Fig. S1. HC and CFS networks have significantly different topology. Three frequency distributions are shown to compare the similar graph edit distances between consensus networks within each diagnostic category (green HC and red CFS), and contrast these with the graph edit distances between consensus networks drawn from different diagnostic categories (blue). The two distributions for HC and CFS diagnoses overlap, and so are stacked. Each indicates the distribution of graph edit distances between consensus networks of the same diagnostic category, and contains n(n-1)/2 = 45 distances, where n = 10 is the number of consensus networks calculated for both HC and CFS. The average graph edit distance between consensus networks is slightly lower in CFS (red) than HC (green), but similar (≈ 0.35). The average graph edit distance between two networks (blue), one HC and one CFS, is significantly larger (≈ 2.0); this distribution contains n×n = 100 distances.

Table S1. **A majority of the cytokines is differentially expressed in CFS**. Mean and median expression (pg/ml) of 16 cytokines in healthy controls and CFS patients including the dispersion of these values in terms of the standard error and median absolute deviation from the median (MAD). Significance of the difference in median (delta median) is estimated using a p-value calculated via the Wilcoxon rank-sum test for two independent samples. Values below the lower detection limit were set to zero.

	Healthy(HC)		CFS		Delta Median
Marker	Mean (std err [a])	Median (MAD [b])	Mean (std err)	Median (MAD)	p-value
IL1a	3.16 (0.48)	2.33 (1.45)	5.07 (8.13)	3.18 (1.32)	0.04
IL1b	17.53 (5.43)	6.25 (2.47)	47.39 (90.57)	13.44 (10.54)	0.04
IL2	4.20 (1.15)	2.50 (0.46)	11.12 (30.95)	2.28 (1.23)	0.42
IL4	1.69 (0.54)	0.51 (0.22)	12.09 (37.47)	1.65 (0.94)	0.00
IL5	6.43 (1.11)	3.84 (0.83)	13.39 (24.92)	7.37 (1.08)	0.00
IL6	6.79 (1.82)	3.24 (1.59)	17.06 (40.95)	6.45 (3.28)	0.00
IL8	19.86 (1.96)	15.40 (5.25)	22.26 (34.27)	8.96 (4.56)	0.00
IL10	7.17 (1.63)	3.58 (1.48)	5.87 (8.66)	3.31 (1.34)	0.75
IL12	3.18 (0.46)	2.03 (0.37)	9.38 (18.44)	4.42 (2.09)	0.00
IL13	0.46 (0.01)	0.44 (0.02)	0.42 (0.26)	0.36 (0.10)	0.00
IL15	43.43 (5.31)	27.38 (12.18)	29.14 (40.96)	13.54 (7.07)	0.00
IL17	7.38 (3.00)	2.86 (1.54)	5.75 (7.01)	3.75 (2.92)	0.78
IL23	641.60 (204.91)	97.84 (73.16)	344.07 (1094.72)	81.97 (12.43)	0.81
IFNg	13.31 (4.19)	2.59 (1.91)	17.02 (38.27)	3.11 (3.11)	0.47
LTa	9.69 (3.92)	2.12 (1.17)	19.36 (35.83)	7.48 (3.13)	0.00
TNFa	18.48 (5.75)	6.37 (1.72)	27.75 (50.15)	7.26 (5.09)	0.95

[a] std err is the standard error of the mean

[b] MAD is the median absolute deviation from the median, a robust dispersion

statistic such that $MAD=\overline{\left|x-\overline{X}^{*}\right|}^{*}$ and $\overline{X}^{*}$ indicates a median value.

Table S2. **A large majority of the cytokines was differentially related in CFS**. The role each node plays among the others within a network is highly influenced by its degree centrality and eigenvector centrality. Consequently, changes in centrality scores are important for understanding the cytokine network in CFS patients. Significance was estimated using a p-value calculated via Welsh's (Student's) t-test for samples with unequal variances.

	Mean Degree			Eigenvector Centrality		
Marker	HC	CFS	p-value	HC	CFS	p-value
IL1a	0.16 (0.01)	0.14 (0.01)	0.216	0.23 (0.02)	0.14 (0.01)	0.000
IL1b	0.32 (0.01)	0.46 (0.01)	0.000	0.44 (0.01)	0.59 (0.00)	0.000
IL2	0.19 (0.01)	0.31 (0.00)	0.000	0.24 (0.01)	0.45 (0.01)	0.000
IL4	0.19 (0.01)	0.37 (0.01)	0.000	0.30 (0.01)	0.49 (0.01)	0.000
IL5	0.23 (0.01)	0.04 (0.01)	0.000	0.30 (0.01)	0.01 (0.00)	0.000
IL6	0.31 (0.02)	0.18 (0.01)	0.000	0.41 (0.01)	0.10 (0.01)	0.000
IL8	0.01 (0.01)	0.03 (0.00)	0.019	0.02 (0.01)	0.04 (0.01)	0.171
IL10	0.02 (0.00)	0.16 (0.01)	0.000	0.03 (0.00)	0.03 (0.01)	0.588
IL12	0.41 (0.01)	0.29 (0.01)	0.000	0.49 (0.01)	0.29 (0.02)	0.000
IL13	0.32 (0.01)	0.07 (0.00)	0.000	0.41 (0.01)	0.03 (0.00)	0.000
IL15	0.43 (0.01)	0.41 (0.01)	0.174	0.53 (0.01)	0.52 (0.01)	0.138
IL17	0.23 (0.01)	0.04 (0.01)	0.000	0.28 (0.01)	0.02 (0.01)	0.000
IL23	0.02 (0.00)	0.05 (0.01)	0.000	0.02 (0.00)	0.01 (0.00)	0.276
IFNg	0.27 (0.01)	0.44 (0.01)	0.000	0.35 (0.01)	0.56 (0.00)	0.000
LTa	0.35 (0.01)	0.35 (0.01)	0.955	0.47 (0.01)	0.38 (0.01)	0.000
TNFa	0.32 (0.01)	0.48 (0.00)	0.000	0.44 (0.01)	0.59 (0.00)	0.000

Table S3. Coefficients of inter and intra-assay variation (CV) along with detection limits for each cytokine assay with the number of observations in the HC (n=59) and the CFS (n=40) groups below the lower limit of detection (LLD*), and the lowest non-zero concentration used for the standard curve (LSC). The LLD for the standard Quansys protocol is also shown for comparison.

| Cytokine | Modified Protocol * | | | | | | | | Standard Quansys Protocol | | |
	CV Inter	CV Intra	LLD* (pg/ml)	#CFS < LLD*	#HC < LLD*	LSC (pg/ml)	#CFS < LSC	#HC < LSC	LLD (pg/ml)	#CFS < LLD	#HC < LLD
IL-1a	0.12	0.05	(-0.72)	0	0	4.70	33	49	2.11	15	28
IL-1b	0.10	0.05	(-2.79)	0	0	5.50	12	25	2.43	6	2
IL-2	0.19	0.07	0.97	4	0	3.90	26	50	2.07	17	12
IL-4	0.19	0.07	(-0.99)	0	0	2.30	26	52	0.95	13	42
IL-5	0.15	0.05	(-0.11)	0	0	5.50	3	44	3.56	0	27
IL-6	0.30	0.08	0.20	0	1	4.30	13	39	3.5	8	32
IL-8	0.19	0.09	(-5.15)	0	0	5.50	11	1	0.22	0	0
IL-10	0.11	0.04	0.16	0	0	3.90	25	33	0.39	0	0
IL-12	0.62	0.36	(-0.45)	0	0	2.00	5	27	1.28	2	0
IL-13	0.23	0.08	(-0.06)	0	0	2.50	40	59	0.53	33	36
IL-15	0.21	0.07	(-4.09)	0	0	3.90	2	2	2.42	0	0
IL-17	0.15	0.10	1.00	11	7	2.70	15	27	1.12	12	7
IL-23	0.15	0.07	(-9.27)	0	0	23.40	2	8	28.55	2	11
IFNg	0.23	0.06	(-2.83)	0	0	2.70	20	32	0.16	11	6
TNFa	0.16	0.05	(-2.77)	0	0	4.70	13	9	1.66	2	0
Lta	0.16	0.07	(-0.31)	0	0	2.30	4	32	1.93	4	28
Avg CV inter-assay	0.20										
Avg CV intra-assay	0.09										

Table S4. Spearman cross-correlation coefficients for the expression of 16 cytokines in the Healthy Control group (HC).

	IL-1a	IL-1b	IL-2	IL-4	IL-5	IL-6	IL-8	IL-10	IL-12	IL-13	IL-15	IL-17	IL-23	IFNy	TNFa	Lta
IL-1a	1.00	0.43	0.46	0.44	0.64	0.51	0.28	0.22	0.70	0.46	0.74	0.52	0.31	0.50	0.51	0.52
IL-1b	0.43	1.00	0.47	0.56	0.41	0.71	0.40	0.20	0.55	0.62	0.60	0.41	0.32	0.69	0.83	0.77
IL-2	0.46	0.47	1.00	0.40	0.49	0.55	0.16	0.13	0.59	0.59	0.45	0.83	0.38	0.53	0.37	0.53
IL-4	0.44	0.56	0.40	1.00	0.33	0.38	0.25	0.27	0.62	0.38	0.60	0.39	0.26	0.52	0.68	0.66
IL-5	0.64	0.41	0.49	0.33	1.00	0.61	0.34	0.38	0.67	0.70	0.65	0.57	0.37	0.44	0.40	0.45
IL-6	0.51	0.71	0.55	0.38	0.61	1.00	0.38	0.37	0.57	0.78	0.59	0.56	0.29	0.58	0.59	0.58
IL-8	0.28	0.40	0.16	0.25	0.34	0.38	1.00	0.13	0.40	0.34	0.37	0.11	-0.03	0.30	0.39	0.39
IL-10	0.22	0.20	0.13	0.27	0.38	0.37	0.13	1.00	0.31	0.27	0.22	0.15	0.32	0.48	0.38	0.22
IL-12	0.70	0.55	0.59	0.62	0.67	0.57	0.40	0.31	1.00	0.61	0.74	0.57	0.40	0.60	0.58	0.65
IL-13	0.46	0.62	0.59	0.38	0.70	0.78	0.34	0.27	0.61	1.00	0.68	0.65	0.36	0.51	0.49	0.57
IL-15	0.74	0.60	0.45	0.60	0.65	0.59	0.37	0.22	0.74	0.68	1.00	0.58	0.35	0.55	0.61	0.66
IL-17	0.52	0.41	0.83	0.39	0.57	0.56	0.11	0.15	0.57	0.65	0.58	1.00	0.39	0.43	0.31	0.51
IL-23	0.31	0.32	0.38	0.26	0.37	0.29	-0.03	0.32	0.40	0.36	0.35	0.39	1.00	0.44	0.38	0.39
IFNy	0.50	0.69	0.53	0.52	0.44	0.58	0.30	0.48	0.60	0.51	0.55	0.43	0.44	1.00	0.77	0.64
TNFa	0.51	0.83	0.37	0.68	0.40	0.59	0.39	0.38	0.58	0.49	0.61	0.31	0.38	0.77	1.00	0.78
Lta	0.52	0.77	0.53	0.66	0.45	0.58	0.39	0.22	0.65	0.57	0.66	0.51	0.39	0.64	0.78	1.00

Table S5. Spearman cross-correlation coefficients for the expression of 16 cytokines in the CFS patient group (HC).

	IL-1a	IL-1b	IL-2	IL-4	IL-5	IL-6	IL-8	IL-10	IL-12	IL-13	IL-15	IL-17	IL-23	IFNy	TNFa	Lta
IL-1a	1.00	0.51	0.43	0.30	0.46	0.40	0.34	0.34	0.47	0.30	0.53	0.26	0.47	0.51	0.58	0.59
IL-1b	0.51	1.00	0.83	0.86	0.31	0.54	0.37	0.42	0.58	0.36	0.83	0.42	0.37	0.89	0.93	0.75
IL-2	0.43	0.83	1.00	0.75	0.17	0.33	0.35	0.33	0.44	0.21	0.81	0.33	0.34	0.77	0.86	0.53
IL-4	0.30	0.86	0.75	1.00	0.17	0.51	0.29	0.40	0.58	0.33	0.70	0.41	0.23	0.87	0.81	0.64
IL-5	0.46	0.31	0.17	0.17	1.00	0.52	0.10	0.44	0.43	0.32	0.40	0.38	0.25	0.24	0.29	0.27
IL-6	0.40	0.54	0.33	0.51	0.52	1.00	0.14	0.69	0.73	0.47	0.50	0.44	0.37	0.53	0.45	0.57
IL-8	0.34	0.37	0.35	0.29	0.10	0.14	1.00	-0.02	0.17	-0.07	0.42	-0.19	0.08	0.43	0.44	0.46
IL-10	0.34	0.42	0.33	0.40	0.44	0.69	-0.02	1.00	0.54	0.60	0.48	0.54	0.55	0.40	0.42	0.45
IL-12	0.47	0.58	0.44	0.58	0.43	0.73	0.17	0.54	1.00	0.52	0.56	0.33	0.32	0.57	0.54	0.63
IL-13	0.30	0.36	0.21	0.33	0.32	0.47	-0.07	0.60	0.52	1.00	0.38	0.34	0.28	0.41	0.33	0.31
IL-15	0.53	0.83	0.81	0.70	0.40	0.50	0.42	0.48	0.56	0.38	1.00	0.29	0.45	0.79	0.90	0.61
IL-17	0.26	0.42	0.33	0.41	0.38	0.44	-0.19	0.54	0.33	0.34	0.29	1.00	0.28	0.36	0.36	0.29
IL-23	0.47	0.37	0.34	0.23	0.25	0.37	0.08	0.55	0.32	0.28	0.45	0.28	1.00	0.30	0.38	0.39
IFNy	0.51	0.89	0.77	0.87	0.24	0.53	0.43	0.40	0.57	0.41	0.79	0.36	0.30	1.00	0.89	0.78
TNFa	0.58	0.93	0.86	0.81	0.29	0.45	0.44	0.42	0.54	0.33	0.90	0.36	0.38	0.89	1.00	0.71
Lta	0.59	0.75	0.53	0.64	0.27	0.57	0.46	0.45	0.63	0.31	0.61	0.29	0.39	0.78	0.71	1.00

Figure S1

Fig.S1. Broderick, Formal Anal. of Cytokine Networks