Data Article

# TH1 and TH2 cytokine data in insulin secretagogues users newly diagnosed with breast cancer

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## ARTICLE INFO

## ABSTRACT

Stimulation of insulin production by insulin secretagogue use may impact T helper cells' cytokine production. This dataset presents the relationship between baseline insulin secretagogues use in women diagnosed with breast cancer and type 2 diabetes mellitus, the T-helper 1 and 2 produced cytokine profiles at the time of breast cancer diagnosis, and subsequent cancer outcomes. A Pearson correlation analysis evaluating the relationship between T-helper cytokines stratified by of insulin secretagogues use and controls is also provided.

## Specifications Table

| | |
|---|---|
| Subject area | Clinical and Translational Research |
| More specific subject area | Biomarker Research, Cancer Epidemiology |
| Type of data | Tables |
| How data was acquired | Tumor registry query was followed by vital status ascertainment, and medical records review |
| | Luminex®-based quantitation from plasma samples was conducted for the following T-helper 1 and T-helper 2 cytokines: Interleukin-2, soluble interleukine-2 receptor α, interleukine-12 subunit p40, interleukine-12 subunit p70, interferon α 2, interferon γ, chemokine ligand 10 (interferon gamma-induced protein 10), chemokine ligand 9 (monokine-induced by interferon γ), chemokine ligand 8 (interleukine-8) interleukine-5, interleukine-10, and interleukine-13. |
| | A Luminex®200™ instrument with Xponent 3.1 software was used to acquire all data |
| Data format | Analyzed |
| Experimental factors | T-helper 1 and 2 produced cytokines were determined from the corresponding plasma samples collected at the time of breast cancer diagnosis |
| Experimental features | The dataset included 97 adult females with diabetes mellitus and newly diagnosed breast cancer (cases) and 194 matched controls (breast cancer only). Clinical and treatment history were evaluated in relationship with cancer outcomes and factor-helper 1 and 2 produced cytokine profiles. A cytokine correlation analysis was also performed. |
| Data source location | United States, Buffalo, NY - 42° 53' 50.3592"N; 78° 52' 2.658"W |
| Data accessibility | The data is with this article |

## Value of the data

- This dataset represents the observed relationship between insulin secretagogues use, circulating T-helper 1 and 2 produced cytokines at breast cancer diagnosis and cancer outcomes
- Presented data has the potential to guide future research exploring the potential use of insulin secretagogues in the modulation of type 1 and type 2 immunity
- Our observations can assist further research exploring the relationship between insulin secretagogues use and T-helper-driven signaling in the occurrence of breast cancer.

## 1. Data

Reported data represents the observed association between pre-existing use of injectable insulin before breast cancer diagnosis and the T-helper 1 and 2 produced cytokine profiles upon cancer diagnosis in women with both breast cancer and diabetes mellitus (Table 1). Data in Table 2 includes the observed correlations between T-helper 1 and 2 cytokines stratified by diabetes mellitus pharmacotherapy and controls.

## 2. Experimental design, materials and methods

Evaluation of the association between profiles of T-helper 1 and 2 produced cytokines, injectable insulin use and BC outcomes was carried out under two protocols approved by both Roswell Park Cancer Institute (EDR154409 and NHR009010) and the State University of New York at Buffalo

**Table 1**
T-Helper 1 and 2 produced cytokines' associations with secretagogue use.

| Biomarker | Biomarker Grouping | Concentration (ng/ml) | Control | No Secretagogue | Any Secretagogue | Unadjusted p-value (MVP) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | p[1] | p[2] | p[3] | Global Tesr |
| IL-2 (pg/ml) | Median | – | 1.60 | 1.60 | 1.60 | 0.420 | 0.760 | 0.400 | 0.650 |
| | (25th–75th) | | (1.60–3.2) | (1.60–3.46) | (1.60–3.20) | (0.100) | (0.970) | (0.300) | (0.170) |
| | OS-Based | 0.10 to 34.18 | 189 (97.4%) | 43 (91.5%) | 49 (98.0%) | 0.080 | 1.000 | 0.200 | 0.140 |
| | Optimization | **35.37 to 516.64** | 5 (2.6%) | 4 (8.5%) | 1 (2.0%) | (0.080) | (0.780) | (0.080) | (0.180) |
| | DFS-Based | **0.10 to 1.94** | 131 (67.5%) | 29 (61.7%) | 34 (68.0%) | 0.450 | 0.950 | 0.520 | 0.730 |
| | Optimization | 1.99 to 516.64 | 63 (32.5%) | 18 (38.3%) | 16 (32.0%) | (0.440) | (0.660) | (0.510) | (0.660) |
| sIL-2Rα (pg/ml) | Median | – | 3.20 | 6.38 | 12.07 | 0.430 | 0.240 | 0.880 | 0.430 |
| | (25th–75th) | | (1.60–47.32) | (1.60–98.14) | (1.60–60.42) | (0.100) | (0.630) | (0.230) | (0.210) |
| | Quartiles | 0.00 to 1.60 | 84 (43.3%) | 20 (42.6%) | 16 (32.0%) | 0.270 | 0.460 | 0.270 | 0.350 |
| | | 1.70 to 7.00 | 16 (8.2%) | 4 (8.5%) | 6 (12.0%) | | | | |
| | | 7.12 to 57.42 | 50 (25.8%) | 7 (14.9%) | 15 (30.0%) | | | | |
| | | 57.68 to ALQ | 44 (22.7%) | 16 (34.0%) | 13 (26.0%) | | | | |
| | OS-Based | 0.00 to 63.34 | 155 (79.9%) | 32 (68.1%) | 37 (74.0%) | 0.080 | 0.370 | 0.520 | 0.190 |
| | Optimization | **63.37 to ALQ*** | 39 (20.1%) | 15 (31.9%) | 13 (26.0%) | (0.070) | (0.070) | (0.900) | (0.100) |
| | DFS-Based | 0.00 to 62.50 | 153 (78.9%) | 32 (68.1%) | 37 (74.0%) | 0.120 | 0.460 | 0.520 | 0.270 |
| | Optimization | **62.65 to ALQ*** | 41 (21.1%) | 15 (31.9%) | 13 (26.0%) | (0.120) | (0.100) | (0.900) | (0.160) |
| IL-12p40 (pg/ml) | Median | – | 8.16 | 16.02 | 10.10 | 0.110 | 0.430 | 0.400 | 0.230 |
| | (25th–75th) | | (1.75–30.81) | (4.59–41.28) | (3.39–28.42) | (0.090) | (0.560) | (0.110) | (0.180) |
| | Quartiles | 1.25 to 3.20 | 74 (38.1%) | 11 (23.4%) | 13 (26.0%) | 0.230 | 0.160 | 0.560 | 0.190 |
| | | 3.94 to 9.74 | 29 (14.9%) | 7 (14.9%) | 12 (24.0%) | | | | |
| | | 9.94 to 30.67 | 42 (21.6%) | 15 (31.9%) | 15 (30.0%) | | | | |
| | | 30.92 to 2045.71 | 49 (25.3%) | 14 (29.8%) | 10 (20.0%) | | | | |
| | OS-Based | 1.25 to 3.12 | 53 (27.3%) | 8 (17.0%) | 9 (18.0%) | 0.150 | 0.180 | 0.900 | 0.180 |
| | Optimization | **3.20 to 2045.71** | 141 (72.7%) | 39 (83.0%) | 41 (82.0%) | (0.210) | (0.210) | (0.480) | (0.320) |
| | DFS-Based | 1.25 to 3.12 | 53 (27.3%) | 8 (17.0%) | 9 (18.0%) | 0.150 | 0.180 | 0.900 | 0.180 |
| | Optimization | **3.20 to 2045.71*** | 141 (72.7%) | 39 (83.0%) | 41 (82.0%) | (0.210) | (0.210) | (0.480) | (0.320) |
| IL-12p70 (pg/ml) | Median | – | 1.60 | 3.20 | 2.12 | 0.013 | 0.440 | 0.190 | 0.047 |
| | (25th–75th) | | (1.60–3.20) | (1.60–7.06) | (1.60–4.40) | (0.023) | (0.980) | (0.270) | (0.053) |
| | OS-Based | **0.10 to 0.59** | 5 (2.6%) | 2 (4.3%) | 4 (8.0%) | 0.620 | 0.090 | 0.680 | 0.140 |
| | Optimization | 0.70 to 2510.07 | 189 (97.4%) | 45 (95.7%) | 46 (92.0%) | (0.460) | (0.190) | (0.740) | (0.450) |

**Table 1** (*continued*)

| Biomarker | Biomarker Grouping | Concentration (ng/ml) | Control | No Secretagogue | Any Secretagogue | | Unadjusted p-value (MVP) | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | $p^1$ | $p^2$ | $p^3$ | Global Test |
| DFS-Based Optimization | 0.10 to 2.20 | 120 (61.9%) | 20 (42.6%) | 25 (50.0%) | 0.018 (0.033) | | 0.130 (0.380) | 0.460 (0.420) | | 0.033 (0.100) |
| | **2.28 to 2510.07** | 74 (38.1%) | 27 (57.4%) | 25 (50.0%) | | | | | | |
| IFN-α2 (pg/ml) | Median (25th–75th) | – | 7.24 (3.20–13.61) | 7.39 (3.20–22.78) | 8.00 (3.87–16.94) | | 0.460 (0.230) | 0.300 (0.830) | 0.980 (0.270) | 0.510 (0.410) |
| | Quartiles | 0.61 to 1.60 | 56 (28.9%) | 15 (31.9%) | 12 (24.0%) | | 0.390 | 0.790 | 0.680 | 0.710 |
| | | 3.47 to 7.40 | 42 (21.6%) | 9 (19.1%) | 12 (24.0%) | | | | | |
| | | 7.43 to 15.15 | 52 (26.8%) | 8 (17.0%) | 12 (24.0%) | | | | | |
| | | 15.32 to 1880.18 | 44 (22.7%) | 15 (31.9%) | 14 (28.0%) | | | | | |
| | OS-Based Optimization | 0.61 to 4.18 | 63 (32.5%) | 17 (36.2%) | 13 (26.0%) | | 0.630 (0.600) | 0.380 (0.990) | 0.280 (0.430) | 0.540 (0.720) |
| | | **4.18 to 1880.18*** | 131 (67.5%) | 30 (63.8%) | 37 (74.0%) | | | | | |
| | DFS-Based Optimization | 0.61 to 2.66 | 29 (14.9%) | 7 (14.9%) | 3 (6.0%) | | 0.990 (0.600) | 0.110 (0.047) | 0.190 (0.130) | 0.240 (0.100) |
| | | **2.93 to 1880.18** | 165 (85.1%) | 40 (85.1%) | 47 (94.0%) | | | | | |
| IFN-γ (pg/ml) | Median (25th–75th) | – | 13.32 (4.70–36.30) | 11.26 (3.20–42.84) | 8.53 (2.80–34.28) | | 0.620 (0.860) | 0.140 (0.420) | 0.550 (0.450) | 0.350 (0.770) |
| | Quartiles | 0.07 to 3.86 | 42 (21.6%) | 13 (27.7%) | 18 (36.0%) | | 0.300 | 0.120 | 0.780 | 0.200 |
| | | 4.03 to 12.43 | 50 (25.8%) | 11 (23.4%) | 12 (24.0%) | | | | | |
| | | 12.55 to 37.33 | 56 (28.9%) | 8 (17.0%) | 8 (16.0%) | | | | | |
| | | 38.74 to 646.43 | 46 (23.7%) | 15 (31.9%) | 12 (24.0%) | | | | | |
| | OS-Based Optimization | 0.07 to 230.77 | 188 (96.9%) | 44 (93.6%) | 49 (98.0%) | | 0.380 (0.350) | 1.000 (0.840) | 0.350 (0.150) | 0.550 (0.490) |
| | | **376.09 to 646.43** | 6 (3.1%) | 3 (6.4%) | 1 (2.0%) | | | | | |
| | DFS-Based Optimization | 0.07 to 187.14 | 187 (96.4%) | 43 (91.5%) | 49 (98.0%) | | 0.230 (0.250) | 1.000 (0.690) | 0.200 (0.080) | 0.250 (0.300) |
| | | **206.34 to 646.43*** | 7 (3.6%) | 4 (8.5%) | 1 (2.0%) | | | | | |
| CXCL-10 (IP-10, pg/ml) | Median (25th–75th) | – | 488 (347–814) | 440 (338–728) | 470 (355–662) | | 0.650 (0.990) | 0.680 (0.210) | 0.910 (0.170) | 0.850 (0.350) |
| | Quartiles | 1.6 to 344.8 | 48 (24.7%) | 13 (27.7%) | 12 (24.0%) | | 0.960 | 0.920 | 0.950 | 0.990 |
| | | 346.1 to 484.3 | 48 (24.7%) | 11 (23.4%) | 14 (28.0%) | | | | | |
| | | 484.5 to 748.4 | 47 (24.2%) | 12 (25.5%) | 13 (26.0%) | | | | | |
| | | 751.0 to 3745.0 | 51 (26.3%) | 11 (23.4%) | 11 (22.0%) | | | | | |
| | OS-Based Optimization | 1.6 to 428.3 | 81 (41.8%) | 22 (46.8%) | 21 (42.0%) | | 0.530 (0.390) | 0.970 (0.910) | 0.630 (0.820) | 0.820 (0.800) |
| | | **428.9 to 3745.0*** | 113 (58.2%) | 25 (53.2%) | 29 (58.0%) | | | | | |
| | DFS-Based Optimization | 1.6 to 549.1 | 114 (58.8%) | 27 (57.4%) | 31 (62.0%) | | 0.870 (0.830) | 0.680 (0.440) | 0.650 (0.500) | 0.890 (0.680) |
| | | **549.1 to 3745.0*** | 80 (41.2%) | 20 (42.6%) | 19 (38.0%) | | | | | |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| CXCL-9 (MIG, pg/ml) | Median (25th–75th) | – | 274 (119–504) | 148 (67–637) | 227 (120–509) | 0.420 (0.220) | 0.730 (0.270) | 0.550 (0.840) | 0.690 (0.410) |
| | Quartiles | 1.9 to 103.9 | 46 (23.7%) | 17 (36.2%) | 10 (20.0%) | 0.090 | 0.600 | 0.200 | 0.190 |
| | | 104.9 to 263.1 | 47 (24.2%) | 10 (21.3%) | 16 (32.0%) | | | | |
| | | 264.3 to 512.2 | 55 (28.4%) | 6 (12.8%) | 11 (22.0%) | | | | |
| | | 519.4 to 2691.0 | 46 (23.7%) | 14 (29.8%) | 13 (26.0%) | | | | |
| | OS-Based Optimization | 1.9 to 120.1 | 49 (25.3%) | 21 (44.7%) | 13 (26.0%) | 0.010 (0.002) | 0.910 (0.470) | 0.060 (0.120) | 0.027 (0.013) |
| | | **121.4 to 2691.0***| 145 (74.7%) | 26 (55.3%) | 37 (74.0%) | | | | |
| | DFS-Based Optimization | 1.9 to 120.1 | 49 (25.3%) | 21 (44.7%) | 13 (26.0%) | 0.010 (0.002) | 0.910 (0.470) | 0.060 (0.120) | 0.027 (0.013) |
| | | **121.4 to 2691.0***| 145 (74.7%) | 26 (55.3%) | 37 (74.0%) | | | | |
| CXCL-8 (IL-8, pg/ml) | Median (25th–75th) | – | 4.44 (2.50–6.86) | 6.07 (3.90–9.12) | 5.72 (4.43–8.35) | 0.008 (0.090) | 0.003 (0.090) | 0.880 (0.960) | 0.001 (0.090) |
| | Quartiles | 0.36 to 3.07 | 61 (31.4%) | 6 (12.8%) | 7 (14.0%) | 0.018 | 0.070 | 0.920 | 0.022 |
| | | 3.15 to 4.89 | 47 (24.2%) | 12 (25.5%) | 13 (26.0%) | | | | |
| | | 4.91 to 7.53 | 47 (24.2%) | 11 (23.4%) | 14 (28.0%) | | | | |
| | | 7.68 to 74.69 | 39 (20.1%) | 18 (38.3%) | 16 (32.0%) | | | | |
| | OS-Based Optimization | 0.36 to 17.15 | 187 (96.4%) | 45 (95.7%) | 49 (98.0%) | 0.690 (0.900) | 1.000 (0.740) | 0.610 (0.270) | 0.800 (0.830) |
| | | **19.66 to 74.69***| 7 (3.6%) | 2 (4.3%) | 1 (2.0%) | | | | |
| | DFS-Based Optimization | 0.36 to 17.15 | 187 (96.4%) | 45 (95.7%) | 49 (98.0%) | 0.690 (0.900) | 1.000 (1.000) | 0.610 (0.270) | 0.800 (0.830) |
| | | **19.66 to 74.69***| 7 (3.6%) | 2 (4.3%) | 1 (2.0%) | | | | |
| IL-5 (pg/ml) | Median, ng/ml (25th–75th) | – | 0.48 (0.35–0.77) | 0.45 (0.3–0.77) | 0.35 (0.3–0.57) | 0.610 (0.680) | 0.011 (0.320) | 0.160 (0.100) | 0.043 (0.320) |
| | Quartiles | 0.08 to 0.30 | 38 (19.6%) | 17 (36.2%) | 21 (42.0%) | 0.017 | 0.008 | 0.230 | 0.005 |
| | | 0.35 to 0.48 | 76 (39.2%) | 8 (17.0%) | 14 (28.0%) | | | | |
| | | 0.57 to 0.77 | 49 (25.3%) | 14 (29.8%) | 7 (14.0%) | | | | |
| | | 0.85 to 118 | 31 (16.0%) | 8 (17.0%) | 8 (16.0%) | | | | |
| | OS-Based Optimization | 0.08 to 0.38 | 66 (34.0%) | 20 (42.6%) | 26 (52.0%) | 0.270 (0.250) | 0.021 (0.170) | 0.350 (0.540) | 0.054 (0.180) |
| | | **0.45 to 118***| 128 (66.0%) | 27 (57.4%) | 24 (48.0%) | | | | |
| | DFS-Based Optimization | 0.08 to 0.38 | 66 (34.0%) | 20 (42.6%) | 26 (52.0%) | 0.270 (0.0250) | 0.021 (0.170) | 0.350 (0.540) | 0.054 (0.180) |
| | | **0.45 to 118** | 128 (66.0%) | 27 (57.4%) | 24 (48.0%) | | | | |
| IL-10 (pg/ml) | Median, ng/ml (25th–75th) | – | 1.60 (1.60–6.59) | 3.20 (1.60–12.91) | 1.95 (1.60–4.70) | 0.220 (0.150) | 0.890 (0.770) | 0.290 (0.210) | 0.440 (0.230) |
| | Quartiles | 0.18 to 1.6 | 100 (51.5%) | 19 (40.4%) | 22 (44.0%) | 0.330 | 0.190 | 0.110 | 0.180 |
| | | 1.61 to 1.78 | 3 (1.5%) | 0 (0%) | 2 (4.0%) | | | | |
| | | 1.82 to 8.80 | 44 (22.7%) | 11 (23.4%) | 17 (34.0%) | | | | |
| | | 8.96 to 1197.53 | 47 (24.2%) | 17 (36.2%) | 9 (18.0%) | | | | |
| | OS-Based Optimization | 0.18 to 3.20 | 114 (58.8%) | 21 (44.7%) | 28 (56.0%) | 0.080 (0.080) | 0.720 (0.600) | 0.270 (0.360) | 0.220 (0.200) |
| | | **3.20 to 1197.53***| 80 (41.2%) | 26 (55.3%) | 22 (44.0%) | | | | |
| | DFS-Based Optimization | 0.18 to 1.90 | 105 (54.1%) | 19 (40.4%) | 25 (50.0%) | 0.090 (0.080) | 0.600 (0.510) | 0.340 (0.380) | 0.240 (0.220) |
| | | **2.00 to 1197.53***| 89 (45.9%) | 28 (59.6%) | 25 (50.0%) | | | | |

**Table 1** (*continued* )

| Biomarker | Biomarker Grouping | Concentration (ng/ml) | Control | No Secretagogue | Any Secretagogue | Unadjusted p-value (MVP) | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | p[1] | p[2] | p[3] | Global Tesr |
| IL-13 (pg/ml) | Median, ng/ml | – | 1.60 | 1.60 | 1.60 | 0.810 | 0.290 | 0.590 | 0.580 |
| | (25th–75th) | | (1.60–4.49) | (1.60–4.38) | (1.60–3.13) | (0.760) | (0.330) | (0.140) | (0.520) |
| | OS-Based | 0.00 to 1.55 | 24 (12.4%) | 7 (14.9%) | 8 (16.0%) | 0.640 | 0.500 | 0.880 | 0.760 |
| | Optimization | **1.60 to 1239.25***| 170 (87.6%) | 40 (85.1%) | 42 (84.0%) | (0.450) | (0.410) | (0.550) | (0.570) |
| | DFS-Based | 0.00 to 1.01 | 19 (9.8%) | 5 (10.6%) | 5 (10.0%) | 0.790 | 1.000 | 1.000 | 0.960 |
| | Optimization | **1.16 to 1239.25** | 175 (90.2%) | 42 (89.4%) | 45 (90.0%) | (0.720) | (0.970) | (0.620) | (0.900) |

\* Overall survival (OS)- and disease-free survival (DFS)-optimized biomarker ranges associated with poorer outcomes are represented in bold. ALQ=above limit of quantitation. MVP= p-value of the multivariate adjusted analysis. Interleukine-2, IL-2; soluble interleukine-2 receptor α, sIL-2Rα; interleukine-12 subunit p40, IL-12p40; interleukine-12 subunit p70, IL-12p70; interferon α 2, IFN-α2; interferon γ, IFN-γ; chemokine ligand 10, CXCL-10 (interferon gamma-induced protein 10, IP-10); chemokine ligand 9, CXCL-9 (monokine-induced by interferon γ, MIG); chemokine ligand 8, CXCL-8 (interleukine-8, IL-8); interleukine-5, IL-5; interleukine-10, IL-10; interleukine-13, IL-13.

**Table 2**
T-Helper 1 and 2 produced cytokines' correlations by secretagogue use.

| Compared Biomarkers | | Group | Unadjusted Correlation | | | Adjusted Correlation | | |
|---|---|---|---|---|---|---|---|---|
| | | | Pearson Correlation | 95% Confidence Interval | p-value | Pearson Correlation | 95% Confidence Interval | p-value |
| IL-2 | sIL-2Rα | All Subjects (n=291) | **0.268** | **0.158 to 0.371** | **<0.001** | **0.278** | **0.168 to 0.381** | **<0.001** |
| | | Controls (n=194) | **0.197** | **0.058 to 0.329** | **0.006** | **0.212** | **0.072 to 0.344** | **0.003** |
| | | No Secretagogue (n=43) | **0.486** | **0.218 to 0.686** | **<0.001** | **0.478** | **0.196 to 0.687** | **0.001** |
| | | Any Secretagogue (n=54) | -0.068 | -0.330 to 0.204 | 0.624 | -0.024 | -0.298 to 0.253 | 0.865 |
| IL-2 | IL-12p40 | All Subjects (n=291) | **0.454** | **0.357 to 0.540** | **<0.001** | **0.454** | **0.357 to 0.541** | **<0.001** |
| | | Controls (n=194) | **0.711** | **0.634 to 0.775** | **<0.001** | **0.722** | **0.647 to 0.784** | **<0.001** |
| | | No Secretagogue (n=43) | **0.411** | **0.126 to 0.633** | **0.005** | **0.431** | **0.138 to 0.655** | **0.004** |
| | | Any Secretagogue (n=54) | **0.672** | **0.494 to 0.797** | **<0.001** | **0.646** | **0.451 to 0.782** | **<0.001** |
| IL-2 | IL-12p70 | All Subjects (n=291) | **0.250** | **0.139 to 0.354** | **<0.001** | **0.253** | **0.142 to 0.358** | **<0.001** |
| | | Controls (n=194) | **0.461** | **0.342 to 0.565** | **<0.001** | **0.463** | **0.344 to 0.568** | **<0.001** |
| | | No Secretagogue (n=43) | 0.212 | -0.094 to 0.482 | 0.168 | 0.243 | -0.074 to 0.516 | 0.126 |
| | | Any Secretagogue (n=54) | 0.117 | -0.156 to 0.373 | 0.398 | 0.096 | -0.185 to 0.362 | 0.501 |
| IL-2 | IFN-α2 | All Subjects (n=291) | **0.339** | **0.233 to 0.437** | **<0.001** | **0.339** | **0.232 to 0.437** | **<0.001** |
| | | Controls (n=194) | **0.494** | **0.380 to 0.594** | **<0.001** | **0.493** | **0.378 to 0.594** | **<0.001** |
| | | No Secretagogue (n=43) | **0.631** | **0.407 to 0.783** | **<0.001** | **0.645** | **0.417 to 0.796** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.110 | -0.162 to 0.367 | 0.426 | 0.099 | -0.182 to 0.364 | 0.488 |
| IL-2 | IFN-γ | All Subjects (n=291) | **0.379** | **0.276 to 0.473** | **<0.001** | **0.387** | **0.285 to 0.481** | **<0.001** |
| | | Controls (n=194) | **0.529** | **0.419 to 0.623** | **<0.001** | **0.531** | **0.421 to 0.626** | **<0.001** |
| | | No Secretagogue (n=43) | **0.604** | **0.370 to 0.765** | **<0.001** | **0.639** | **0.409 to 0.793** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.163 | -0.109 to 0.413 | 0.235 | 0.146 | -0.135 to 0.405 | 0.305 |
| IL-2 | CXCL-10 (IP-10) | All Subjects (n=291) | -0.027 | -0.142 to 0.088 | 0.641 | -0.031 | -0.146 to 0.085 | 0.603 |
| | | Controls (n=194) | 0.011 | -0.130 to 0.152 | 0.874 | 0.009 | -0.130 to 0.151 | 0.898 |
| | | No Secretagogue (n=43) | -0.059 | -0.353 to 0.246 | 0.706 | -0.034 | -0.342 to 0.280 | 0.834 |
| | | Any Secretagogue (n=54) | -0.148 | -0.400 to 0.124 | 0.281 | -0.169 | -0.424 to 0.055 | 0.111 |
| IL-2 | CXCL-9 (MIG) | All Subjects (n=291) | **0.192** | **0.079 to 0.300** | **0.001** | **0.183** | **0.069 to 0.293** | **0.002** |
| | | Controls (n=194) | **0.170** | **0.030 to 0.303** | **0.018** | **0.160** | **0.018 to 0.295** | **0.027** |
| | | No Secretagogue (n=43) | **0.382** | **0.092 to 0.612** | **0.010** | **0.387** | **0.086 to 0.623** | **0.012** |
| | | Any Secretagogue (n=54) | -0.029 | -0.295 to 0.240 | 0.832 | -0.107 | -0.372 to 0.174 | 0.452 |
| IL-2 | CXCL-8 (IL-8) | All Subjects (n=291) | **0.163** | **0.049 to 0.273** | **0.005** | **0.159** | **0.044 to 0.270** | **0.007** |
| | | Controls (n=194) | **0.379** | **0.252 to 0.494** | **<0.001** | **0.396** | **0.269 to 0.509** | **<0.001** |
| | | No Secretagogue (n=43) | **0.333** | **0.037 to 0.576** | **0.027** | **0.317** | **0.006 to 0.572** | **0.043** |
| | | Any Secretagogue (n=54) | -0.160 | -0.410to 0.113 | 0.245 | -0.224 | -0.470 to 0.055 | 0.111 |
| IL-2 | IL-5 | All Subjects (n=291) | 0.082 | -0.034 to 0.195 | 0.164 | 0.080 | -0.036 to 0.193 | 0.177 |
| | | Controls (n=194) | 0.060 | -0.082 to 0.199 | 0.406 | 0.057 | -0.086 to 0.197 | 0.433 |
| | | No Secretagogue (n=43) | 0.207 | -0.099 to 0.478 | 0.178 | 0.216 | -0.102 to 0.494 | 0.176 |
| | | Any Secretagogue (n=54) | -0.069 | -0.331 to 0.202 | 0.616 | -0.082 | -0.350 to 0.198 | 0.566 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| IL-2 | IL-10 | All Subjects (n=291) | **0.174** | **0.060 to 0.283** | **0.003** | **0.180** | **0.066 to 0.289** | **0.002** |
| | | Controls (n=194) | **0.553** | **0.447 to 0.644** | **<0.001** | **0.565** | **0.460 to 0.654** | **<0.001** |
| | | No Secretagogue (n=43) | 0.109 | -0.197 to 0.397 | 0.482 | 0.134 | -0.186 to 0.427 | 0.408 |
| | | Any Secretagogue (n=54) | **0.550** | **0.331 to 0.713** | **<0.001** | **0.521** | **0.286 to 0.696** | **<0.001** |
| IL-2 | IL-13 | All Subjects (n=291) | 0.102 | -0.013 to 0.214 | 0.082 | 0.111 | -0.005 to 0.224 | 0.059 |
| | | Controls (n=194) | **0.235** | **0.098 to 0.364** | **<0.001** | **0.241** | **0.103 to 0.371** | **<0.001** |
| | | No Secretagogue (n=43) | 0.213 | -0.093 to 0.483 | 0.166 | 0.239 | -0.079 to 0.512 | 0.134 |
| | | Any Secretagogue (n=54) | **0.415** | **0.166 to 0.614** | **0.002** | **0.380** | **0.116 to 0.593** | **0.005** |
| sIL-2Rα | IL-12p40 | All Subjects (n=291) | **0.355** | **0.251 to 0.452** | **<0.001** | **0.357** | **0.252 to 0.454** | **<0.001** |
| | | Controls (n=194) | **0.142** | **0.001 to 0.277** | **0.048** | **0.145** | **0.003 to 0.281** | **0.044** |
| | | No Secretagogue (n=43) | **0.689** | **0.490 to 0.820** | **<0.001** | **0.720** | **0.527 to 0.843** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.124 | -0.379 to 0.149 | 0.371 | -0.117 | -0.380 to 0.164 | 0.413 |
| sIL-2Rα | IL-12p70 | All Subjects (n=291) | **0.210** | **0.097 to 0.317** | **<0.001** | **0.208** | **0.095 to 0.316** | **<0.001** |
| | | Controls (n=194) | 0.009 | -0.132 to 0.150 | 0.896 | 0.012 | -0.130 to 0.154 | 0.868 |
| | | No Secretagogue (n=43) | **0.491** | **0.224 to 0.690** | **<0.001** | **0.543** | **0.278 to 0.731** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.006 | -0.273 to 0.262 | 0.967 | 0.025 | -0.253 to 0.298 | 0.862 |
| sIL-2Rα | IFN-α2 | All Subjects (n=291) | **0.164** | **0.050 to 0.274** | **0.005** | **0.165** | **0.050 to 0.275** | **0.005** |
| | | Controls (n=194) | 0.042 | -0.100 to 0.182 | 0.563 | 0.046 | -0.096 to 0.187 | 0.526 |
| | | No Secretagogue (n=43) | **0.665** | **0.455 to 0.804** | **<0.001** | **0.688** | **0.480 to 0.823** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.013 | -0.280 to 0.255 | 0.923 | 0.026 | -0.251 to 0.300 | 0.854 |
| sIL-2Rα | IFN-γ | All Subjects (n=291) | **0.468** | **0.373 to 0.553** | **<0.001** | **0.466** | **0.371 to 0.552** | **<0.001** |
| | | Controls (n=194) | **0.466** | **0.348 to 0.569** | **<0.001** | **0.469** | **0.350 to 0.572** | **<0.001** |
| | | No Secretagogue (n=43) | **0.569** | **0.324 to 0.742** | **<0.001** | **0.628** | **0.394 to 0.786** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.111 | -0.161 to 0.368 | 0.421 | 0.180 | -0.101 to 0.434 | 0.203 |
| sIL-2Rα | CXCL-10 (IP-10) | All Subjects (n=291) | -0.039 | -0.153 to 0.077 | 0.511 | -0.032 | -0.147 to 0.084 | 0.587 |
| | | Controls (n=194) | -0.038 | -0.178 to 0.104 | 0.599 | -0.027 | -0.168 to 0.115 | 0.709 |
| | | No Secretagogue (n=43) | -0.052 | -0.347 to 0.253 | 0.741 | -0.037 | -0.344 to 0.278 | 0.821 |
| | | Any Secretagogue (n=54) | -0.068 | -0.329 to 0.204 | 0.625 | 0.016 | -0.261 to 0.290 | 0.912 |
| sIL-2Rα | CXCL-9 (MIG) | All Subjects (n=291) | **0.119** | **0.004 to 0.231** | **0.042** | **0.123** | **0.007 to 0.235** | **0.037** |
| | | Controls (n=194) | **0.150** | **0.009 to 0.285** | **0.036** | **0.158** | **0.016 to 0.293** | **0.029** |
| | | No Secretagogue (n=43) | 0.104 | -0.202 to 0.392 | 0.503 | 0.097 | -0.221 to 0.397 | 0.549 |
| | | Any Secretagogue (n=54) | 0.043 | -0.227 to 0.307 | 0.756 | 0.066 | -0.213 to 0.336 | 0.641 |
| sIL-2Rα | CXCL-8 (IL-8) | All Subjects (n=291) | **0.146** | **0.032 to 0.257** | **0.012** | **0.155** | **0.040 to 0.266** | **0.008** |
| | | Controls (n=194) | **0.149** | **0.008 to 0.284** | **0.038** | **0.150** | **0.008 to 0.286** | **0.037** |
| | | No Secretagogue (n=43) | 0.241 | -0.064 to 0.504 | 0.116 | 0.224 | -0.095 to 0.500 | 0.161 |
| | | Any Secretagogue (n=54) | -0.041 | -0.305 to 0.230 | 0.769 | 0.055 | -0.224 to 0.326 | 0.698 |
| sIL-2Rα | IL-5 | All Subjects (n=291) | 0.091 | -0.024 to 0.204 | 0.121 | 0.092 | -0.023 to 0.206 | 0.117 |
| | | Controls (n=194) | -0.023 | -0.163 to 0.118 | 0.752 | -0.020 | -0.161 to 0.123 | 0.788 |
| | | No Secretagogue (n=43) | **0.660** | **0.449 to 0.802** | **<0.001** | **0.678** | **0.465 to 0.817** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.022 | -0.247 to 0.288 | 0.871 | 0.019 | -0.258 to 0.293 | 0.893 |

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|---|---|---|---|---|---|---|---|
| sIL-2Rα | IL-10 | All Subjects (n=291) | **0.236** | **0.124 to 0.341** | **<0.001** | **0.234** | **0.122 to 0.340** | **<0.001** |
| | | Controls (n=194) | 0.054 | -0.088 to 0.193 | 0.456 | 0.053 | -0.090 to 0.193 | 0.470 |
| | | No Secretagogue (n=43) | **0.496** | **0.230 to 0.693** | **<0.001** | **0.541** | **0.276 to 0.730** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.029 | -0.295 to 0.240 | 0.833 | 0.059 | -0.221 to 0.329 | 0.681 |
| sIL-2Rα | IL-13 | All Subjects (n=291) | 0.050 | -0.065 to 0.164 | 0.391 | 0.046 | -0.070 to 0.161 | 0.433 |
| | | Controls (n=194) | -0.014 | -0.155 to 0.127 | 0.841 | -0.019 | -0.161 to 0.123 | 0.792 |
| | | No Secretagogue (n=43) | **0.438** | **0.158 to 0.652** | **0.003** | **0.489** | **0.209 to 0.695** | **0.001** |
| | | Any Secretagogue (n=54) | -0.081 | -0.341 to 0.191 | 0.560 | -0.015 | -0.289 to 0.262 | 0.919 |
| IL-12p40 | IL-12p70 | All Subjects (n=291) | **0.853** | **0.819 to 0.882** | **<0.001** | **0.854** | **0.819 to 0.883** | **<0.001** |
| | | Controls (n=194) | **0.653** | **0.564 to 0.727** | **<0.001** | **0.655** | **0.565 to 0.729** | **<0.001** |
| | | No Secretagogue (n=43) | **0.927** | **0.869 to 0.960** | **<0.001** | **0.930** | **0.871 to 0.963** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.286** | **0.019 to 0.514** | **0.034** | **0.283** | **0.009 to 0.519** | **0.041** |
| IL-12p40 | IFN-α2 | All Subjects (n=291) | **0.591** | **0.510 to 0.661** | **<0.001** | **0.590** | **0.510 to 0.661** | **<0.001** |
| | | Controls (n=194) | **0.721** | **0.645 to 0.782** | **<0.001** | **0.725** | **0.649 to 0.786** | **<0.001** |
| | | No Secretagogue (n=43) | **0.930** | **0.875 to 0.962** | **<0.001** | **0.934** | **0.877 to 0.965** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.341** | **0.081 to 0.558** | **0.010** | **0.357** | **0.090 to 0.576** | **0.009** |
| IL-12p40 | IFN-γ | All Subjects (n=291) | **0.492** | **0.399 to 0.574** | **<0.001** | **0.493** | **0.400 to 0.575** | **<0.001** |
| | | Controls (n=194) | **0.473** | **0.356 to 0.576** | **<0.001** | **0.482** | **0.365 to 0.584** | **<0.001** |
| | | No Secretagogue (n=43) | **0.755** | **0.588 to 0.860** | **<0.001** | **0.771** | **0.604 to 0.873** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.209 | -0.062 to 0.451 | 0.126 | 0.211 | -0.068 to 0.460 | 0.133 |
| IL-12p40 | CXCL-10 (IP-10) | All Subjects (n=291) | 0.041 | -0.074 to 0.155 | 0.484 | 0.044 | -0.72 to 0.159 | 0.458 |
| | | Controls (n=194) | 0.082 | -0.059 to 0.221 | 0.252 | 0.077 | -0.066 to 0.217 | 0.290 |
| | | No Secretagogue (n=43) | 0.065 | -0.240 to 0.358 | 0.678 | 0.063 | -0.253 to 0.367 | 0.698 |
| | | Any Secretagogue (n=54) | 0.113 | -0.160 to 0.369 | 0.414 | 0.149 | -0.132 to 0.408 | 0.293 |
| IL-12p40 | CXCL-9 (MIG) | All Subjects (n=291) | **0.172** | **0.058 to 0.281** | **0.003** | **0.169** | **0.054 to 0.280** | **0.004** |
| | | Controls (n=194) | **0.248** | **0.111 to 0.376** | **<0.001** | **0.249** | **0.111 to 0.378** | **<0.001** |
| | | No Secretagogue (n=43) | 0.251 | -0.054 to 0.512 | 0.101 | 0.259 | -0.057 to 0.528 | 0.103 |
| | | Any Secretagogue (n=54) | -0.038 | -0.302 to 0.233 | 0.787 | -0.140 | -0.400 to 0.141 | 0.323 |
| IL-12p40 | CXCL-8 (IL-8) | All Subjects (n=291) | **0.292** | **0.183 to 0.394** | **<0.001** | **0.295** | **0.186 to 0.397** | **<0.001** |
| | | Controls (n=194) | **0.571** | **0.467 to 0.659** | **<0.001** | **0.572** | **0.468 to 0.660** | **<0.001** |
| | | No Secretagogue (n=43) | **0.350** | **0.055 to 0.588** | **0.020** | **0.369** | **0.065 to 0.611** | **0.017** |
| | | Any Secretagogue (n=54) | -0.050 | -0.313 to 0.221 | 0.720 | -0.096 | -0.362 to 0.184 | 0.499 |
| IL-12p40 | IL-5 | All Subjects (n=291) | **0.297** | **0.188 to 0.398** | **<0.001** | **0.296** | **0.187 to 0.398** | **<0.001** |
| | | Controls (n=194) | 0.070 | -0.071 to 0.209 | 0.329 | 0.071 | -0.072 to 0.211 | 0.328 |
| | | No Secretagogue (n=43) | **0.907** | **0.833 to 0.949** | **<0.001** | **0.915** | **0.844 to 0.954** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.061 | -0.323 to 0.210 | 0.661 | -0.086 | -0.353 to 0.194 | 0.545 |
| IL-12p40 | IL-10 | All Subjects (n=291) | **0.909** | **0.886 to 0.927** | **<0.001** | **0.910** | **0.888 to 0.928** | **<0.001** |
| | | Controls (n=194) | **0.904** | **0.874 to 0.927** | **<0.001** | **0.905** | **0.875 to 0.928** | **<0.001** |
| | | No Secretagogue (n=43) | **0.924** | **0.864 to 0.958** | **<0.001** | **0.926** | **0.863 to 0.960** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.625** | **0.428 to 0.764** | **<0.001** | **0.618** | **0.412 to 0.763** | **<0.001** |

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|---|---|---|---|---|---|---|---|---|
| IL-12p40 | IL-13 | All Subjects (n=291) | **0.374** | **0.271 to 0.469** | **<0.001** | **0.376** | **0.273 to 0.471** | **<0.001** |
| | | Controls (n=194) | **0.444** | **0.323 to 0.550** | **<0.001** | **0.449** | **0.327 to 0.555** | **<0.001** |
| | | No Secretagogue (n=43) | **0.865** | **0.764 to 0.925** | **<0.001** | **0.871** | **0.768 to 0.930** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.587** | **0.379 to 0.739** | **<0.001** | **0.578** | **0.360 to 0.736** | **<0.001** |
| IL-12p70 | IFN-α2 | All Subjects (n=291) | **0.749** | **0.693 to 0.795** | **<0.001** | **0.749** | **0.693 to 0.796** | **<0.001** |
| | | Controls (n=194) | **0.944** | **0.926 to 0.958** | **<0.001** | **0.944** | **0.926 to 0.958** | **<0.001** |
| | | No Secretagogue (n=43) | **0.816** | **0.682 to 0.896** | **<0.001** | **0.823** | **0.688 to 0.903** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.897** | **0.828 to 0.939** | **<0.001** | **0.898** | **0.826 to 0.941** | **<0.001** |
| IL-12p70 | IFN-γ | All Subjects (n=291) | **0.526** | **0.438 to 0.605** | **<0.001** | **0.526** | **0.437 to 0.605** | **<0.001** |
| | | Controls (n=194) | **0.506** | **0.393 to 0.604** | **<0.001** | **0.508** | **0.394 to 0.606** | **<0.001** |
| | | No Secretagogue (n=43) | **0.678** | **0.475 to 0.813** | **<0.001** | **0.683** | **0.471 to 0.820** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.816** | **0.701 to 0.889** | **<0.001** | **0.813** | **0.693 to 0.890** | **<0.001** |
| IL-12p70 | CXCL-10 (IP-10) | All Subjects (n=291) | 0.047 | -0.069 to 0.161 | 0.426 | 0.053 | -0.063 to 0.168 | 0.367 |
| | | Controls (n=194) | 0.059 | -0.082 to 0.199 | 0.411 | 0.063 | -0.080 to 0.203 | 0.386 |
| | | No Secretagogue (n=43) | 0.087 | -0.219 to 0.377 | 0.577 | 0.078 | -0.239 to 0.380 | 0.630 |
| | | Any Secretagogue (n=54) | 0.074 | -0.197 to 0.336 | 0.591 | 0.050 | -0.229 to 0.321 | 0.725 |
| IL-12p70 | CXCL-9 (MIG) | All Subjects (n=291) | **0.235** | **0.124 to 0.341** | **<0.001** | **0.235** | **0.123 to 0.342** | **<0.001** |
| | | Controls (n=194) | **0.377** | **0.249 to 0.492** | **<0.001** | **0.371** | **0.242 to 0.487** | **<0.001** |
| | | No Secretagogue (n=43) | 0.233 | -0.073 to 0.498 | 0.129 | 0.250 | -0.067 to 0.521 | 0.116 |
| | | Any Secretagogue (n=54) | -0.061 | -0.324 to 0.210 | 0.660 | -0.075 | -0.343 to 0.205 | 0.599 |
| IL-12p70 | CXCL-8 (IL-8) | All Subjects (n=291) | **0.182** | **0.069 to 0.291** | **0.002** | **0.188** | **0.074 to 0.297** | **<0.001** |
| | | Controls (n=194) | **0.203** | **0.064 to 0.335** | **0.004** | **0.210** | **0.070 to 0.342** | **0.003** |
| | | No Secretagogue (n=43) | 0.293 | -0.008 to 0.545 | 0.053 | 0.260 | -0.017 to 0.500 | 0.063 |
| | | Any Secretagogue (n=54) | 0.254 | -0.014 to 0.489 | 0.061 | **0.329** | **0.019 to 0.581** | **0.036** |
| IL-12p70 | IL-5 | All Subjects (n=291) | **0.254** | **0.143 to 0.358** | **<0.001** | **0.255** | **0.143 to 0.360** | **<0.001** |
| | | Controls (n=194) | 0.030 | -0.111 to 0.171 | 0.674 | 0.033 | -0.109 to 0.174 | 0.649 |
| | | No Secretagogue (n=43) | **0.877** | **0.782 to 0.932** | **<0.001** | **0.896** | **0.811 to 0.944** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.042 | -0.306 to 0.229 | 0.765 | -0.026 | -0.299 to 0.252 | 0.858 |
| IL-12p70 | IL-10 | All Subjects (n=291) | **0.897** | **0.872 to 0.917** | **<0.001** | **0.897** | **0.872 to 0.918** | **<0.001** |
| | | Controls (n=194) | **0.709** | **0.631 to 0.773** | **<0.001** | **0.709** | **0.630 to 0.773** | **<0.001** |
| | | No Secretagogue (n=43) | **0.970** | **0.945 to 0.984** | **<0.001** | **0.970** | **0.944 to 0.984** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.817** | **0.703 to 0.890** | **<0.001** | **0.827** | **0.714 to 0.898** | **<0.001** |
| IL-12p70 | IL-13 | All Subjects (n=291) | **0.412** | **0.312 to 0.503** | **<0.001** | **0.413** | **0.312 to 0.504** | **<0.001** |
| | | Controls (n=194) | **0.375** | **0.247 to 0.490** | **<0.001** | **0.380** | **0.252 to 0.495** | **<0.001** |
| | | No Secretagogue (n=43) | **0.964** | **0.933 to 0.980** | **<0.001** | **0.966** | **0.936 to 0.982** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.501** | **0.269 to 0.677** | **<0.001** | **0.492** | **0.250 to 0.676** | **<0.001** |
| IFN-α2 | IFN-γ | All Subjects (n=291) | **0.620** | **0.544 to 0.686** | **<0.001** | **0.622** | **0.546 to 0.688** | **<0.001** |
| | | Controls (n=194) | **0.571** | **0.468 to 0.659** | **<0.001** | **0.571** | **0.467 to 0.660** | **<0.001** |
| | | No Secretagogue (n=43) | **0.796** | **0.652 to 0.885** | **<0.001** | **0.823** | **0.688 to 0.903** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.823** | **0.713 to 0.894** | **<0.001** | **0.821** | **0.706 to 0.894** | **<0.001** |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| IFN-α2 | CXCL-10 (IP-10) | All Subjects (n=291) | 0.047 | -0.068 to 0.161 | 0.424 | 0.053 | -0.063 to 0.167 | 0.370 |
| | | Controls (n=194) | 0.056 | -0.086 to 0.195 | 0.440 | 0.0616 | -0.081 to 0.202 | 0.396 |
| | | No Secretagogue (n=43) | 0.046 | -0.258 to 0.341 | 0.769 | 0.064 | -0.253 to 0.368 | 0.694 |
| | | Any Secretagogue (n=54) | -0.085 | -0.345 to 0.187 | 0.540 | -0.122 | -0.385 to 0.159 | 0.390 |
| IFN-α2 | CXCL-9 (MIG) | All Subjects (n=291) | **0.345** | **0.240 to 0.443** | **<0.001** | **0.342** | **0.236 to 0.441** | **<0.001** |
| | | Controls (n=194) | **0.413** | **0.289 to 0.524** | **<0.001** | **0.406** | **0.280 to 0.518** | **<0.001** |
| | | No Secretagogue (n=43) | **0.445** | **0.167 to 0.657** | **0.002** | **0.457** | **0.169 to 0.673** | **0.002** |
| | | Any Secretagogue (n=54) | -0.096 | -0.355 to 0.176 | 0.486 | -0.103 | -0.368 to 0.178 | 0.471 |
| IFN-α2 | CXCL-8 (IL-8) | All Subjects (n=291) | **0.397** | **0.296 to 0.490** | **<0.001** | **0.403** | **0.302 to 0.496** | **<0.001** |
| | | Controls (n=194) | **0.396** | **0.270 to 0.508** | **<0.001** | **0.409** | **0.283 to 0.521** | **<0.001** |
| | | No Secretagogue (n=43) | **0.479** | **0.209 to 0.681** | **<0.001** | **0.495** | **0.218 to 0.699** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.258 | -0.010 to 0.492 | 0.057 | 0.253 | -0.025 to 0.494 | 0.071 |
| IFN-α2 | IL-5 | All Subjects (n=291) | **0.146** | **0.032 to 0.257** | **0.012** | **0.147** | **0.032 to 0.258** | **0.012** |
| | | Controls (n=194) | 0.043 | -0.099 to 0.182 | 0.554 | 0.045 | -0.097 to 0.186 | 0.533 |
| | | No Secretagogue (n=43) | **0.829** | **0.704 to 0.904** | **<0.001** | **0.831** | **0.702 to 0.908** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.004 | -0.271 to 0.264 | 0.978 | 0.008 | -0.268 to 0.283 | 0.956 |
| IFN-α2 | IL-10 | All Subjects (n=291) | **0.655** | **0.584 to 0.716** | **<0.001** | **0.657** | **0.586 to 0.718** | **<0.001** |
| | | Controls (n=194) | **0.813** | **0.758 to 0.855** | **<0.001** | **0.480** | **0.362 to 0.582** | **<0.001** |
| | | No Secretagogue (n=43) | **0.783** | **0.631 to 0.877** | **<0.001** | **0.790** | **0.635 to 0.884** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.750** | **0.604 to 0.848** | **<0.001** | **0.760** | **0.612 to 0.856** | **<0.001** |
| IFN-α2 | IL-13 | All Subjects (n=291) | **0.556** | **0.471 to 0.630** | **<0.001** | **0.560** | **0.475 to 0.635** | **<0.001** |
| | | Controls (n=194) | **0.538** | **0.429 to 0.631** | **<0.001** | **0.545** | **0.437 to 0.637** | **<0.001** |
| | | No Secretagogue (n=43) | **0.790** | **0.642 to 0.881** | **<0.001** | **0.803** | **0.655 to 0.891** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.551** | **0.332 to 0.713** | **<0.001** | **0.547** | **0.320 to 0.715** | **<0.001** |
| IFN-γ | CXCL-10 (IP-10) | All Subjects (n=291) | 0.062 | -0.054 to 0.175 | 0.295 | 0.068 | -0.048 to 0.182 | 0.251 |
| | | Controls (n=194) | 0.085 | -0.057 to 0.223 | 0.239 | 0.103 | -0.040 to 0.241 | 0.156 |
| | | No Secretagogue (n=43) | -0.056 | -0.351 to 0.248 | 0.719 | -0.079 | -0.381 to 0.238 | 0.626 |
| | | Any Secretagogue (n=54) | 0.066 | -0.206 to 0.328 | 0.635 | 0.019 | -0.258 to 0.293 | 0.892 |
| IFN-γ | CXCL-9 (MIG) | All Subjects (n=291) | **0.287** | **0.178 to 0.389** | **<0.001** | **0.291** | **0.181 to 0.393** | **<0.001** |
| | | Controls (n=194) | **0.358** | **0.228 to 0.475** | **<0.001** | **0.354** | **0.224 to 0.473** | **<0.001** |
| | | No Secretagogue (n=43) | **0.347** | **0.053 to 0.587** | **0.020** | **0.375** | **0.071 to 0.614** | **0.015** |
| | | Any Secretagogue (n=54) | -0.033 | -0.298 to 0.237 | 0.812 | -0.039 | -0.311 to 0.240 | 0.787 |
| IFN-γ | CXCL-8 (IL-8) | All Subjects (n=291) | **0.432** | **0.334 to 0.521** | **<0.001** | **0.442** | **0.344 to 0.530** | **<0.001** |
| | | Controls (n=194) | **0.485** | **0.370 to 0.586** | **<0.001** | **0.504** | **0.390 to 0.603** | **<0.001** |
| | | No Secretagogue (n=43) | **0.325** | **0.027 to 0.569** | **0.031** | **0.347** | **0.040 to 0.594** | **0.026** |
| | | Any Secretagogue (n=54) | 0.192 | -0.080 to 0.438 | 0.160 | 0.180 | -0.100 to 0.434 | 0.202 |
| IFN-γ | IL-5 | All Subjects (n=291) | **0.136** | **0.022 to 0.247** | **0.020** | **0.136** | **0.021 to 0.248** | **0.021** |
| | | Controls (n=194) | 0.047 | -0.094 to 0.188 | 0.514 | 0.049 | -0.093 to 0.190 | 0.497 |
| | | No Secretagogue (n=43) | **0.613** | **0.383 to 0.771** | **<0.001** | **0.658** | **0.436 to 0.805** | **<0.001** |
| | | Any Secretagogue (n=54) | 0.001 | -0.267 to 0.269 | 0.995 | 0.022 | -0.255 to 0.296 | 0.876 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| IFN-γ | IL-10 | All Subjects (n=291) | **0.477** | **0.383 to 0.561** | **<0.001** | **0.476** | **0.382 to 0.561** | **<0.001** |
| | | Controls (n=194) | **0.475** | **0.358 to 0.577** | **<0.001** | **0.480** | **0.362 to 0.582** | **<0.001** |
| | | No Secretagogue (n=43) | **0.620** | **0.393 to 0.776** | **<0.001** | **0.618** | **0.380 to 0.780** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.681** | **0.506 to 0.803** | **<0.001** | **0.678** | **0.495 to 0.804** | **<0.001** |
| IFN-γ | IL-13 | All Subjects (n=291) | **0.492** | **0.400 to 0.575** | **<0.001** | **0.490** | **0.397 to 0.573** | **<0.001** |
| | | Controls (n=194) | **0.503** | **0.390 to 0.601** | **<0.001** | **0.504** | **0.389 to 0.603** | **<0.001** |
| | | No Secretagogue (n=43) | **0.660** | **0.448 to 0.801** | **<0.001** | **0.647** | **0.420 to 0.798** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.459** | **0.218 to 0.647** | **<0.001** | **0.443** | **0.190 to 0.640** | **<0.001** |
| CXCL-10 (IP-10) | CXCL-9 (MIG) | All Subjects (n=291) | 0.093 | -0.022 to 0.206 | 0.114 | 0.102 | -0.014 to 0.215 | 0.084 |
| | | Controls (n=194) | 0.089 | -0.052 to 0.227 | 0.216 | 0.097 | -0.046 to 0.235 | 0.183 |
| | | No Secretagogue (n=43) | 0.213 | -0.093 to 0.483 | 0.165 | 0.214 | -0.104 to 0.493 | 0.180 |
| | | Any Secretagogue (n=54) | 0.048 | -0.222 to 0.312 | 0.727 | 0.082 | -0.198 to 0.350 | 0.565 |
| CXCL-10 (IP-10) | CXCL-8 (IL-8) | All Subjects (n=291) | 0.108 | -0.007 to 0.220 | 0.065 | 0.095 | -0.021 to 0.208 | 0.108 |
| | | Controls (n=194) | 0.121 | -0.020 to 0.258 | 0.092 | 0.110 | -0.032 to 0.248 | 0.129 |
| | | No Secretagogue (n=43) | 0.112 | -0.195 to 0.399 | 0.473 | 0.130 | -0.190 to 0.424 | 0.422 |
| | | Any Secretagogue (n=54) | 0.005 | -0.263 to 0.273 | 0.970 | -0.029 | -0.302 to 0.248 | 0.838 |
| CXCL-10 (IP-10) | IL-5 | All Subjects (n=291) | 0.000 | -0.115 to 0.115 | 0.996 | -0.002 | -0.117 to 0.114 | 0.975 |
| | | Controls (n=194) | -0.007 | -0.148 to 0.134 | 0.918 | -0.013 | -0.155 to 0.129 | 0.857 |
| | | No Secretagogue (n=43) | 0.049 | -0.255 to 0.344 | 0.755 | 0.068 | -0.249 to 0.372 | 0.674 |
| | | Any Secretagogue (n=54) | -0.167 | -0.416 to 0.106 | 0.224 | -0.143 | -0.403 to 0.138 | 0.314 |
| CXCL-10 (IP-10) | IL-10 | All Subjects (n=291) | 0.058 | -0.057 to 0.172 | 0.324 | 0.061 | -0.055 to 0.175 | 0.302 |
| | | Controls (n=194) | 0.067 | -0.075 to 0.206 | 0.353 | 0.070 | -0.073 to 0.209 | 0.338 |
| | | No Secretagogue (n=43) | 0.107 | -0.200 to 0.394 | 0.493 | 0.095 | -0.224 to 0.394 | 0.559 |
| | | Any Secretagogue (n=54) | 0.156 | -0.117 to 0.407 | 0.257 | 0.124 | -0.157 to 0.386 | 0.385 |
| CXCL-10 (IP-10) | IL-13 | All Subjects (n=291) | **0.140** | **0.026 to 0.251** | **0.016** | **0.144** | **0.029 to 0.255** | **0.014** |
| | | Controls (n=194) | 0.140 | -0.001 to 0.275 | 0.051 | **0.149** | **0.008 to 0.285** | **0.038** |
| | | No Secretagogue (n=43) | 0.142 | -0.165 to 0.424 | 0.360 | 0.131 | -0.188 to 0.425 | 0.418 |
| | | Any Secretagogue (n=54) | **0.270** | **0.003 to 0.502** | **0.046** | 0.253 | -0.024 to 0.494 | 0.070 |
| CXCL-9 (MIG) | CXCL-8 (IL-8) | All Subjects (n=291) | **0.118** | **0.003 to 0.230** | **0.043** | **0.122** | **0.007 to 0.234** | **0.038** |
| | | Controls (n=194) | 0.107 | -0.035 to 0.244 | 0.137 | 0.119 | -0.023 to 0.257 | 0.100 |
| | | No Secretagogue (n=43) | **0.392** | **0.104 to 0.620** | **0.008** | **0.393** | **0.093 to 0.628** | **0.011** |
| | | Any Secretagogue (n=54) | -0.052 | -0.315 to 0.219 | 0.710 | -0.099 | -0.364 to 0.182 | 0.488 |
| CXCL-9 (MIG) | IL-5 | All Subjects (n=291) | 0.038 | -0.077 to 0.153 | 0.515 | 0.037 | -0.079 to 0.152 | 0.527 |
| | | Controls (n=194) | -0.025 | -0.165 to 0.117 | 0.734 | -0.023 | -0.164 to 0.119 | 0.752 |
| | | No Secretagogue (n=43) | **0.356** | **0.062 to 0.593** | **0.017** | **0.363** | **0.058 to 0.606** | **0.019** |
| | | Any Secretagogue (n=54) | 0.159 | -0.114 to 0.409 | 0.248 | 0.140 | -0.141 to 0.400 | 0.324 |
| CXCL-9 (MIG) | IL-10 | All Subjects (n=291) | **0.149** | **0.035 to 0.260** | **0.011** | **0.153** | **0.038 to 0.264** | **0.009** |
| | | Controls (n=194) | **0.274** | **0.139 to 0.400** | **<0.001** | **0.274** | **0.137 to 0.400** | **<0.001** |
| | | No Secretagogue (n=43) | 0.126 | -0.181 to 0.411 | 0.417 | 0.138 | -0.181 to 0.431 | 0.393 |
| | | Any Secretagogue (n=54) | -0.077 | -0.338 to 0.195 | 0.577 | -0.139 | -0.399 to 0.142 | 0.329 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| CXCL-9 (MIG) | IL-13 | All Subjects (n=291) | **0.159** | **0.045 to 0.269** | **0.006** | **0.166** | **0.052 to 0.277** | **0.004** |
| | | Controls (n=194) | **0.186** | **0.047 to 0.319** | **0.009** | **0.191** | **0.051 to 0.324** | **0.008** |
| | | No Secretagogue (n=43) | 0.232 | -0.073 to 0.498 | 0.130 | 0.251 | -0.065 to 0.522 | 0.114 |
| | | Any Secretagogue (n=54) | 0.069 | -0.203 to 0.331 | 0.619 | 0.027 | -0.251 to 0.300 | 0.850 |
| CXCL-8 (IL-8) | IL-5 | All Subjects (n=291) | **0.125** | **0.010 to 0.237** | **0.033** | **0.125** | **0.010 to 0.237** | **0.033** |
| | | Controls (n=194) | 0.107 | -0.034 to 0.245 | 0.135 | 0.107 | -0.036 to 0.245 | 0.141 |
| | | No Secretagogue (n=43) | **0.336** | **0.039 to 0.578** | **0.025** | **0.351** | **0.045 to 0.598** | **0.024** |
| | | Any Secretagogue (n=54) | 0.058 | -0.213 to 0.320 | 0.677 | 0.035 | -0.243 to 0.308 | 0.805 |
| CXCL-8 (IL-8) | IL-10 | All Subjects (n=291) | **0.402** | **0.301 to 0.494** | **<0.001** | **0.408** | **0.307 to 0.500** | **<0.001** |
| | | Controls (n=194) | **0.672** | **0.586 to 0.742** | **<0.001** | **0.677** | **0.592 to 0.747** | **<0.001** |
| | | No Secretagogue (n=43) | **0.316** | **0.018 to 0.563** | **0.036** | **0.347** | **0.040 to 0.594** | **0.026** |
| | | Any Secretagogue (n=54) | 0.142 | -0.131 to 0.395 | 0.303 | 0.090 | -0.191 to 0.356 | 0.529 |
| CXCL-8 (IL-8) | IL-13 | All Subjects (n=291) | **0.640** | **0.567 to 0.703** | **<0.001** | **0.651** | **0.579 to 0.713** | **<0.001** |
| | | Controls (n=194) | **0.687** | **0.605 to 0.755** | **<0.001** | **0.695** | **0.613 to 0.761** | **<0.001** |
| | | No Secretagogue (n=43) | **0.366** | **0.073 to 0.600** | **0.014** | **0.398** | **0.099 to 0.632** | **0.009** |
| | | Any Secretagogue (n=54) | 0.012 | -0.256 to 0.279 | 0.929 | -0.040 | -0.312 to 0.238 | 0.780 |
| IL-5 | IL-10 | All Subjects (n=291) | **0.308** | **0.200 to 0.408** | **<0.001** | **0.309** | **0.200 to 0.410** | **<0.001** |
| | | Controls (n=194) | 0.134 | -0.007 to 0.270 | 0.270 | 0.138 | -0.004 to 0.275 | 0.056 |
| | | No Secretagogue (n=43) | **0.867** | **0.767 to 0.926** | **<0.001** | **0.887** | **0.795 to 0.939** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.111 | -0.368 to 0.162 | 0.422 | -0.113 | -0.377 to 0.167 | 0.425 |
| IL-5 | IL-13 | All Subjects (n=291) | **0.134** | **0.020 to 0.245** | **0.022** | **0.134** | **0.018 to 0.246** | **0.023** |
| | | Controls (n=194) | 0.065 | -0.076 to 0.204 | 0.364 | 0.066 | -0.077 to 0.206 | 0.363 |
| | | No Secretagogue (n=43) | **0.811** | **0.675 to 0.893** | **<0.001** | **0.842** | **0.718 to 0.914** | **<0.001** |
| | | Any Secretagogue (n=54) | -0.022 | -0.288 to 0.247 | 0.874 | -0.019 | -0.293 to 0.258 | 0.894 |
| IL-10 | IL-13 | All Subjects (n=291) | **0.513** | **0.423 to 0.593** | **<0.001** | **0.512** | **0.422 to 0.593** | **<0.001** |
| | | Controls (n=194) | **0.596** | **0.497 to 0.680** | **<0.001** | **0.601** | **0.501 to 0.684** | **<0.001** |
| | | No Secretagogue (n=43) | **0.942** | **0.895 to 0.968** | **<0.001** | **0.942** | **0.893 to 0.969** | **<0.001** |
| | | Any Secretagogue (n=54) | **0.654** | **0.468 to 0.784** | **<0.001** | **0.628** | **0.426 to 0.770** | **<0.001** |

Significant correlations are displayed in bolded text. The differences that are only significant in either adjusted or unadjusted correlations are further denoted by an outline. Interleukin-2, IL-2; soluble interleukin-2 receptor α, sIL-2Rα; interleukin-12 subunit p40, IL-12p40; interleukine-12 subunit p70, IL-12p70; interferon α 2, IFN-α2; interferon γ, IFN-γ; chemokine ligand 10, CXCL-10 (interferon gamma-induced protein 10, IP-10); chemokine ligand 9, CXCL-9 (monokine-induced by interferon γ, MIG); chemokine ligand 8, CXCL-8 (interleukin-8, IL-8); interleukin-5, IL-5; interleukin-10, IL-10; interleukin-13, IL-13.

(PHP0840409E). Demographic and clinical patient information was linked with cancer outcomes and profiles of T-helper 1 and 2 produced cytokines of corresponding plasma specimen harvested at BC diagnosis and banked in the Roswell Park Cancer Institute Data Bank and Bio-Repository.

## 2.1. Study population

All incident breast cancer cases diagnosed at Roswell Park Cancer Institute (01/01/2003-12/31/2009) were considered for inclusion ($n=2194$). Medical and pharmacotherapy history were used to determine the baseline presence of diabetes.

## 2.2. Inclusion and exclusion criteria

All adult women with pre-existing diabetes at breast cancer diagnosis having available banked treatment-naïve plasma specimens (blood collected prior to initiation of any cancer-related therapy - surgery, radiation or pharmacotherapy) in the Institute's Data Bank and Bio-Repository were included.

Subjects were excluded if they had prior cancer history or unclear date of diagnosis, incomplete clinical records, type 1 or unclear diabetes status. For a specific breakdown of excluded subjects, please see the original research article by Wintrob et al. [1].

A total of 97 female subjects with breast cancer and baseline diabetes mellitus were eligible for inclusion in this analysis.

## 2.3. Control-matching approach

Each of the 97 adult female subjects with breast cancer and diabetes mellitus (defined as "cases") was matched with two other female subjects diagnosed with breast cancer, but without baseline diabetes mellitus (defined as "controls"). The following matching criteria were used: age at diagnosis, body mass index category, ethnicity, menopausal status and tumor stage (as per the American Joint Committee on Cancer). Some matching limitations applied [1].

## 2.4. Demographic and clinical data collection

Clinical and treatment history was documented as previously described [1]. Vital status was obtained from the Institute's Tumor Registry, a database updated biannually with data obtained from the National Comprehensive Cancer Networks' Oncology Outcomes Database. Outcomes of interest were breast cancer recurrence and/or death.

## 2.5. Plasma specimen storage and retrieval

All the plasma specimens retrieved from long-term storage were individually aliquoted in color coded vials labeled with unique, subject specific barcodes. Overall duration of freezing time was accounted for all matched controls ensuring that the case and matched control specimens had similar overall storage conditions. Only two instances of freeze-thaw were allowed between biobank retrieval and biomarker analyses: aliquoting procedure step and actual assay.

## 2.6. Luminex® assays

A total of 12 biomarkers - interleukine-2, soluble interleukine-2 receptor α, interleukine-12 subunit p40, interleukine-12 subunit p70, interferon α 2, interferon γ, chemokine ligand 10 (interferon gamma-induced protein 10), chemokine ligand 9 (monokine-induced by interferon γ), chemokine ligand 8 (interleukine-8), interleukine-5, interleukine-10, and interleukine-13 - were quantified according to the manufacturer protocol. The Luminex® HCYTOMAG-60K panel (Millipore Corporation, Billerica, MA) was used in this study.

## 2.7. Biomarker-pharmacotherapy association analysis

Biomarker cut-point optimization was performed for each analyzed biomarker. Biomarker levels constituted the continuous independent variable that was subdivided into two groups that optimized the log rank test among all possible cut-point selections yielding a minimum of 10 patients in any resulting group. Quartiles were also constructed. The resultant biomarker categories were then tested for association with type 2 diabetes mellitus therapy and controls by Fisher's exact test. The continuous biomarker levels were also tested for association with diabetes therapy and controls across groups by the Kruskall-Wallis test and pairwise by the Wilcoxon rank sum. Multivariate adjustments were performed accounting for age, tumor stage, body mass index, estrogen receptor status, and cumulative comorbidity. The biomarker analysis was performed using R Version 2.15.3. Please see the original article for an illustration of the analysis workflow [1].

Correlations between biomarkers stratified by type 2 diabetes mellitus pharmacotherapy and controls were assessed by the Pearson method. Correlation models were constructed both with and without adjustment for age, body mass index, and the combined comorbidity index. Correlation analyses were performed using SAS Version 9.4.

## Funding sources

## Acknowledgements

## Transparency document. Supporting information

Transparency data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2017.02.044.

## Reference

[1] Z. Wintrob, J.P. Hammel, T. Khoury, G.K. Nimako, H.-W. Fu, Z.S. Fayazi, D.P. Gaile, A. Forrest, A.C. Ceacareanu, Insulin use, adipokine profiles and breast cancer prognosis, Cytokine (2017) 45–61. http://dx.doi.org/10.1016/j.cyto.2016.10.017.