284	***0.0330***	0.8234	0.9006	0.1451	0.39230
GM-CSF	0.10	0.10	0.08	0.4457	0.1081	0.8232	0.9006	0.2850	0.41140
IFN-g	23.77	27.51	26.04	0.0576	0.0573	0.3724	0.8719	0.2481	0.39612
MCP-1	44.98	64.62	43.12	0.1465	0.0850	0.8361	0.9006	0.1453	0.39230
MIP-1a	0.85	0.89	0.91	0.1653	0.0881	0.4349	0.8719	0.7351	0.59853
MIP-1b	1.23	1.20	1.25	0.6895	0.1153	0.5450	0.9006	0.3650	0.44351
RANTES	2.34	2.66	2.56	0.1442	0.0850	0.3809	0.8719	0.5940	0.52393
TNF-a	3.80	4.20	3.97	0.0709	0.0617	0.7741	0.9006	0.1451	0.39230
VEGF	15.93	17.27	16.65	0.4288	0.1081	0.4168	0.8719	0.8870	0.59928
CTACK	104.86	94.18	82.78	0.2278	0.0881	0.1388	0.8719	0.4665	0.44889
GROa	3.73	3.73	3.45	0.7997	0.1185	0.3985	0.8719	0.1309	0.39230
ICAM-1	828.72	831.64	827.01	0.3447	0.1081	0.9113	0.9325	0.4039	0.44351
IL-1a	0.13	0.12	0.13	0.7505	0.1162	0.4978	0.9006	0.2620	0.39612
IL-2Ra	49.19	45.35	46.20	0.2248	0.0881	0.6444	0.9006	0.1606	0.39230
IL-3	71.01	69.32	64.54	0.6783	0.1153	0.6558	0.9006	0.3604	0.44351
IL-12p40	216.90	219.76	189.39	0.8718	0.1248	0.2086	0.8719	0.2411	0.39612
IL-16	185.68	188.22	189.44	0.4655	0.1081	0.7989	0.9006	0.6316	0.54202
IL-18	6.08	5.22	4.04	0.8900	0.1248	0.8610	0.9006	0.9575	0.63342
LIF	1.92	1.82	1.98	0.6782	0.1153	0.7866	0.9006	1.0000	0.63507
MCP-3	16.09	17.08	13.39	0.2218	0.0881	0.6907	0.9006	0.1357	0.39230
M-CSF	0.33	0.32	0.33	0.8959	0.1248	1.0000	0.9414	0.9929	0.63507
MIF	75.35	96.61	88.26	0.0825	0.0639	0.3477	0.8719	0.4140	0.44351
MIG	452.94	436.38	469.03	0.6176	0.1153	0.2790	0.8719	0.4451	0.44631
b-NGF	7.32	7.38	6.47	0.6448	0.1153	0.2517	0.8719	0.2010	0.39612
SCF	82.52	71.04	94.45	0.3069	0.1081	0.4937	0.9006	0.1606	0.39230
SCGF	1261.96	1216.32	1118.20	0.3770	0.1081	0.9619	0.9414	0.5578	0.50608
SDF-1a	49.09	51.09	51.82	0.6067	0.1153	1.0000	0.9414	0.7091	0.59258
TNFb	0.32	0.32	0.32	0.4115	0.1081	0.5954	0.9006	0.2393	0.39612
TRAIL	32.60	31.65	23.94	0.6952	0.1153	0.0370	0.8719	0.1887	0.39612
VCAM-1	1156.08	1212.30	1068.50	0.7762	0.1175	0.1151	0.8719	0.1061	0.39230
HGF	331.54	342.44	359.96	0.1942	0.0881	0.3642	0.8719	0.8382	0.59928
IFNa2	17.43	16.94	16.24	0.6783	0.1153	0.2386	0.8719	0.3420	0.44351

Table S2. Pair-wise Wilcoxon rank-sum tests – ASRM Staging

	Median Concentration (pg/mL)			ASRM I/II vs. Controls		ASRM III/IV vs. Controls		ASRM III/IV vs. I/II	
Cytokine	Controls	Minimal/Mild	Moderate/Severe	Unadjusted	BH	Unadjusted	BH	Unadjusted	BH
PDGF-bb	2.50	2.32	3.03	0.5566	0.9805	0.0550	0.0744	0.0190	0.0531
IL-1b	0.23	0.24	0.30	0.3395	0.9805	0.0004	***0.0032***	0.0095	0.0478
IP-10	667.11	707.89	707.97	0.6700	0.9805	0.6192	0.2534	0.9476	0.4864
IL-1ra	12.27	12.27	13.86	0.9708	0.9805	0.0870	0.0777	0.0502	0.1147
IL-2	0.15	0.14	0.16	0.9805	0.9805	0.4640	0.2149	0.4776	0.3475
IL-4	0.32	0.34	0.48	0.5575	0.9805	0.0002	***0.0032***	0.0017	0.0416
IL-5	0.52	0.50	0.55	0.9708	0.9805	0.5290	0.2315	0.4852	0.3475
IL-6	10.22	9.60	28.06	0.6878	0.9805	0.0769	0.0777	0.0345	0.0866
IL-7	4.93	4.98	5.45	0.6005	0.9805	0.4559	0.2149	0.6742	0.4095
IL-8	2.72	3.10	10.56	0.3941	0.9805	0.0009	***0.0032***	0.0181	0.0531
IL-9	2.81	3.11	3.61	0.0299	0.9805	0.0113	***0.0260***	0.3712	0.2977
IL-10	2.08	1.95	2.48	0.8170	0.9805	0.0899	0.0777	0.0902	0.1417
IL-12(p70)	2.45	2.45	2.97	0.9224	0.9805	0.0927	0.0777	0.0621	0.1274
IL-13	0.64	0.67	0.73	0.5504	0.9805	0.1073	0.0859	0.1675	0.1832
IL-15	1.26	1.45	1.28	0.4801	0.9805	0.8264	0.3030	0.7826	0.4374
IL-17	0.70	0.76	0.78	0.1098	0.9805	0.0118	0.0260	0.2108	0.2097
Eotaxin	70.03	88.90	92.30	0.5507	0.9805	0.3131	0.1604	0.6085	0.3825
FGFb	0.90	0.94	0.97	0.2778	0.9805	0.0870	0.0777	0.5025	0.3475
G-CSF	1.69	1.86	2.90	0.5180	0.9805	0.0007	***0.0032***	0.0065	0.0478
GM-CSF	0.10	0.10	0.10	0.7142	0.9805	0.3190	0.1604	0.5617	0.3622
IFN-g	23.77	24.10	32.65	0.8264	0.9805	0.0009	***0.0032***	0.0086	0.0478
MCP-1	44.98	64.62	86.72	0.2894	0.9805	0.1398	0.1026	0.3647	0.2977
MIP-1a	0.85	0.89	0.92	0.4860	0.9805	0.0737	0.0777	0.2563	0.2242
MIP-1b	1.23	1.09	1.28	0.2838	0.9805	0.6087	0.2534	0.2585	0.2242
RANTES	2.34	2.34	4.81	0.9126	0.9805	0.0034	***0.0101***	0.0035	0.0445
TNF-a	3.80	4.06	4.59	0.3297	0.9805	0.0242	***0.0426***	0.2168	0.2097
VEGF	15.93	16.06	17.52	0.7608	0.9805	0.2603	0.1432	0.4306	0.3282
CTACK	104.86	95.20	91.00	0.6879	0.9805	0.0722	0.0777	0.1412	0.1693
GROa	3.73	3.73	4.73	0.7421	0.9805	0.3722	0.1820	0.1481	0.1693
ICAM-1	828.72	806.21	979.12	0.8170	0.9805	0.0365	0.0536	0.0156	0.0531
IL-1a	0.13	0.12	0.12	0.9593	0.9805	0.4962	0.2239	0.2053	0.2097
IL-2Ra	49.19	45.78	39.44	0.5508	0.9805	0.1144	0.0875	0.2531	0.2242
IL-3	71.01	69.32	69.64	0.7149	0.9805	0.7367	0.2882	0.8233	0.4501
IL-12p40	216.90	223.82	216.59	0.8076	0.9805	0.5392	0.2315	0.5113	0.3475
IL-16	185.68	170.73	267.55	0.5187	0.9805	0.0294	***0.0470***	0.0130	0.0531
IL-18	6.08	5.47	4.11	0.8171	0.9805	1.0000	0.3520	0.9895	0.4977
LIF	1.92	2.28	1.17	0.6968	0.9805	0.2034	0.1279	0.0659	0.1274
MCP-3	16.09	16.36	18.26	0.3937	0.9805	0.1982	0.1279	0.7228	0.4227
M-CSF	0.33	0.32	0.33	0.9319	0.9805	0.8951	0.3215	0.9371	0.4864
MIF	75.35	94.57	210.55	0.4954	0.9805	0.0135	***0.0264***	0.1062	0.1483
MIG	452.94	432.04	533.47	0.7240	0.9805	0.1649	0.1161	0.0806	0.1352
b-NGF	7.32	7.48	7.20	0.7516	0.9805	0.2033	0.1279	0.1377	0.1693
SCF	82.52	72.73	61.65	0.9127	0.9805	0.0722	0.0777	0.1448	0.1693
SCGF	1261.96	1191.07	1355.14	0.6878	0.9805	0.2364	0.1342	0.3788	0.2977
SDF-1a	49.09	57.54	46.12	0.2785	0.9805	0.7589	0.2884	0.0979	0.1448
TNFb	0.32	0.32	0.32	0.6825	0.9805	0.2926	0.1560	0.5360	0.3547
TRAIL	32.60	31.65	32.38	0.7424	0.9805	0.7367	0.2882	0.7625	0.4358
VCAM-1	1156.08	1061.17	1303.37	0.6006	0.9805	0.2364	0.1342	0.0806	0.1352
HGF	331.54	329.31	376.77	0.2895	0.9805	0.2364	0.1342	0.6839	0.4095
IFNa2	17.43	16.94	17.36	0.6878	0.9805	0.7700	0.2884	0.9476	0.4864

Table S3. Pair-wise Wilcoxon rank-sum tests – Cycle Phase

	Median Concentration (pg/mL)				Controls		Endometriosis	
Cytokine	Follicular (-)	Luteal (-)	Follicular (+)	Luteal (+)	Unadjusted	BH	Unadjusted	BH
PDGF-bb	2.50	2.35	2.50	2.50	0.5930	1.0000	0.9685	0.8925
IL-1b	0.23	0.22	0.26	0.27	0.3959	0.9166	0.9685	0.8925
IP-10	588.31	903.94	674.08	841.48	0.1965	0.8983	0.0719	0.4128
IL-1ra	12.27	12.27	13.46	12.27	1.0000	1.0000	0.8232	0.8747
IL-2	0.15	0.14	0.12	0.15	0.9393	1.0000	0.0849	0.4211
IL-4	0.33	0.31	0.36	0.35	0.8189	1.0000	0.7721	0.8747
IL-5	0.51	0.52	0.52	0.52	0.7893	1.0000	0.7321	0.8747
IL-6	8.19	18.42	13.15	8.76	0.3047	0.8983	0.1761	0.5351
IL-7	4.87	5.33	4.98	5.07	0.7322	1.0000	0.7625	0.8747
IL-8	2.07	2.83	3.33	3.63	0.3619	0.9048	1.0000	0.8925
IL-9	2.95	2.57	2.95	3.72	0.9696	1.0000	0.0030	0.0660
IL-10	1.67	2.27	2.53	1.93	0.1105	0.8983	0.1485	0.5097
IL-12(p70)	2.76	2.35	2.76	2.53	0.2545	0.8983	0.6268	0.8747
IL-13	0.67	0.62	0.72	0.66	0.5423	1.0000	0.1306	0.5097
IL-15	1.06	1.56	1.58	1.21	0.0333	0.8983	0.0740	0.4128
IL-17	0.68	0.72	0.76	0.79	0.6728	1.0000	0.1431	0.5097
Eotaxin	58.41	82.86	88.90	95.93	0.2871	0.8983	0.7033	0.8747
FGFb	0.91	0.89	0.94	0.93	1.0000	1.0000	0.7825	0.8747
G-CSF	1.74	1.69	2.39	1.90	0.9391	1.0000	0.3244	0.8042
GM-CSF	0.06	0.10	0.09	0.12	0.3410	0.8983	0.0109	0.1623
IFN-g	23.00	25.73	27.51	30.79	0.7322	1.0000	0.6361	0.8747
MCP-1	28.78	51.40	64.47	65.59	0.4033	0.9166	0.4230	0.8505
MIP-1a	0.89	0.84	0.89	0.98	0.4931	1.0000	0.0646	0.4128
MIP-1b	1.14	1.26	1.14	1.36	0.3414	0.8983	0.0247	0.2752
RANTES	1.84	2.34	3.06	2.59	0.2227	0.8983	0.4945	0.8747
TNF-a	3.85	3.74	4.14	4.64	0.8786	1.0000	0.2370	0.6610
VEGF	16.65	14.48	17.43	16.29	0.7038	1.0000	0.6363	0.8747
CTACK	104.66	111.05	90.61	102.75	0.9394	1.0000	0.0979	0.4368
GROa	3.40	3.89	3.73	4.57	0.2386	0.8983	0.1799	0.5351
ICAM-1	825.79	831.64	831.64	833.30	0.5687	1.0000	0.7327	0.8747
IL-1a	0.13	0.13	0.12	0.12	0.4946	1.0000	0.9891	0.8925
IL-2Ra	48.81	50.61	42.32	45.42	0.7040	1.0000	0.9476	0.8925
IL-3	73.62	68.40	68.78	73.85	0.5949	1.0000	0.8029	0.8747
IL-12p40	213.41	218.61	212.14	223.94	1.0000	1.0000	0.4700	0.8738
IL-16	184.78	200.19	184.78	191.96	0.5947	1.0000	0.4384	0.8505
IL-18	8.65	5.44	4.53	5.88	0.1286	0.8983	0.6646	0.8747
LIF	1.47	2.02	1.60	2.33	0.2875	0.8983	0.0551	0.4128
MCP-3	12.86	16.55	18.14	16.62	0.0805	0.8983	0.8851	0.8925
M-CSF	0.32	0.34	0.30	0.38	1.0000	1.0000	0.0021	0.0660
MIF	95.59	60.67	117.40	87.56	0.1106	0.8983	0.2994	0.7860
MIG	278.30	462.03	482.08	416.41	0.3233	0.8983	0.7229	0.8747
b-NGF	7.28	7.32	7.37	7.43	0.9697	1.0000	0.6269	0.8747
SCF	96.38	71.04	69.49	71.31	0.2241	0.8983	0.4306	0.8505
SCGF	1284.13	1239.79	1191.07	1347.98	0.7040	1.0000	0.8233	0.8747
SDF-1a	51.24	46.94	51.09	54.22	1.0000	1.0000	0.4383	0.8505
TNFb	0.32	0.32	0.32	0.32	0.3185	0.8983	0.5097	0.8747
TRAIL	26.24	34.54	32.74	29.80	0.1286	0.8983	0.4383	0.8505
VCAM-1	1101.68	1262.57	1212.30	1172.52	0.1489	0.8983	0.5902	0.8747
HGF	347.02	270.51	370.93	333.56	1.0000	1.0000	0.9686	0.8925
IFNa2	17.16	17.61	16.94	17.42	0.9394	1.0000	0.8955	0.8925

Table S4. Pair-wise Wilcoxon rank-sum tests – Recurrence Status

	Median Concentration (pg/mL)		Recurrent Disease vs. Initial Diagnosis	
Cytokine	**Initial Diagnosis**	**Recurrent Disease**	**Unadjusted**	**BH**
PDGF-bb	2.5	2.5	0.5778	1.0000
IL-1b	0.26	0.27	0.6741	1.0000
IP-10	674.08	777.26	0.2284	1.0000
IL-1ra	13.46	12.985	0.9137	1.0000
IL-2	0.13	0.155	0.1160	1.0000
IL-4	0.35	0.36	0.5151	1.0000
IL-5	0.5	0.55	0.2221	1.0000
IL-6	14.91	9.86	0.5976	1.0000
IL-7	4.49	5.29	0.5606	1.0000
IL-8	3.76	3.405	0.8817	1.0000
IL-9	3.11	3.58	0.0782	1.0000
IL-10	2.3	2.175	1.0000	1.0000
IL-12(p70)	2.62	2.71	0.9784	1.0000
IL-13	0.72	0.685	0.6068	1.0000
IL-15	1.24	1.435	0.5697	1.0000
IL-17	0.76	0.76	0.8477	1.0000
Eotaxin	89.44	90.645	0.8603	1.0000
FGFb	0.88	0.96	0.0527	1.0000
G-CSF	2.03	2.185	0.9030	1.0000
GM-CSF	0.1	0.1	0.9892	1.0000
IFN-g	27.51	27.955	0.6549	1.0000
MCP-1	43.11	85.98	0.1103	1.0000
MIP-1a	0.89	0.92	0.8704	1.0000
MIP-1b	1.15	1.22	0.1632	1.0000
RANTES	3.83	2.56	0.3433	1.0000
TNF-a	4.2	4.17	0.7970	1.0000
VEGF	16.06	17.435	0.3366	1.0000
CTACK	94.18	92.67	0.7351	1.0000
GROa	4.35	3.645	0.2969	1.0000
ICAM-1	831.64	845.67	0.7556	1.0000
IL-1a	0.12	0.12	0.4742	1.0000
IL-2Ra	45.35	43.605	0.9892	1.0000
IL-3	79.96	67.81	0.1133	1.0000
IL-12p40	223.82	213.41	0.3717	1.0000
IL-16	179.21	205.625	0.4901	1.0000
IL-18	5.1	5.38	0.2973	1.0000
LIF	1.99	1.795	0.8710	1.0000
MCP-3	18.37	16.985	0.7452	1.0000
M-CSF	0.32	0.33	0.8495	1.0000
MIF	117.4	92.38	0.6552	1.0000
MIG	435.18	458.115	0.8817	1.0000
b-NGF	7.38	7.38	1.0000	1.0000
SCF	71.04	71.09	0.6650	1.0000
SCGF	1216.32	1236.435	0.6650	1.0000
SDF-1a	51.09	51.605	0.7970	1.0000
TNFb	0.35	0.32	0.2858	1.0000
TRAIL	32.01	31.65	0.6165	1.0000
VCAM-1	1237.57	1123.315	0.8180	1.0000
HGF	297.14	375.135	0.1553	1.0000
IFNa2	18.98	16.73	0.1593	1.0000

Table S5. Pair-wise Wilcoxon rank-sum tests – Lesion Distribution

	Median Concentration (pg/mL)				Peritoneal vs. Controls		Ovarian vs. Controls		Deep vs. Controls	
Cytokine	Controls	Peritoneal	Ovarian	Deep	Unadjusted	BH	Unadjusted	BH	Unadjusted	BH
PDGF-bb	2.43	2.50	1.86	2.31	0.8165	1.0000	0.0343	0.8201	0.7596	0.9786
IL-1b	0.22	0.23	0.21	0.25	0.5203	1.0000	0.3056	0.9257	0.0956	0.4316
IP-10	706.02	736.40	838.86	786.78	1.0000	1.0000	0.5823	0.9751	0.2128	0.6130
IL-1ra	12.63	13.00	11.87	15.06	0.9805	1.0000	0.5970	0.9751	0.1145	0.4316
IL-2	0.14	0.14	0.14	0.13	0.9414	1.0000	0.9297	1.0000	0.7792	0.9786
IL-4	0.31	0.34	0.32	0.31	0.7503	1.0000	0.8945	1.0000	0.7580	0.9786
IL-5	0.51	0.52	0.47	0.53	0.7507	1.0000	0.9649	1.0000	0.8185	0.9786
IL-6	9.72	9.60	6.43	8.98	0.9127	1.0000	0.0989	0.9257	1.0000	1.0000
IL-7	5.15	5.14	5.28	6.37	0.9320	1.0000	0.8430	1.0000	0.2524	0.6130
IL-8	2.25	2.46	2.07	3.36	0.6966	1.0000	0.1724	0.9257	0.0793	0.4316
IL-9	2.81	2.91	3.11	3.21	0.6000	1.0000	0.2079	0.9257	0.0705	0.4316
IL-10	1.83	1.88	1.59	2.65	0.9514	1.0000	0.1525	0.9257	0.8587	0.9786
IL-12(p70)	2.41	2.47	2.29	2.47	0.7421	1.0000	0.3906	0.9257	0.9797	1.0000
IL-13	0.63	0.64	0.64	0.64	0.8167	1.0000	1.0000	1.0000	0.5083	0.8301
IL-15	1.01	0.96	0.98	1.84	0.8169	1.0000	0.3669	0.9257	0.0118	0.2897
IL-17	0.70	0.76	0.71	0.76	0.6836	1.0000	0.9294	1.0000	0.0845	0.4316
Eotaxin	46.98	47.26	49.15	105.09	0.9708	1.0000	0.5822	0.9751	0.0394	0.4316
FGFb	0.91	0.94	0.87	1.05	0.3729	1.0000	0.5375	0.9751	0.2627	0.6130
G-CSF	1.69	1.81	1.68	2.11	0.4632	1.0000	0.7914	1.0000	0.0190	0.3102
GM-CSF	0.12	0.12	0.10	0.11	0.6335	1.0000	0.5955	0.9751	0.5568	0.8553
IFN-g	23.93	24.10	24.10	22.74	0.6786	1.0000	0.9649	1.0000	0.9391	1.0000
MCP-1	41.01	40.81	50.72	81.55	0.9127	1.0000	0.8776	1.0000	0.0446	0.4316
MIP-1a	0.87	0.89	0.79	0.97	0.6516	1.0000	0.3649	0.9257	0.3868	0.7285
MIP-1b	1.20	1.21	1.05	1.10	0.9030	1.0000	0.3328	0.9257	0.1544	0.5042
RANTES	2.34	2.34	2.10	2.83	0.6688	1.0000	0.1786	0.9257	0.3590	0.7285
TNF-a	3.79	3.85	3.99	4.03	0.7140	1.0000	0.4142	0.9257	0.7404	0.9786
VEGF	14.25	15.20	10.64	13.73	0.7513	1.0000	0.2711	0.9257	0.5586	0.8553
CTACK	107.48	108.09	116.27	75.14	0.9320	1.0000	0.4156	0.9257	0.0984	0.4316
GROa	3.88	3.90	3.28	3.91	0.8357	1.0000	0.3219	0.9257	0.8189	0.9786
ICAM-1	837.80	831.64	889.34	826.38	0.9127	1.0000	0.7084	1.0000	0.7410	0.9786
IL-2Ra	49.19	45.49	44.02	57.23	0.4574	1.0000	0.5234	0.9751	0.2525	0.6130
IL-3	69.20	67.01	65.16	68.29	0.8934	1.0000	0.9824	1.0000	0.9190	1.0000
IL-12p40	216.89	215.19	215.35	214.53	0.9223	1.0000	0.8430	1.0000	1.0000	1.0000
IL-16	185.67	188.80	137.29	206.36	0.6173	1.0000	0.0209	0.8201	0.3467	0.7285
IL-18	4.77	4.52	3.31	5.32	0.9320	1.0000	0.4156	0.9257	0.4305	0.7534
LIF	2.40	2.38	2.54	3.75	1.0000	1.0000	0.6920	1.0000	0.2855	0.6358
MCP-3	13.39	13.41	12.72	12.73	0.7057	1.0000	0.7917	1.0000	0.9594	1.0000
M-CSF	0.33	0.33	0.31	0.38	1.0000	1.0000	0.4540	0.9551	0.1088	0.4316
MIF	70.06	90.30	59.13	98.48	0.7057	1.0000	0.3670	0.9257	0.1472	0.5042
MIG	452.94	451.86	433.61	569.86	0.8742	1.0000	0.4156	0.9257	0.2525	0.6130
b-NGF	7.52	7.48	7.40	8.42	0.9903	1.0000	0.7917	1.0000	0.5933	0.8810
SCF	76.00	79.66	62.09	86.57	0.6522	1.0000	0.3011	0.9257	0.8190	0.9786
SCGF	1261.77	1284.13	1061.32	1430.55	0.8169	1.0000	0.4678	0.9551	0.4014	0.7285
SDF-1a	51.90	57.23	52.74	65.75	0.6260	1.0000	0.8950	1.0000	0.1092	0.4316
TNFb	0.33	0.34	0.34	0.33	0.8153	1.0000	0.7905	1.0000	0.8574	0.9786
TRAIL	36.52	38.69	27.00	43.35	0.7607	1.0000	0.0502	0.8201	0.4014	0.7285
VCAM-1	1081.96	1110.15	1065.03	834.71	0.9127	1.0000	0.7414	1.0000	0.1947	0.5963
HGF	324.22	327.65	246.95	536.20	0.6522	1.0000	0.1657	0.9257	0.0029	0.1436
IFNa2	17.43	17.61	16.70	16.10	0.9223	1.0000	0.9124	1.0000	0.4609	0.7787

Table S6. Pair-wise Wilcoxon rank-sum tests – Primary Indication

	Median Concentration (pg/mL)		Infertility vs. Pain	
Cytokine	Pain Only	Infertility -/+ Pain	Unadjusted	BH
PDGF-bb	2.5	2.13	0.4126	0.8618
IL-1b	0.26	0.285	0.4466	0.8618
IP-10	707.89	689.47	0.5569	0.8618
IL-1ra	13.06	13.455	0.5188	0.8618
IL-2	0.14	0.165	0.6566	0.8872
IL-4	0.35	0.445	0.2334	0.8192
IL-5	0.55	0.48	0.9199	0.9738
IL-6	10.97	12.645	0.5007	0.8618
IL-7	5.06	5.145	0.4916	0.8618
IL-8	3.79	3.1	0.7965	0.9738
IL-9	3.11	3.35	0.2174	0.8192
IL-10	2.12	2.62	0.6160	0.8801
IL-12(p70)	2.62	2.96	0.5097	0.8618
IL-13	0.72	0.695	1.0000	1.0000
IL-15	1.42	0.985	0.0855	0.8192
IL-17	0.76	0.76	0.8731	0.9738
Eotaxin	102.89	67.645	0.1184	0.8192
FGFb	0.94	0.935	0.9428	0.9738
G-CSF	2.34	1.82	0.5860	0.8618
GM-CSF	0.12	0.09	0.0615	0.8192
IFN-g	27.51	28.54	0.5567	0.8618
MCP-1	51.41	92.495	0.1253	0.8192
MIP-1a	0.89	0.94	0.7955	0.9738
MIP-1b	1.2	1.12	0.4737	0.8618
RANTES	2.66	2.81	0.8075	0.9738
TNF-a	4.2	4.01	0.5006	0.8618
VEGF	15.36	21.44	0.2126	0.8192
CTACK	92.91	100.1	0.6989	0.9196
GROa	4.35	3.2	0.1599	0.8192
ICAM-1	818.72	950.84	0.2233	0.8192
IL-1a	0.12	0.115	0.0249	0.8192
IL-2Ra	45.49	39.33	0.3821	0.8618
IL-3	69.32	72.485	0.8974	0.9738
IL-12p40	219.76	216.585	0.4737	0.8618
IL-16	198.74	167.4	0.2126	0.8192
IL-18	4.89	6.485	0.4307	0.8618
LIF	1.99	1.605	0.2458	0.8192
MCP-3	17.64	16.49	0.4915	0.8618
M-CSF	0.32	0.31	0.2015	0.8192
MIF	114.75	81.015	0.6364	0.8838
MIG	482.08	336.64	0.3517	0.8618
b-NGF	7.38	7.32	0.9543	0.9738
SCF	71.48	54.61	0.1253	0.8192
SCGF	1202.35	1366.225	0.9087	0.9738
SDF-1a	57.54	48.245	0.1922	0.8192
TNFb	0.32	0.32	0.8487	0.9738
TRAIL	31.65	31.83	0.8298	0.9738
VCAM-1	1091.14	1274.385	0.2956	0.8618
HGF	342.44	412.09	0.5763	0.8618
IFNa2	16.86	18.37	0.2826	0.8618

Table S7. Reported associations between peritoneal cytokines, chemokines, growth factors and pelvic endometriosis.

	Endometriosis vs. Controls			
	Increased	No Difference	Decreased	Transient
Interleukins				
IL-1		Koyama 1993		
IL-1α	Kondera-Anasz 2005	Dziunycz 2009		
IL-1β	Fakih 1987	Keenan 1989		
	Taketani 1992	Kalu 2007		
	Ho 1996	Bedaiwy 2002		
	Sukhikh 2004	Oku 2004		
	Mier-Cabrerra 2010	Milewski 2008		
	Michaud 2011			
	Sikora 2012			
IL-1Ra	Kondera-Anasz 2005	Ho 1996	Zhang 2007	
		Bersinger 2012	Mier-Cabrerra 2010	
IL-1 sRII			Kondera-Anasz 2005	
			Michaud 2011	
sIL1RAcP			Michaud 2011	
IL-2		Punnonen 1996	Hsu 1997	
		Oku 2004		
		Podgaec 2007		
		Hassa 2009		
		Mier-Cabrerra 2010		
IL-2Ra				
IL-3				
IL-4	Hsu 1997	Punnonen 1996		
		Oku 2004		
		Podgaec 2007		
		Hassa 2009		
		Mier-Cabrerra 2010		
IL-5	Koyama 1993	Punnonen 1996		
IL-6	Koyama 1993	Keenan 1989		
	Rier 1995	Oku 2004		
	Ho 1996			
	Punnonen 1996			
	Harada 1997			
	Bedaiwy 2002			
	Khan 2002			
	Kalu 2007			
	Milewski 2008			
	Dziunycz 2009			
	Mier-Cabrerra 2010			
	Velasco 2010			
	Drosdzol-Cop 2012			
	Bersinger 2012			
IL-6sR			Rier 1995	
IL-7				
IL-9				
IL-10	Punnonen 1996	Rana 1996		Ho 1997
	Tabibzadeh 2003	Hsu 1997		
	Kondera-Anasz 2004	Oku 2004		
	Podgaec 2007	Hassa 2009		
	Mier-Cabrerra 2010	Andreoli 2011		
		Bersinger 2012		
IL-11		Gazvani 2001		
IL-12(p70)	Mazzeo 1998	Zeyneloglu 1998		Ho 1997
	Gallinelli 2004	Gazvani 2001		
	Fairbanks 2009	Mier-Cabrerra 2010		
		Andreoli 2011		
		Bersinger 2012		
IL-12(p40)		Mazzeo 1998		
IL-13		Bedaiwy 2002	McLaren 1997	
		Mier-Cabrerra 2010	Gallinelli 2004	
		Velasco 2010		
IL-14				
IL-15		Bersinger 2012	Mier-Cabrerra 2010	Arici 2003
IL-16	Koga 2005			

IL-17		Velasco 2010 Andreoli 2011		Zhang 2005
IL-18	Oku 2004 Bersinger 2012	Fairbanks 2009 Glitz 2009	Zhang 2004 Sikora 2012	Arici 2003
IL-19				
IL-20				
IL-21				
IL-22				
IL-23	Andreoli 2011			
IL-24				
IL-25				
IL-26				
IL-27				
IL-28				
IL-29				
IL-30				
IL-31				
IL-32				
IL-33	Santulli 2012			
IL-35				
IL-36				
IL-37				
IL-38				
MIF	Kats 2002 Mahutta 2004			
IFNα2		Sukhikh 2004		
IFNγ	Podgaec 2007	Keenan 1989 Khorram 1993 Oku 2004 Sukhikh 2004 Milewski 2008 Hassa 2009	Ho 1996 Hsu 1997 Wu 1998 Mier-Cabrerra 2010	
TNF Superfamily				
TNFα	Rana 1996 Ho 1996 Overton 1996 Harada 1997 Bedaiwy 2002 Sukhikh 2004 Mier-Cabrerra 2010 Drosdzol-Cop 2012	Keenan 1989 Calhaz-Jorge 2000 Oku 2004 Kalu 2007 Podgaec 2007 Milewski 2008 Dziunycz 2009		Pizzo 2002
TNFRSF1A/B/sTNFR	Koga 2000			
TNFRSF11B/OPG	Harada 2004 Bersinger 2006			
TNFβ				
TRAIL				Harada 2004
sFas		Kalu 2007		
sFasL		Kalu 2007		
ICAM-1		Somigliana 1996 Daniel 2000 Bersinger 2012		
VCAM-1		Daniel 2000 Bersinger 2012		
TGFβ	Oosterlynck 1994 Kupker 1998 Pizzo 2002			
Hematopoetic				
LIF				
G-CSF		Bersinger 2012		
GM-CSF		Punnonen 1996 Oku 2004		
CSF1/M-CSF	Fukaya 1994 Budrys 2012		Weinberg 1991	
SCGF				
SCF				Osuga 2000
Tissue Remodeling				
bFGF	Bourlev 2006	Bersinger 2012		
PDGF-bb		Overton 1996		
VEGF	McLaren 1996 Kupker 1998	Kalu 2007 Dziunycz 2009		

	Mier-Cabrerra 2010	Bersinger 2012		
HGF	Osuga 1999 Khan 2002			
b-NGF		Bersinger 2012		
EGF	Sukhikh 2004	De Leon 1986		
Chemokines				
CCL1/TCA-3				
CCL2/MCP-1	Arici 1997 Pizzo 2002 Kalu 2007 Mier-Cabrerra 2010 Bersinger 2012	Laudanski 2006		
CCL3/MIP-1α		Laudanski 2006		
CCL4/MIP-1β		Laudanski 2006		
CCL5/RANTES	Khorram 1993 Bersinger 2005 Mier-Cabrerra 2010	Laudanski 2006 Kalu 2007 Bersinger 2012		
CCL6/MRP-2				
CCL7/MCP-3				
CCL8/MCP-2				
CCL9(10)/CCF18				
CCL11/Eotaxin	Mier-Cabrerra 2010 Bersinger 2012			
CCL12/MCP-5				
CCL13/MCP-4				
CCL14/HCC-1				
CCL15/MIP-1δ		Laudanski 2006		
CCL16/LEC				
CCL17/TARC		Laudanski 2006		
CCL18/PARC				
CCL19/MIP-3β	Laudanski 2006			
CCL20/MIP-3α		Laudanski 2006		
CCL21/SLC				
CCL22/MDC		Laudanski 2006		
CCL23/MPIF-1				
CCL24/MPIF-2				
CCL25/TECK				
CCL26/MIP-4a				
CCL27/CTACK				
CCL28/MEC				
CXCL1/GROα	Szamatowicz 2002 Bersinger 2012			
CXCL2/GROβ				
CXCL3/GRO3				
CXCL4/PF-4				
CXCL5/ENA-78	Mueller 2003 Suzumori 2004			
CXCL6/GCP-2				
CXCL7NAP-2				
CXCL8/IL-8	Ryan 1995 Rana 1996 Arici 1996 Iwabe 1998 Bedaiwy 2002 Pizzo 2002 Bersinger 2005 Kalu 2007 Mier-Cabrerra 2010 Malhotra 2012	Oku 2004 Velasco 2010 Bersinger 2012		Gazvani 2001
CXCL9/MIG				
CXCL10/IP-10		Bersinger 2012	Yoshino 2003 Galleri 2009	
CXCL11/I-TAC				
CXCL12/SDF-1α				
CXCL13/BCA-1				
CXCL14/BRAK				
CXCL15/Lungkine				
CXCL16/SRPSOX				
CXCL17/DMC				
XCL1/Lymphotactin a				

Table S8. Over-representation of transcriptional binding sites among macrophage secreted cytokines.

Transcription Factor	All Motifs	Consensus Sequence(s)	Co-expression Profile P-Value IRIS	Co-expression Profile P-Value HICT	Co-expression Profile FDR IRIS	Co-expression Profile FDR HICT
C/EBPbeta	<0.0001	V$CEBPB_01	0.0000	0.0000	0.1330	0.0645
		V$CEBPB_02	0.0022	0.0000	0.1448	0.0392
		V$CEBP_Q2_01	0.0129	0.1626	0.2820	0.4249
		V$CEBP_Q3	0.2298	0.3982	0.6020	0.7252
		V$CEBPB_Q6	NA	NA	NA	NA
RelA-p65-isoform1	0.0026	V$NFKAPPAB65_01	0.0021	0.0000	***0.0749***	***0.0078***
		V$NFKAPPAB_01	0.0000	0.0000	***0.0371***	***0.0015***
		V$NFKB_Q6_01	0.0000	0.0000	***0.0456***	***0.0089***
		V$RELA_Q6	NA	NA	NA	NA
CREB1	0.0047	V$CREB_01	0.9017	0.8568	0.9857	1.0000
		V$CREB_Q2	0.6960	0.1106	0.9826	0.3907
		V$CREB_Q4	0.7767	0.8489	1.0000	1.0000
		V$CREB_02	0.0895	0.7080	0.4423	1.0000
		V$TAXCREB_01	0.8693	0.1147	0.9997	0.3401
		V$TAXCREB_02	0.4063	0.2286	0.7197	0.3837
		V$CREB_Q2_01	0.6716	0.7511	0.9015	0.9338
		V$CREB_Q4_01	0.2041	0.3401	0.5608	0.6951
		V$CREB_Q3	0.2981	0.1549	0.7330	0.7430
		V$CREBATF_Q6	NA	NA	NA	NA
		V$CREB1_01	NA	NA	NA	NA
		V$CREB1_Q6	NA	NA	NA	NA
NF-kappaB1-p50:RelA-p65	0.0095	V$P50RELAP65_Q5_01	NA	NA	NA	NA
ATF-2	0.0186	V$CREBP1_01	0.6869	0.9660	0.9999	1.0000
		V$CREBP1CJUN_01	0.7810	0.6883	NA	NA
		V$CREBP1_Q2	0.8366	0.4664	0.9642	0.7473
		V$CREB_Q3	0.2981	0.1549	NA	NA
		V$CREBATF_Q6	NA	NA	NA	NA
		V$ATF2_Q5	NA	NA	NA	NA
NF-kappaB1-p50	0.0198	V$NFKAPPAB50_01	NA	NA	NA	NA
		V$NFKAPPAB_01	0.0000	0.0000	***0.0371***	***0.0015***
		V$NFKB_Q6	0.0000	0.0000	***0.0300***	***0.0064***
		V$NFKB_C	0.0022	0.0000	***0.0982***	***0.0128***
		V$NFKB_Q6_01	0.0000	0.0000	***0.0456***	***0.0089***
		V$P50_Q6	NA	NA	NA	NA
c-Fos:c-Jun	0.0274	V$CFOSCJUN_Q5	NA	NA	NA	NA
c-Ets-1	0.0286	V$CETS1P54_01	0.2140	0.7336	0.6859	0.9423
		V$CETS1P54_02	NA	NA	NA	NA
		V$ETS1_B	0.0712	0.0319	0.4129	0.3434
		V$ETS_B	NA	NA	NA	NA
		V$ETS_Q6	NA	NA	NA	NA
		V$ETS_Q4	0.0000	0.0000	***0.0035***	***0.0131***
		V$CETS1P54_03	NA	NA	NA	NA
		V$CETS1_Q6	NA	NA	NA	NA
		V$CETS1_02	NA	NA	NA	NA
		V$ETS1_02	NA	NA	NA	NA
AP-1	0.0417	V$AP1FJ_Q2	0.0044	0.0000	0.1437	0.1090
		V$AP1_Q2	0.0713	0.0050	0.3912	0.1115
		V$AP1_Q6	0.0000	0.0041	0.0835	0.1088
		V$AP1_Q4	0.0000	0.0000	0.1027	0.1030
		V$AP1_C	0.0000	0.4241	0.1214	0.7488
		V$AP1_01	0.0000	0.0000	***0.0159***	***0.0796***
		V$AP1_Q2_01	0.0109	0.0807	0.2366	0.3499
		V$AP1_Q6_01	0.0066	0.0449	0.1453	0.2619
		V$AP1_Q4_01	0.0000	0.0000	***0.0488***	***0.0730***
		V$AP1_Q6_02	NA	NA	NA	NA
STAT1	0.0444	V$STAT1_01	0.3418	0.4359	0.7391	1.0000
		V$STAT_01	0.0146	0.0000	0.1433	0.0385
		V$STAT1_02	0.5580	0.1652	0.8404	0.4480
		V$STAT1_03	0.8896	0.7739	0.9931	1.0000
		V$STAT_Q6	0.6152	0.8502	0.8555	0.9888
		V$STAT1_05	NA	NA	NA	NA
		V$STAT1_Q6	NA	NA	NA	NA

NA – Not Annotated in MSigDB v4.0

176 **Table S9.** Luminex Targets and Assay Performance Characteristics
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Panel	Analyte	HUGO Gene Symbol	xMAP Region	LoD, pg/mL	Intra-Assay CV, %	Inter-Assay CV, %
Group I - 27-plex	IL-1b	IL1B	39	0.02	0.7	2.5
	IL-1ra	IL1RA	25	1.28	0.9	5.7
	IL-2	IL2	38	0.34	0.8	3.6
	IL-4	IL4	52	0.02	2	3.5
	IL-5	IL5	33	0.03	1.7	4.5
	IL-6	IL6	19	0.13	0.7	3.2
	IL-7	IL7	74	0.07	1.4	3.2
	IL-8	IL8	54	0.06	2.4	2.9
	IL-9	IL9	77	0.83	1	4.3
	IL-10	IL10	56	0.12	0.4	6.4
	IL-12 (p70)	IL12A,B	75	3.10	2.2	1.8
	IL-13	IL13	51	0.05	1.2	4.4
	IL-15	IL15	73	0.62	0.4	4.5
	IL-17	IL17	76	0.59	0.8	7.5
	Eotaxin	CCL11	43	0.52	1.2	8
	bFGF	FGFB	44	0.47	0.7	6.1
	G-CSF	CSF3	57	0.21	1.5	3.7
	GM-CSF	CSF2	34	0.65	0.4	3.4
	IFNg	IFNG	21	0.52	1.3	2.9
	IP-10	CXCL10	48	0.63	1.1	3.8
	MCP-1	CCL2	53	0.23	0.5	4
	MIP-1a	CCL3	55	0.22	0.6	5.3
	MIP-1b	CCL4	18	0.21	0.5	2.5
	PDGF	PDGF	47	0.45	2	3.8
	RANTES	CCL5	37	0.46	1	6.5
	TNFa	TNF	36	1.55	1.4	3.6
	VEGF	VEGF	45	0.47	1.1	4.1
Group II - 21-plex	IFNa2	IFNA2	20	0.93	1.7	9
	IL-1a	IL1A	63	0.13	1.1	3.3
	IL-2ra	IL2RA	13	0.70	1.1	11.1
	IL-3	IL3	64	1.64	0.9	6.4
	IL-12 (p40)	IL12B	28	0.40	1.4	7.6
	IL-16	IL16	27	0.51	1.3	6.8
	IL-18	IL18	42	0.09	6	8.6
	CTACK	CCL27	72	1.10	2.5	6.1
	GRO-a	CXCL1	61	1.87	1	5.6
	HGF	HGF	62	0.74	0.9	6
	LIF	LIF	29	0.54	0.9	2.9
	MCP-3	CCL7	26	0.31	1.5	10.9
	M-CSF	CSF1	67	0.53	1	4.8
	MIF	MIF	35	1.38	4.6	7.9
	MIG	CXCL9	14	1.50	1.3	9.7
	b-NGF	NGFB	46	0.21	0.9	5
	SCF	SCF	65	0.38	1.3	3.8
	SCGF-b	CLEC11A	78	5.72	1.5	5.8
	SDF-1a	CXCL12	22	1.19	1.3	12.3
	TNFb	TNFB	30	0.51	0.4	3.8
	TRAIL	TNFSF10	66	0.79	1.5	6.3
ICAM-1 singleplex	ICAM-1	ICAM1	12	0.95	1.3	5.4
VCAM-1 singleplex	VCAM-1	VCAM1	15	0.70	1.8	9.4

Table S10. Leukocyte Sub-populations Among Peritoneal Aspirates

Population	Surface Staining	Peripheral Blood[1]	Peritoneal Aspirate		
			Total	Adherent	Non-adherent
Leukocytes	CD45+	85%	98	98	98
Granulocytes	CD14+ CD68- CD10+	59 ± 20	<1	<1	<1
Monocytes/Macrophages	CD14+ CD68+ CD10-	6 ± 2	64 ± 7 74 ± 8**	96 ± 7	41 ± 6
Lymphocytes	CD14- CD68- CD10-	34 ± 8	20 ± 6	<5	60 ± 13

Values are mean ± s.d. percent composition of three donors.

[1]Peripheral blood values are reference ranges for healthy adults (Reichert et al. 1991, Bain 1996)

Table S11. Kinase Inhibitor Treatments

Inhibitor	Primary Target(s)	IC50 (nM)	Experimental Dose (uM)
LY294002	PI3Kβ	310	10
	PI3Kα	730	
	PI3Kδ	1,060	
	PI3Kγ	6,600	
PD98059	MEK1	4,000	50
	MEK2	50,000	
SB203580	p38α/MAPK14	50	10
	p38β/MAPK11	500	
SP600125	JNK1	40	10
	JNK2	40	
	JNK3	90	
BMS-345541	IKK2	300	10
	IKK1	4,000	
SU6656	SRC	280	10
	Fyn	170	
	Yes	20	
	Lyn	130	
JAK Inhibitor I	JAK1	15 (murine)	10
	JAK2	1	
	JAK3	5 (Ki50)	
	Tyk2	1	
Gö6983	PKCα	7	10
	PKCβ	7	
	PKCγ	6	
	PKCδ	10	
	PKCζ	60	