Data Article

Circulating adipokines data associated with insulin secretagogue use in breast cancer patients

Zachary A.P. Wintroba, Jeffrey P. Hammel, George K. Nimako, Zahra S. Fayazi, Dan P. Gaile, Alan Forrest, Alice C. Ceacareanu

State University of New York at Buffalo, Department of Pharmacy Practice, NYS Center of Excellence in Bioinformatics and Life Sciences, 701 Ellicott Street, Buffalo, NY 14203, United States

Cleveland Clinic, Department of Biostatistics and Epidemiology, 9500 Euclid Ave., Cleveland, OH 44195, United States

State University of New York at Buffalo, Department of Biostatistics, 718 Kimball Tower, Buffalo, NY 14214, United States

The UNC Eshelman School of Pharmacy, Division of Pharmacotherapy and Experimental Therapeutics, Campus Box 7568, Chapel Hill, NC 27599, United States

Roswell Park Cancer Institute, Department of Pharmacy Services, Elm & Carlton Streets, Buffalo, NY 14263, United States

Article history:
Received 31 October 2016
Received in revised form 14 November 2016
Accepted 16 November 2016
Available online 22 November 2016

Keywords:
Adipokine
Insulin
Secretagogue
Breast cancer
Diabetes
Cancer outcomes
Cancer prognosis

Abstract
Oral drugs stimulating endogenous insulin production (insulin secretagogues) may have detrimental effects on breast cancer outcomes. The data presented shows the relationship between pre-existing insulin secretagogues use, adipokine profiles at the time of breast cancer (BC) diagnosis and subsequent cancer outcomes in women diagnosed with BC and type 2 diabetes mellitus (T2DM). The Pearson correlation analysis evaluating the relationship between adipokines stratified by T2DM pharmacotherapy and controls is also provided. This information is the extension of the data presented and discussed in “Insulin use, adipokine profiles and breast cancer prognosis” (Wintrob et al., in press) [1].

© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

DOI of original article: http://dx.doi.org/10.1016/j.cyto.2016.10.017

* Correspondence author at: State University of New York at Buffalo, Department of Pharmacy Practice, NYS Center of Excellence in Bioinformatics and Life Sciences, 701 Ellicott Street, Buffalo, NY 14203, United States. Fax: +1 716 849 6651.
E-mail address: ACC36@BUFFALO.EDU (A.C. Ceacareanu).

http://dx.doi.org/10.1016/j.dib.2016.11.060
2352-3409/© 2016 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).
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®- or enzyme-linked immunosorbent assay-based quantitation of adipokines (adiponectin, leptin, C-reactive protein, interleukine-6, interleukine-1β, interleukine-1Ra, tumor necrosis factor-α, and C-peptide) from plasma samples was conducted.
|                                                      | A Luminex®/200™ instrument with Xponent 3.1 software was used to acquire all data except for C-reactive protein determinations which have been done using a Synergy 2 BioTek multi-mode reader
| Data format                                       | Analyzed
| Experimental factors                             | Adipokines 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 adipokine profiles. A biomarker 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

- Presented data shows the relationship between pre-existing insulin secretagogues use, adipokine production at the time of cancer diagnosis and breast cancer outcomes.
- This data serves as a benchmark for future investigations targeting pharmacotherapy-induced adipokine modulation in breast cancer.
- The data described here can assist study design of further biomarker evaluation in relationship with the safety and effectiveness of diabetes pharmacotherapy.

1. Data

Reported data represents the observed association between insulin secretagogues’ utilization and the adipokine profiles at the time of breast cancer diagnosis in women with diabetes mellitus (Table 1). Data in Table 2 includes the observed correlations between adipokines stratified by type 2 diabetes mellitus pharmacotherapy and controls.

2. Experimental design, materials and methods

Evaluation of adipokine profile association with insulin secretagogue 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 (PHP0840409E). Demographic and clinical patient information was linked with cancer outcomes and adipokine profiles of corresponding plasma specimen harvested at BC diagnosis and banked in the Roswell Park Cancer Institute Data Bank and Bio-Repository.
# Table 1
Adipokines associations with insulin secretagogue use.

| Biomarker | Biomarker Grouping | Concentration | Control | No Secretagogue | Any Secretagogue | Unadjusted p-value (MVP) |
|-----------|--------------------|---------------|---------|-----------------|------------------|-------------------------|
|           |                    |               |         |                 |                  |                         |
| Adiponectin (ng/ml) | Median (25–75th) Quartiles | - | 14.9 (10.7–22.6) | 11.3 (6.89–20.9) | 11.7 (8.10–17.6) | <0.015 (0.022) 0.008 (0.210) 0.810 (0.770) 0.005 (0.046) |
|           | OS-Based Optimization | 179–715 | 19 (9.8%) | 13 (27.7%) | 7 (14.0%) | 0.002 (0.007) 0.390 (0.780) 0.100 (0.120) 0.005 (0.018) |
|           | DFS-Based Optimization | 179–719 | 124 (63.9%) | 33 (70.2%) | 39 (78.0%) | 0.420 (0.560) 0.060 (0.210) 0.380 (0.350) 0.150 (0.340) |
| Leptin (ng/ml) | Median (25–75th) Quartiles | - | 26.0 (16.9–38.0) | 23.0 (15.4–44.1) | 32.0 (21.8–50.1) | 0.820 (0.330) 0.050 (0.120) 0.210 (0.700) 0.150 (0.160) |
|          | OS-Based Optimization | BLQ to 617 | 14 (7.2%) | 3 (6.4%) | 1 (2.0%) | 1.000 (0.640) 0.320 (0.890) 0.350 (0.740) 0.450 (0.850) |
|          | DFS-Based Optimization | BLQ to 50.82 | 155 (79.9%) | 37 (79.0%) | 39 (78.0%) | 0.860 (0.070) 0.770 (0.002) 0.930 (0.070) 0.950 (0.002) |
| CRP (μg/ml) | Median (25–75th) Quartiles | - | 2.10 (0.80–4.65) | 2.80 (1.10–5.30) | 3.05 (1.30–9.15) | 0.340 (0.670) 0.022 (0.370) 0.260 (0.890) 0.060 (0.750) |
|           | OS-Based Optimization | BLQ to 8.30 | 173 (89.2%) | 41 (87.2%) | 34 (68.0%) | 0.001 (0.390) 0.710 (0.580) 0.028 (0.250) 0.001 (0.530) |
|           | DFS-Based Optimization | BLQ to 16.60 | 186 (95.9%) | 46 (97.9%) | 45 (90.0%) | 1.000 (0.300) 0.150 (0.670) 0.210 (0.180) 0.190 (0.470) |
| IL-6 (pg/ml) | Median (25–75th) Quartiles | - | 0.7 (0.44–1.76) | 1.49 (0.59–3.72) | 1.14 (0.51–3.10) | 0.010 (0.090) 0.170 (0.740) 0.330 (0.048) 0.024 (0.180) |
|           | OS-Based Optimization | BLQ to 8.30 | 173 (89.2%) | 41 (87.2%) | 34 (68.0%) | 0.001 (0.390) 0.710 (0.580) 0.028 (0.250) 0.001 (0.530) |
|           | DFS-Based Optimization | BLQ to 16.60 | 186 (95.9%) | 46 (97.9%) | 45 (90.0%) | 1.000 (0.300) 0.150 (0.670) 0.210 (0.180) 0.190 (0.470) |
| Biomarker         | Median (25–75th) | Quartiles | OS-Based Optimization | BLQ<sup>*</sup> | 0.34–138.00 | 176 (90.7%) | 47 (100%) | 49 (98%) | 0.028 (0.010) | 1.000 (0.999) | 0.140 (0.300) | 0.022 (0.031) | DFS-Based Optimization | BLQ<sup>*</sup> | 0.34–138.00 | 176 (90.7%) | 49 (98%) |
|-------------------|------------------|-----------|-----------------------|----------------|-------------|-------------|-----------|---------|----------------|----------------|----------------|----------------|-----------------------|----------------|-------------|-------------|---------|
| TNF-α (pg/ml)     | 5.55 (3.86–8.22) | 4.21–5.66 | 5.67–8.73            | 8.90–77.00     | 9.00–77.00* | 153 (78.9%) | 31 (66%) | 36 (72%) | 0.060 (0.080) | 1.000 (0.020) | 0.080 (0.420) | 0.850 (0.300) | 0.070 (0.170) | 0.34              | 138.00       | 176 (90.7%) | 49 (98%) |
| IL-1β (pg/ml)     | 1.60 (1.60–3.20) | 1.29–1.82 | 1.83–2.68            | 2.68–9.02      | 0.14–0.75*  | 14 (7.2%)  | 0 (0%)   | 0 (0%)   | 0.050 (0.760) | <0.001 (0.041) | 0.330 (0.060) | <0.001 (0.090) | 0.043              | <0.001        | 1 (2.0%)   | 0 (0%)    |
| C-peptide (ng/ml) | 1.67 (1.17–2.42) | 1.29–1.82 | 1.83–2.68            | 2.68–9.02      | 0.14–0.75*  | 14 (7.2%)  | 0 (0%)   | 0 (0%)   | 0.140 (0.037) | 0.080 (0.130) | 0.005 (0.001) | 0.013 (0.008) | 0.140 (0.037) | 0.080 (0.130) | 0.005 (0.001) | 0.013 (0.008) |

C-reactive protein (CRP), interleukine-6 (IL-6), interleukine-1β (IL-1β), interleukine-1Ra (IL-1Ra), tumor necrosis factor-α (TNF-α).

* Overall survival (OS)- and disease-free survival (DFS)-optimized biomarker ranges associated with poorer outcomes are represented in bold. BLQ=below limit of quantitation. MVP=p-value of the multivariate adjusted analysis.
| Compared biomarkers | Group                      | Unadjusted correlation                  | Adjusted correlation                  |
|---------------------|----------------------------|----------------------------------------|---------------------------------------|
|                     |                           | Pearson correlation 95% CI p-value      | Pearson correlation 95% CI p-value    |
| C-peptide           | IL-1β                     | All Subjects (n=291)                   |                                      |
|                     |                            | −0.089 −0.202 to 0.027 0.132           | −0.081 −0.194 to 0.034 0.168         |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | −0.003 −0.145 to 0.139 0.967           | 0.01 −0.131 to 0.151 0.891           |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | −0.265 −0.532 to 0.051 0.095           | −0.285 −0.539 to 0.017 0.061         |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | −0.069 −0.338 to 0.211 0.63            | −0.105 −0.363 to 0.167 0.446         |
| C-peptide           | IL-1Ra                    | All Subjects (n=291)                   |                                      |
|                     |                            | −0.081 −0.195 to 0.034 0.167           | −0.073 −0.187 to 0.042 0.212         |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | −0.075 −0.214 to 0.068 0.304           | 0.063 −0.202 to 0.079 0.382          |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | −0.171 −0.458 to 0.148 0.287           | −0.18 −0.455 to 0.128 0.245          |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | 0.064 −0.215 to 0.334 0.653            | 0.004 −0.264 to 0.272 0.977          |
| C-peptide           | IL-6                      | All Subjects (n=291)                   |                                      |
|                     |                            | −0.053 −0.168 to 0.063 0.368           | −0.068 −0.182 to 0.047 0.244         |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | −0.046 −0.187 to 0.097 0.528           | 0.059 −0.198 to 0.083 0.414          |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | −0.146 −0.437 to 0.174 0.366           | −0.159 −0.438 to 0.149 0.306         |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | −0.022 −0.295 to 0.255 0.879           | 0.032 −0.238 to 0.297 0.819          |
| C-peptide           | Adiponectin               | All Subjects (n=291)                   |                                      |
|                     |                            | −0.163 −0.274 to −0.048 0.005          | −0.178 −0.287 to −0.064 0.002        |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | −0.145 −0.281 to −0.003 0.045          | −0.119 −0.255 to 0.022 0.098         |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | −0.343 −0.591 to −0.035 0.028          | −0.388 −0.617 to −0.1 0.009          |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | −0.086 −0.353 to 0.194 0.547           | −0.068 −0.33 to 0.203 0.621          |
| C-peptide           | Leptin                    | All Subjects (n=291)                   |                                      |
|                     |                            | 0.161 0.047 to 0.272 0.006             | 0.238 0.126 to 0.343 < 0.001         |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | 0.278 0.141 to 0.404 0.001             | 0.314 0.181 to 0.436 < 0.001         |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | −0.042 −0.349 to 0.273 0.795           | −0.001 −0.301 to 0.299 0.995         |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | 0.03 −0.248 to 0.303 0.834             | 0.144 −0.129 to 0.396 0.297          |
| C-peptide           | CRP                       | All Subjects (n=291)                   |                                      |
|                     |                            | −0.075 −0.188 to 0.041 0.207           | 0.023 −0.092 to 0.137 0.698          |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | −0.117 −0.254 to 0.026 0.107           | 0.042 −0.182 to 0.099 0.556          |
|                     |                            | No Secretagogue (n=43)                 |                                      |
|                     |                            | 0.192 −0.127 to 0.475 0.231           | 0.207 −0.099 to 0.478 0.179          |
|                     |                            | Any Secretagogue (n=54)                |                                      |
|                     |                            | −0.086 −0.353 to 0.194 0.545           | −0.014 −0.281 to 0.255 0.92          |
| C-peptide           | TNFα                      | All Subjects (n=291)                   |                                      |
|                     |                            | −0.012 −0.127 to 0.104 0.839           | 0.035 −0.08 to 0.15 0.55             |
|                     |                            | Control (n=194)                        |                                      |
|                     |                            | 0.086 −0.056 to 0.226 0.234           | 0.125 −0.016 to 0.261 0.082          |
|                | IL-1β   | IL-1Ra   |
|----------------|---------|----------|
| **IL-1β**      | **IL-1Ra** |
| **No Secretagogue (n=43)** | -0.3 | -0.559 to 0.013 | 0.057 | -0.277 | -0.533 to 0.026 | 0.069 |
| **Any Secretagogue (n=54)** | 0.265 | -0.011 to 0.504 | 0.057 | 0.227 | -0.043 to 0.467 | 0.096 |
| **All Subjects (n=291)** | 0.753 | 0.698 to 0.799 | < 0.001 | 0.75 | 0.695 to 0.797 | < 0.001 |
| **Controls (n=194)** | 0.436 | 0.313 to 0.544 | < 0.001 | 0.435 | 0.313 to 0.542 | < 0.001 |
| **No Secretagogue (n=43)** | 0.932 | 0.874 to 0.964 | < 0.001 | 0.929 | 0.871 to 0.961 | < 0.001 |
| **Any Secretagogue (n=54)** | 0.367 | 0.101 to 0.583 | 0.007 | 0.384 | 0.13 to 0.591 | 0.004 |
| **IL-1β** | **IL-6** |
| **No Secretagogue (n=43)** | 0.69 | 0.482 to 0.824 | < 0.001 | 0.682 | 0.481 to 0.816 | < 0.001 |
| **Any Secretagogue (n=54)** | 0.042 | -0.237 to 0.314 | 0.771 | 0.055 | -0.216 to 0.318 | 0.694 |
| **IL-1β** | **Adiponectin** |
| **No Secretagogue (n=43)** | -0.038 | -0.153 to 0.077 | 0.515 | -0.024 | -0.138 to 0.091 | 0.685 |
| **Any Secretagogue (n=54)** | -0.055 | -0.195 to 0.088 | 0.451 | -0.031 | -0.171 to 0.11 | 0.665 |
| **All Subjects (n=291)** | -0.047 | -0.335 to 0.269 | 0.773 | -0.001 | -0.301 to 0.3 | 0.996 |
| **Controls (n=194)** | -0.033 | -0.306 to 0.245 | 0.818 | -0.054 | -0.317 to 0.217 | 0.695 |
| **IL-1β** | **Leptin** |
| **No Secretagogue (n=43)** | -0.038 | -0.116 to 0.115 | 0.994 | -0.009 | -0.124 to 0.106 | 0.88 |
| **Any Secretagogue (n=54)** | -0.045 | -0.351 to 0.27 | 0.782 | -0.092 | -0.382 to 0.214 | 0.553 |
| **All Subjects (n=291)** | -0.019 | -0.16 to 0.124 | 0.799 | -0.001 | -0.151 to 0.131 | 0.891 |
| **Controls (n=194)** | -0.013 | -0.322 to 0.228 | 0.724 | -0.14 | -0.393 to 0.133 | 0.31 |
| **IL-1β** | **CRP** |
| **No Secretagogue (n=43)** | 0.038 | -0.276 to 0.346 | 0.813 | -0.009 | -0.309 to 0.292 | 0.953 |
| **Any Secretagogue (n=54)** | -0.023 | -0.139 to 0.092 | 0.693 | -0.029 | -0.143 to 0.086 | 0.623 |
| **All Subjects (n=291)** | -0.019 | -0.16 to 0.124 | 0.799 | -0.001 | -0.151 to 0.131 | 0.891 |
| **Controls (n=194)** | -0.045 | -0.351 to 0.27 | 0.782 | -0.092 | -0.382 to 0.214 | 0.553 |
| **IL-1β** | **TNFα** |
| **No Secretagogue (n=43)** | 0.196 | 0.055 to 0.328 | 0.007 | 0.208 | 0.069 to 0.339 | 0.004 |
| **Any Secretagogue (n=54)** | 0.487 | 0.394 to 0.571 | < 0.001 | 0.484 | 0.391 to 0.568 | < 0.001 |
| **All Subjects (n=291)** | 0.668 | 0.45 to 0.811 | < 0.001 | 0.618 | 0.39 to 0.775 | < 0.001 |
| **Controls (n=194)** | -0.065 | -0.334 to 0.215 | 0.651 | -0.007 | -0.274 to 0.261 | 0.961 |
| **IL-1Ra** | **IL-6** |
| **No Secretagogue (n=43)** | 0.319 | 0.186 to 0.441 | < 0.001 | 0.31 | 0.177 to 0.432 | < 0.001 |
| **Any Secretagogue (n=54)** | 0.759 | 0.587 to 0.866 | < 0.001 | 0.749 | 0.578 to 0.856 | < 0.001 |
| **All Subjects (n=291)** | 0.021 | -0.256 to 0.295 | 0.882 | -0.029 | -0.294 to 0.241 | 0.836 |
| **IL-1Ra** | **Adiponectin** |
| **No Secretagogue (n=43)** | -0.043 | -0.158 to 0.073 | 0.467 | -0.049 | -0.163 to 0.067 | 0.407 |
| **Any Secretagogue (n=54)** | -0.015 | -0.37 to 0.175 | 0.46 | -0.147 | -0.399 to 0.126 | 0.287 |
| Compared biomarkers | Group | Unadjusted correlation | Adjusted correlation |
|---------------------|-------|------------------------|---------------------|
|                     |       | Pearson correlation    | 95% CI              | p-value | Pearson correlation | 95% CI | p-value |
| IL-1Ra              |       |                        |                     |         |                     |        |         |
|                     |       |                        |                     |         |                     |        |         |
| IL-1Ra              | Leptin | All Subjects (n=291)  | 0.021              | –0.095 to 0.136 | 0.727 | 0.028              | –0.087 to 0.143 | 0.63 |
|                     |       | Controls (n=194)      | 0.017              | –0.125 to 0.159 | 0.812 | 0.055              | –0.087 to 0.194 | 0.447 |
|                     |       | No Secretagogue (n=43)| 0.046              | –0.269 to 0.353 | 0.774 | 0.004              | –0.296 to 0.304 | 0.977 |
|                     |       | Any Secretagogue (n=54)| –0.101            | –0.366 to 0.18  | 0.478 | –0.131            | –0.385 to 0.142 | 0.344 |
| IL-1Ra              | CRP    | All Subjects (n=291)  | 0.066              | –0.05 to 0.18   | 0.263 | 0.071              | –0.045 to 0.184 | 0.229 |
|                     |       | Controls (n=194)      | 0.147              | 0.005 to 0.283  | 0.042 | 0.166              | 0.026 to 0.3    | 0.02 |
|                     |       | No Secretagogue (n=43)| 0.058              | –0.259 to 0.363 | 0.722 | 0.042              | –0.262 to 0.338 | 0.79 |
|                     |       | Any Secretagogue (n=54)| –0.081            | –0.349 to 0.199 | 0.569 | –0.1              | –0.358 to 0.172 | 0.47 |
| IL-1Ra              | TNFα   | All Subjects (n=291)  | 0.529              | 0.441 to 0.608  | < 0.001 | 0.516              | 0.426 to 0.596  | < 0.001 |
|                     |       | Controls (n=194)      | 0.456              | 0.336 to 0.562  | < 0.001 | 0.449              | 0.329 to 0.555  | < 0.001 |
|                     |       | No Secretagogue (n=43)| 0.623              | 0.386 to 0.782  | < 0.001 | 0.578              | 0.335 to 0.748  | < 0.001 |
|                     |       | Any Secretagogue (n=54)| 0.202             | –0.078 to 0.452 | 0.152 | 0.203              | –0.068 to 0.447 | 0.138 |
| IL-6                | Adiponectin | All Subjects (n=291) | –0.062             | –0.176 to 0.054 | 0.294 | –0.05              | –0.164 to 0.066 | 0.398 |
|                     |       | Controls (n=194)      | –0.103             | –0.242 to 0.039 | 0.155 | –0.088            | –0.226 to 0.054 | 0.222 |
|                     |       | No Secretagogue (n=43)| 0.076              | –0.242 to 0.378 | 0.64  | 0.112             | –0.195 to 0.399 | 0.472 |
|                     |       | Any Secretagogue (n=54)| –0.07             | –0.339 to 0.209 | 0.623 | –0.043            | –0.307 to 0.228 | 0.759 |
| IL-6                | Leptin | All Subjects (n=291)  | 0.055              | –0.061 to 0.169 | 0.354 | 0.015             | –0.101 to 0.129 | 0.804 |
|                     |       | Controls (n=194)      | 0.054              | –0.089 to 0.195 | 0.457 | 0.01               | –0.131 to 0.151 | 0.888 |
|                     |       | No Secretagogue (n=43)| 0.069              | –0.248 to 0.372 | 0.672 | 0.081             | –0.225 to 0.372 | 0.603 |
|                     |       | Any Secretagogue (n=54)| 0.104             | –0.176 to 0.369 | 0.464 | 0.081             | –0.191 to 0.341 | 0.559 |
| IL-6                | CRP    | All Subjects (n=291)  | 0.096              | –0.02 to 0.209  | 0.104 | 0.059             | –0.056 to 0.173 | 0.315 |
|                     |       | Controls (n=194)      | 0.141              | –0.001 to 0.277 | 0.051 | 0.095             | –0.047 to 0.233 | 0.188 |
|                     |       | No Secretagogue (n=43)| –0.093             | –0.394 to 0.225 | 0.564 | –0.09             | –0.38 to 0.216  | 0.562 |
|                     |       | Any Secretagogue (n=54)| 0.302             | 0.028 to 0.533  | 0.029 | 0.268             | 0.001 to 0.5    | 0.047 |
| IL-6                | TNFα   | All Subjects (n=291)  | 0.243              | 0.131 to 0.349  | < 0.001 | 0.224              | 0.112 to 0.33   | < 0.001 |
|                     |       | Controls (n=194)      | 0.262              | 0.124 to 0.389  | < 0.001 | 0.24              | 0.102 to 0.368  | 0.001 |
|                     |       | No Secretagogue (n=43)| 0.43               | 0.137 to 0.654  | 0.005 | 0.437             | 0.157 to 0.652  | 0.003 |
|                  | All Subjects (n=291) | Controls (n=194) | No Secretagogue (n=43) | Any Secretagogue (n=54) |
|------------------|----------------------|------------------|------------------------|-------------------------|
| **Adiponectin**  |                      |                  |                        |                         |
|                  | -0.085               | -0.235           | -0.222                 | -0.32                   |
| **Leptin**       | -0.198 to 0.031      | -0.365 to -0.096 | -0.228 to 0.391        | -0.547 to -0.049        |
| **CRP**          | 0.152                | 0.001            | 0.577                  | 0.795                   |
| **All Subjects** | -0.15                | -0.362           | -0.299                 | -0.309                  |
|                  | -0.261 to -0.036     | -0.389 to -0.126 | -0.298 to 0.303        | -0.533 to -0.045        |
| **0.039 to 0.528**| 0.01                 | 0.001            | 0.986                  | 0.021                   |
| **0.024**        |                      |                  |                        |                         |

**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. C-reactive protein (CRP), interleukine-6 (IL-6), interleukine-1β (IL-1β), interleukine-1Ra (IL-1Ra), tumor necrosis factor-α (TNF-α), confidence interval (CI).**
2.1. Study population

As described in the original research article by Wintrob et al. [1], 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

Inclusion criteria were as follows: minimum 18 years of age at diagnosis, presence of pre-existing diabetes at breast cancer diagnosis, and having available banked treatment-naïve plasma specimens in the Institute's Data Bank and Bio-Repository. That is, the blood had to be collected prior to the initiation of any cancer-related therapy (surgery, radiation or pharmacotherapy).

Subjects were excluded if they were male, 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 by medical chart review. Vital status was obtained from the Institute's Tumor Registry, a local 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. For additional details concerning data collection, specific definitions regarding censoring and drug use, and a comprehensive demographic report, please see the original article [1].

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. Enzyme-linked immunosorbent assay and Luminex® assays

A total of 7 biomarkers (adiponectin, leptin, C-reactive protein, interleukine-6, interleukine-1β, interleukine-1Ra, tumor necrosis factor-α, and C-peptide) were quantified using either enzyme-linked immunosorbent or Luminex® assays, as described by Wintrob et al. [1]. A quantitative colorimetric enzyme-linked immunosorbent assay was performed for detection of C-reactive protein, according to manufacturer protocol (Genway Biotek Inc., San Diego, CA). The following Luminex® biomarker panels were utilized in this study: human cytokine/chemokine panel I (MPXHCYTO-60K for interleukine-1β and interleukine-1Ra), human high sensitivity cytokine/chemokine panel (HSCYTO-60SK for interleukine-6 and tumor necrosis factorα), human cardiovascular disease panel I
(HCVD1-67AK for adiponectin), and human endocrine panel (HENDO-65K for leptin and c-peptide) produced by Millipore Corporation, Billerica, MA.

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

This research was funded by the following Grant awards: Wadsworth Foundation Peter Rowley Breast Cancer Grant awarded to A.C.C. (UB Grant Number 55705, Contract CO26588), the New York State Council of Health-system Pharmacists Research and Education Foundation (NYSCHP-REF) Oncology Leadership Grant awarded to A.C.C. (UB Grant Number 50151), and the NYSCHP-REF Clinical Pharmacy Award TO A.C.C. (UB Grant Number 53967).

Acknowledgements

Authors acknowledge the valuable help of Dr. Chi-Chen Hong with case-control matching.

Transparency document. Supplementary material

Transparency data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2016.11.060.

Reference

[1] Z.A.P. 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 (2016), http://dx.doi.org/10.1016/j.cyto.2016.10.017 (in press).