Data Article

mRNA expression data in breast cancers before and after consumption of walnut by women

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Abstract

This article contains supporting data for the research paper entitled: ‘Dietary walnut altered gene expressions related to tumor growth, survival, and metastasis in breast cancer patients: a pilot clinical trial’ [1] Hardman et al., 2019. Included are tables for all mapped genes and all unmapped loci identifications that were significantly changed in breast cancers by consumption of walnut for about 2 weeks. All gene networks that were identified by Ingenuity Pathway Analyses as modified are shown in table 3. Files containing the raw reads, along with a shell script describing the complete data analysis pipeline, were deposited to the Gene Expression Omnibus (GEO) at the National Center for Biotechnology Information (NCBI) and can be obtained via accession number GSE111073. https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE111073.

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1. Data

The data in Table 1 present the known genes in which the log ratio of [(gene expressions in the breast tumor at surgery) divided by (the expression of that gene in the initial biopsy)] in the subjects who consumed walnut divided by the [(gene expressions in the breast tumor at surgery) divided by (the expression of that gene in the initial biopsy)] in the subjects who did not consume walnut.
| Expr log ratio | ID          | Symbol       | Entrez gene name                                                                 | Location       | Type(s)     | Drug(s)     |
|---------------|-------------|--------------|----------------------------------------------------------------------------------|----------------|-------------|-------------|
| 28.23         | ENSG00000255277  | ABCG6P2      | ATP binding cassette subfamily C member 6 pseudogene 2                            | Other          | other       |             |
| 27.99         | ENSG00000144827  | ABHD10       | abhydrolase domain containing 10                                                 | Cytoplasm      | enzyme      |             |
| −26.16        | ENSG00000165660  | ABRAXAS2     | abraxas 2, BRISC complex subunit                                                  | Nucleus        | other       |             |
| −27.92        | ENSG00000226359  | ACTG1P24     | actin gamma 1 pseudogene 2                                                        | Other          | other       |             |
| −23.18        | ENSG00000168594  | ADAM29       | ADAM metallopeptidase domain 29                                                  | Plasma Membrane | peptidase   |             |
| −26.19        | ENSG00000274376  | ADAMTS7P1    | ADAMTS7 pseudogene 1                                                              | Other          | other       |             |
| −16.27        | ENSG00000065457  | ADAT1        | adenosine deaminase, tRNA specific 1                                             | Other          | enzyme      |             |
| 26.85         | ENSG00000204818  | ADGRF5P2     | adhesion G protein-coupled receptor F5 pseudogene 2                               | Other          | other       |             |
| 25.98         | ENSG00000156920  | ADGRG4       | adhesion G protein-coupled receptor                                              | Plasma Membrane | G-protein coupled receptor | other       |
| −28.07        | ENSG00000243289  | AGAP13P      | ArfGAP with GTPase domain, ankyrin repeat and PH domain 13, pseudogene           | Other          | other       |             |
| 30.00         | ENSG00000196581  | AJAP1        | adherens junctions associated protein 1                                           | Plasma Membrane | other       |             |
| 26.13         | ENSG00000140057  | AK7          | adenylate kinase 7                                                               | Cytoplasm      | kinase      |             |
| −29.86        | ENSG00000108602  | ALDH1A1      | aldehyde dehydrogenase 3 family member A1                                        | Cytoplasm      | enzyme      |             |
| −26.69        | ENSG00000163046  | ANKRD3OB     | ankyrin repeat domain 30B like                                                   | Other          | other       |             |
| −26.36        | ENSG00000224309  | ANKRD3OBP2   | ankyrin repeat domain 30B                                                         | Other          | other       |             |
| 29.60         | ENSG00000184945  | AQP12A/AQP12B | aquaporin 12A                                                                    | Cytoplasm      | transporter |             |
| 30.00         | ENSG00000198576  | ARC          | activity regulated cytoskeleton associated protein                               | Cytoplasm      | other       |             |
| 29.58         | ENSG00000127249  | ATP13A4      | ATPase 13A4                                                                       | Cytoplasm      | transporter |             |
| 27.73         | ENSG00000228847  | ATP5G2P4     | ATP synthase, H+ transporting, mitochondrial Fo complex subunit C2 (subunit 9) pseudogene 4 | Other          | other       |             |
| 20.55         | ENSG00000230223  | ATXN8OS      | ATXN8 opposite strand (non-protein coding)                                       | Other          | other       |             |
| 27.05         | ENSG00000148090  | AUH          | AU RNA binding methylglutaconyl-CoA hydratase                                     | Cytoplasm      | enzyme      |             |
| −29.79        | ENSG00000198049  | AVPR1B       | arginine vasopressin receptor 1B                                                  | Plasma Membrane | G-protein coupled receptor | AVP, lypressin |
| −29.84        | ENSG00000187172  | BAGE2        | BAGE family member 2                                                             | Other          | other       |             |
| −25.63        | ENSG00000106739  | BDKRB1       | bradykinin receptor B1                                                            | Plasma Membrane | G-protein coupled receptor | other       |
| −27.71        | ENSG00000224809  | BEND3P2      | BEN domain containing 3 pseudogene 2                                             | Other          | other       |             |
| 25.09         | ENSG00000204960  | BLACE        | B-cell acute lymphoblastic leukemia expressed                                    | Other          | other       |             |
| −29.71        | ENSG00000186222  | BLOC1S4      |                                                                         | Cytoplasm      | other       |             |

(continued on next page)
| Expr log ratio | Expr false discovery rate (q-value) | ID | Flags | Symbol | Entrez gene name | Location | Type(s) | Drug(s) |
|---------------|-----------------------------------|----|-------|--------|-----------------|----------|---------|---------|
| -29.92        | 4.30E-03                          | ENSG00000125845 |          | BMP2    | bone morphogenetic protein 2 | Extracellular Space | growth factor |
| -26.19        | 9.18E-03                          | ENSG00000198183 |          | BIPA1   | BPI fold containing family A member 1 | Extracellular Space | other |
| 28.23         | 5.54E-03                          | ENSG00000224775 |          | BRAF    | BRAF pseudogene 1 | Other | Other |
| -29.84        | 4.30E-03                          | ENSG00000224913 |          | BSN-A52 | BSN antisense RNA 2 (head to head) | Other | Other |
| -30.00        | 4.30E-03                          | ENSG00000137656 |          | BUD13   | BUD13 homolog | Nucleus | other |
| -26.19        | 7.91E-03                          | ENSG00000173237 |          | C1orf86 | chromosome 11 open reading frame 86 | Other | Other |
| -28.54        | 5.52E-03                          | ENSG00000157330 |          | C1orf58 | chromosome 1 open reading frame 158 | Other | Other |
| -25.71        | 9.87E-03                          | ENSG00000188511 |          | C2orf84 | chromosome 22 open reading frame 34 | Other | Other |
| -26.19        | 7.91E-03                          | ENSG00000173557 |          | C2orf70 | chromosome 2 open reading frame 70 | Nuclear | other |
| -30.00        | 4.30E-03                          | ENSG00000237787 |          | C3orf79 | chromosome 3 open reading frame 79 | Other | Other |
| 26.46         | 5.52E-03                          | ENSG00000082213 |          | C5orf22 | chromosome 5 open reading frame 22 | Other | Other |
| 26.5          | 6.09E-02                          | ENSG00000256462 |          | CALML3  | calmodulin like 3 | Cytoplasm | other |
| -26.19        | 7.91E-03                          | ENSG00000141688 |          | CBLN2   | cerebellin 2 precursor | Extracellular Space | other |
| -26.49        | 7.91E-03                          | ENSG00000183287 |          | CCBE1   | collagen and calcium binding EGF domains 1 | Extracellular Space | other |
| -28.54        | 5.52E-03                          | ENSG00000100147 |          | CCDC134 | coiled-coil domain containing 134 | Other | other |
| 28.23         | 5.54E-03                          | ENSG00000163081 |          | CCDC140 | coiled-coil domain containing 140 | Other | other |
| -28.49        | 5.52E-03                          | ENSG00000248712 |          | CCDC153 | coiled-coil domain containing 153 | Other | other |
| -28.00        | 5.54E-03                          | ENSG00000276409 |          | CCL14   | C-C motif chemokine ligand 14 | Extracellular Space | cytokine |
| -29.96        | 4.30E-03                          | ENSG00000133101 |          | CCNA1   | cyclin A1 | Nucleus | other |
| -28.80        | 5.52E-03                          | ENSG00000238241 |          | CCR12P  | C-C motif chemokine receptor 12 pseudogene | Other | other |
| -26.36        | 7.91E-03                          | ENSG00000204933 |          | CD177P1 | CD177 molecule pseudogene 1 | Other | other |
| -27.06        | 6.99E-03                          | ENSG00000158477 |          | CD1A    | CD1a molecule | Plasma Membrane | other |
| -26.69        | 7.63E-03                          | ENSG00000184661 |          | CDC2A   | cell division cycle associated 2 | Nucleus | other |
| -27.06        | 6.99E-03                          | ENSG00000145526 |          | CDH18   | catherin 18 | Plasma Membrane | other |
| 17.96         | 2.14E-03                          | ENSG00000113100 |          | CDH9    | catherin 9 | Plasma Membrane | other |
| 26.76         | 7.20E-03                          | ENSG00000170312 |          | CDK1    | cyclin dependent kinase 1 | Nucleus | kinase |
| -25.71        | 9.87E-03                          | ENSG00000230666 |          | CEACAM22P | carcinoembryonic antigen related cell adhesion molecule 22, pseudogene | Other | other |
| -26.19        | 7.91E-03                          | ENSG00000273203 |          | CECR7   | cataract eye syndrome chromosome region, candidate 7 (non-protein coding) | Other | other |
| 19.24         | 6.08E-02                          | ENSG00000264448 |          | CEL5    | CUGBP Elav-like family member 5 | Nucleus | other |
| 25.98         | 8.69E-02                          | ENSG00000273203 |          | CEP206  | cilium and flagella associated protein 206 | Cytoplasm | other |
| -27.02        | 7.01E-03                          | ENSG00000258469 |          | CHMP4BP1 | charged multivesicular body protein 4B pseudogene 1 | Other | other |
| -14.77        | 7.91E-03                          | ENSG00000181072 |          | CHRM2   | cholinergic receptor muscarinic 2 | Plasma Membrane | G-protein coupled receptor |

Table 1 (continued)
| Change |
|--------|
| -2792  |
| -28.07 |
| -30.00 |
| -25.71 |
| 26.50  |
| -27.92 |
| -27.42 |
| 29.36  |
| -16.35 |

| Gene ID | Accession | Description | Location |
|---------|-----------|-------------|----------|
| ENSG00000172322 | CLEC12A | C-type lectin domain family 12 member A | Plasma Membrane |
| ENSG00000111729 | CLEC4A | C-type lectin domain family 4 member A | Plasma Membrane |
| ENSG00000104038 | CLEC4M | C-type lectin domain family 4 member M | Plasma Membrane |
| ENSG00000205057 | CLL1OS | chronic lymphocytic leukemia up-regulated 1 opposite strand | Other |
| ENSG00000155052 | CNTNAP5 | contactin associated protein like 5 | Other |
| ENSG0000023159 | COX10 | heme A:cytochrome c oxidase assembly factor | Cytoplasm |
| ENSG00000258981 | COX5AP2 | cytochrome c oxidase subunit 5A pseudogene 2 | Other |
| ENSG00000117322 | CR2 | complement C3d receptor 2 | Plasma Membrane |
| ENSG00000276076 | CRYA/LOC102724652 | crystallin alpha A | Cytoplasm |
| Expr log ratio | Expr false discovery rate (q-value) | ID | Flags | Symbol | Entrez gene name | Location | Type(s) | Drug(s) |
|---------------|------------------------------------|----|--------|--------|-----------------|----------|---------|---------|
| 28.23         | 5.54E-03                           | ENSG00000135222 | CSN2   | casein beta    | Extracellular Space | kinase    |         |         |
| -29.34        | 4.45E-03                           | ENSG00000170367 | CST5   | cytostatin D   | Cytoplasm           | other     |         |         |
| -29.44        | 4.37E-03                           | ENSG00000228836 | CT45A10/CT45A5 | cancer/testis antigen family 45 member A5 | Other | other |         |
| -26.69        | 7.56E-03                           | ENSG00000235857 | CTBP2P1 | C-terminal binding protein 2 pseudogene 1 | Other | other |         |
| -26.36        | 7.91E-03                           | ENSG00000234993 | CUBN2  | cubulin pseudogene 2 | Other | other |         |
| -25.71        | 9.87E-03                           | ENSG00000120280 | CXorf21 | chromosome X open reading frame 21 | Other | enzyme |         |
| -26.19        | 7.91E-03                           | ENSG00000179305 | CYLC1  | cylin 1       | Cytoplasm           | other     |         |         |
| 27.73         | 5.66E-03                           | ENSG00000158333 | CYLC2  | cylin 2       | Other               | other     |         |         |
| 26.19         | 7.91E-03                           | ENSG00000036530 | CYP46A1 | cytochrome P450 family 46 subfamily A member 1 | Other | enzyme |         |
| -27.43        | 5.90E-03                           | ENSG00000173406 | DAB1   | DAB1, reelin adaptor protein | Cytoplasm | other |         |
| -26.36        | 7.91E-03                           | ENSG00000172844 | DAND5  | DAn domain BMP antagonist family member 5 | Extracellular Space | other |         |
| 26.19         | 7.91E-03                           | ENSG00000236709 | DAPK1-IT1 | DAPK1 intronic transcript 1 | Other | other |         |
| 30.00         | 4.30E-03                           | ENSG00000152670 | DDX4   | DEAD-box helicase 4 | Nucleus | enzyme |         |
| 27.24         | 6.98E-03                           | ENSG00000164822 | DEFA6  | defensin alpha 6 | Extracellular Space | other |         |
| -29.77        | 3.00E-03                           | ENSG00000205883 | DEFB135 | defensin beta 135 | Other | other |         |
| 28.47         | 7.91E-03                           | ENSG00000038866 | DGKG   | diacylglycerol kinase gamma | Cytoplasm | kinase |         |
| -26.36        | 7.91E-03                           | ENSG00000104808 | DHDH   | dihydridiol dehydrogenase | Other | enzyme |         |
| -17.70        | 6.24E-02                           | ENSG00000187908 | DMBT1  | deleted in malignant brain tumors 1 | Plasma Membrane | transmembrane receptor |         |
| -26.19        | 7.91E-03                           | ENSG00000157851 | DPP5L5 | dihydroptimidinase like 5 | Cytoplasm | enzyme |         |
| -25.71        | 9.87E-03                           | ENSG00000125821 | DT1    | D-lysyl-RNA deacetylase 1 | Cytoplasm | enzyme |         |
| 25.98         | 8.69E-03                           | ENSG00000198842 | DUSP27 | dual specificity phosphatase 27, atypical | Other | phosphatase |         |
| -30.00        | 4.30E-03                           | ENSG00000229798 | DYNTL3P2 | dynnein light chain Tctex-type 3 pseudogene 2 | Other | other |         |
| -22.51        | 3.61E-02                           | ENSG00000104823 | ECH1   | eukaryotic translation elongation factor 1 alpha 1 pseudogene 7 | Other | other |         |
| -28.07        | 5.54E-03                           | ENSG00000268222 | EEF1A1P7 | eukaryotic translation elongation factor 1 alpha 1 pseudogene 7 | Other | other |         |
| -28.80        | 5.52E-03                           | ENSG00000235549 | EF1P2  | eukaryotic translation initiation factor 1 pseudogene 2 | Other | other |         |
| -25.71        | 9.87E-03                           | ENSG00000227925 | ELL2P1 | elongation factor for RNA polymerase II 2 pseudogene 1 | Other | other |         |
| -25.63        | 1.10E-02                           | ENSG00000144488 | ESNPL  | espin like | Extracellular Space | other |         |
| -28.07        | 5.54E-03                           | ENSG00000253831 | ETV3L  | ETS variant 3 like | Other | other |         |
| 28.19         | 5.52E-03                           | ENSG00000231882 | F10-AS1 | F10 antisense RNA 1 | Other | other |         |
| -26.19        | 7.91E-03                           | ENSG00000226766 | FABP7P1 | fatty acid binding protein 7 | Other | other |         |
| -26.96        | 7.09E-03                           | ENSG00000183508 | FAM46C | family with sequence similarity 46 member C | Extracellular Space | other |         |
| 30.00         | 4.30E-03                           | ENSG00000174678 | FAM47DP |         | Other | other |         |
-27.40 6.75E-03 ENSG00000197872 FAM49A family with sequence similarity 47 member D, pseudogene
-26.50 7.91E-03 ENSG00000253488 FAM60BP family with sequence similarity 49 member A
-26.47 7.91E-03 ENSG00000227410 D FAM90A26 (includes others) family with sequence similarity 50, member A26, pseudogene
-26.47 7.91E-03 ENSG00000231656 D FAM90A26 (includes others) family with sequence similarity 50, member A26, pseudogene
-26.47 7.91E-03 ENSG00000237122 D FAM90A26 (includes others) family with sequence similarity 50, member A26, pseudogene
-22.53 4.68E-02 ENSG00000231060 FRSBP1 phenylalanine-tRNA synthetase beta subunit pseudogene 1
29.24 4.62E-03 ENSG00000132185 FCRLA Fc receptor like A Plasma Membrane other
19.89 5.10E-02 ENSG00000181171 FER1L6-AS1 FER1L6 antisense RNA 1 Other other
30.00 4.30E-03 ENSG00000146618 FERD3L Fe3+ like BH4H transcription factor Nucleus transcription regulator
28.56 5.52E-03 ENSG00000168546 GFRA2 GDNF family receptor alpha 2 Plasma Membrane transmembrane receptor
26.47 7.91E-03 ENSG00000257800 D FAM90A26 (includes others) family with sequence similarity 50, member A26, pseudogene
25.71 4.68E-02 ENSG00000086205 FOLH1 folate hydrolase 1 Plasma Membrane peptidase capromab pendetide
-6.35 7.87E-02 ENSG00000110195 FOLR1 folate receptor 1 Plasma Membrane transporter farletuzumab
-26.96 7.09E-03 ENSG00000258421 FXNPI frataxin pseudogene 1 Other other
27.73 5.66E-03 ENSG00000177736 FXNIP2 frataxin pseudogene 2 Other other
26.13 8.21E-03 ENSG00000136750 GAD2 glutamate decarboxylase 2 Cytoplasm enzyme valproic acid
26.50 7.91E-03 ENSG00000257594 GALNT4 polypeptide N-acetylgalactosaminyltransferase 4 Cytoplasm enzyme
25.98 8.69E-03 ENSG00000109534 GAR1 GAR1 ribonuclease specific 1 like 1 pseudogene 2 Nucleus other
30.00 4.30E-03 ENSG00000223876 GAS2L1P2 G protein nucleolar 2 pseudogene 1 Other other
-25.63 1.10E-02 ENSG00000272695 GNAS-AS2 GNAS antisense RNA 2 (head to head) Other other
26.85 7.20E-03 ENSG00000168546 GFRα2 GDNF family receptor alpha 2 Plasma Membrane transmembrane receptor
-26.19 7.91E-03 ENSG00000125861 GFRα4 GDNF family receptor alpha 4 Plasma Membrane transmembrane receptor
-29.72 4.37E-03 ENSG00000197421 GGT3P gamma-glutamyltransferase 3 pseudogene Extracellular Space other
-28.54 5.52E-03 ENSG00000223893 GNL2PI G protein nucleolar 2 pseudogene 1 Other other
-27.08 6.99E-03 ENSG0000011171 GOLT1B golgi transport 1B Cytoplasm other
-27.02 7.01E-03 ENSG00000235984 GPC5-AS1 GPC5 antisense RNA 1 Other other
28.58 5.52E-03 ENSG00000232885 GPC5-AS2 GPC5 antisense RNA 2 Other other
-26.36 7.91E-03 ENSG00000182771 GRID1 glutamate ionotropic receptor delta type subunit 1 Plasma Membrane ion channel
27.43 6.04E-03 ENSG00000140307 GTF2A2 general transcription factor IA subunit 2 Nucleus transcription regulator
-26.19 7.91E-03 ENSG00000153767 GTF2E1 general transcription factor IE subunit 1 Nucleus transcription regulator
-29.44 4.45E-03 ENSG00000237099 GYG1P2 glycogenin 1 pseudogene 2 Other other
21.02 7.22E-02 ENSG00000145649 GZMA granzyme A Cytoplasm peptidase
28.14 5.52E-03 ENSG00000270604 HCG17 (continued on next page)
Table 1 (continued)

| Expr log ratio | ID          | Symbol | Entrez gene name                                                                 | Location       | Type(s)            | Drug(s)                                                                 |
|----------------|-------------|--------|----------------------------------------------------------------------------------|----------------|--------------------|--------------------------------------------------------------------------|
| -30.00         | ENSG00000164588 HCN1 | hyperpolarization activated cyclic nucleotide gated potassium channel 1 (non-protein coding) | Plasma Membrane | ion channel        |                                                                           |
| 26.47          | ENSG00000281831 HCP5B | HLA complex P5B (non-protein coding) | Other              | Other              |                                                                           |
| -28.32         | ENSG00000113924 HGD | homogenisate 1,2-dioxygenase | Cytoplasm         | enzyme             |                                                                           |
| 28.23          | ENSG00000273703 HIST1H2BM | histone cluster 1H2B family member | Nucleus           | other              |                                                                           |
| -29.72         | ENSG00000274641 HIST1H2BO | histone cluster 1H2B family member | Nucleus           | other              |                                                                           |
| -30.00         | ENSG0000024557 HLA-DPB2 | major histocompatibility complex, class II, DP beta 2 (pseudogene) | Plasma Membrane | transmembrane receptor | iloperidone, asenapine, sulthiame, lurasidone, vortioxetine, brexpiprazole, eletriptan, almotriptan, almotriptan, amoxapine, fenfluramine, methysergide, ergotamine |
| 28.15          | ENSG00000220557 HMGB1P13 | high mobility group box 1 pseudogene 13 | Other              | other              |                                                                           |
| 28.15          | ENSG00000253516 HMGB1P41 | high mobility group box 1 pseudogene 41 | Other              | other              |                                                                           |
| -28.07         | ENSG00000237285 HNRNPA1P2 | heterogeneous nuclear ribonucleoprotein A1 pseudogene 2 | Other              | other              |                                                                           |
| 29.41          | ENSG00000249271 HNRNPA1P44 | heterogeneous nuclear ribonucleoprotein A1 pseudogene 44 | Other              | other              |                                                                           |
| -26.80         | ENSG00000120075 HOXB5 | homeobox box B5 | Nuclear regulation | transcription regulator |                                                                           |
| -29.82         | ENSG00000123407 HOXC12 | homeobox C12 | Nuclear regulation | transcription regulator |                                                                           |
| 28.24          | ENSG00000228355 HRAF1 | heart tissue-associated transcript 92 | Other              | other              |                                                                           |
| -26.19         | ENSG00000248159 HSPA1P11 | heat shock protein family A (Hsp70) member 8 pseudogene 11 | Other              | other              |                                                                           |
| 26.13          | ENSG00000250356 HSPE1P23 | heat shock protein family E (Hsp10) member 1 pseudogene 23 | Other              | other              |                                                                           |
| 25.69          | ENSG00000232015 HSPE1P25 | heat shock protein family E (Hsp10) member 1 pseudogene 25 | Other              | other              |                                                                           |
| -27.92         | ENSG00000148680 HTR7 | 5-hydroxytryptamine receptor 7 | Plasma Membrane | G-protein coupled receptor |                                                                           |
| 30.00          | ENSG00000121351 IAPP | islet amyloid polypeptide | Extracellular Space | other              |                                                                           |
| -29.81         | ENSG00000137965 IFH4 | interferon induced protein 44 | Cytoplasm         | other              |                                                                           |
| -26.19         | ENSG00000273211 IFNL4P1 | interferon lambda 4 pseudogene 1 | Other              | other              |                                                                           |
| -30.00         | ENSG00000163395 IGFN1 | immunoglobulin-like and fibronectin type III domain containing 1 | Nucleus           | other              |                                                                           |
| 26.13          | ENSG00000233855 KKV1-6 | immunoglobulin kappa variable 1-6 | Other              | other              |                                                                           |
| -29.75         | ENSG00000253823 KLV1-62 | immunoglobulin lambda variable 1-6 (pseudogene) | Other              | other              |                                                                           |
| 25.98          | ENSG00000253889 KLV1-38 | Other | Other | other              |                                                                           |
| Ensembl ID          | Gene                                                                 | Description                                 | Chromosome | Score | ENSG00000196083 | IL1RAP | interleukin 1 receptor accessory protein | Plasma Membrane transmembrane receptor | CAN04 |
|---------------------|----------------------------------------------------------------------|----------------------------------------------|------------|-------|-----------------|--------|------------------------------------------|----------------------------------------|-------|
| -26.36 7.91E-03     | ENSG00000196083                                                      | IL1RAP                                       | Plasma Membrane |      |                 |        |                                          |                                        |       |
| -25.71 9.87E-03     | ENSG00000162594                                                      | IL23R                                        | Plasma Membrane |      |                 |        |                                          |                                        |       |
| 26.23 5.54E-03      | ENSG00000217539                                                      | IQCR2P                                       | Other        |       |                 |        |                                          |                                        |       |
| 25.98 8.69E-03      | ENSG00000255679                                                      | JRLK-AS1                                     | Other        |       |                 |        |                                          |                                        |       |
| -15.26 8.56E-03     | ENSG00000242370                                                      | KCNB1-AS1                                    | Other        |       |                 |        |                                          |                                        |       |
| 27.58 5.67E-03      | ENSG00000280650                                                      | KCNP4-IT1                                    | Other        |       |                 |        |                                          |                                        |       |
| -15.90 5.44E-03     | ENSG00000162989                                                      | KCNJ3                                        | Plasma Membrane |      |                 |        |                                          |                                        |       |
| -27.92 5.54E-03     | ENSG00000257069                                                      | KCNK4-TEX40                                   | Other        |       |                 |        |                                          |                                        |       |
| -25.63 1.10E-02     | ENSG00000143603                                                     | KCNNJ                                        | Plasma Membrane |      |                 |        |                                          |                                        |       |
| -22.96 3.92E-02     | ENSG00000150361                                                      | KJH1L1                                       | Cytoplasm    |       |                 |        |                                          |                                        |       |
| 27.01 6.99E-03      | ENSG00000250221                                                      | KRT8P32                                      | Other        |       |                 |        |                                          |                                        |       |
| 27.38 5.67E-03      | ENSG00000198841                                                      | KTH2                                         | Other        |       |                 |        |                                          |                                        |       |
| -27.02 7.01E-03     | ENSG00000217783                                                     | LDHAL6FP                                     | Other        |       |                 |        |                                          |                                        |       |
| 28.32 5.52E-03      | ENSG00000179676                                                     | LINC00305                                    | Other        |       |                 |        |                                          |                                        |       |
| 19.43 1.87E-02      | ENSG00000226250                                                     | LINC00408                                    | Other        |       |                 |        |                                          |                                        |       |
| -26.97 7.01E-03     | ENSG00000236384                                                     | LINC00479                                    | Plasma Membrane |      |                 |        |                                          |                                        |       |
| -25.71 9.87E-03     | ENSG00000251533                                                     | LINC00605                                    | Other        |       |                 |        |                                          |                                        |       |
| 25.98 8.69E-03      | ENSG00000233746                                                     | LINC00656                                    | Other        |       |                 |        |                                          |                                        |       |
| -27.92 5.54E-03     | ENSG00000229404                                                     | LINC00858                                    | Other        |       |                 |        |                                          |                                        |       |
| -14.31 1.94E-02     | ENSG00000214145                                                     | LINC00887                                    | Other        |       |                 |        |                                          |                                        |       |
| -26.19 7.91E-03     | ENSG00000253961                                                     | LINC00927                                    | Other        |       |                 |        |                                          |                                        |       |
| -26.36 7.91E-03     | ENSG00000230174                                                     | LINC01149                                    | Other        |       |                 |        |                                          |                                        |       |
| -26.36 7.91E-03     | ENSG00000274827                                                     | LINC01297                                    | Other        |       |                 |        |                                          |                                        |       |
| -26.19 7.91E-03     | ENSG00000244578                                                     | LINC01391                                    | Other        |       |                 |        |                                          |                                        |       |
| -3.000 4.30E-03     | ENSG00000249306                                                     | LINC01411                                    | Other        |       |                 |        |                                          |                                        |       |
| 26.47 7.91E-03      | ENSG00000254211                                                     | LINC01485                                    | Other        |       |                 |        |                                          |                                        |       |
| -27.43 5.67E-03     | ENSG00000231422                                                     | LINC01516                                    | Other        |       |                 |        |                                          |                                        |       |
| 27.58 5.67E-03      | ENSG00000262468                                                     | LINC01569                                    | Other        |       |                 |        |                                          |                                        |       |
| -27.73 5.54E-03     | ENSG00000227115                                                     | LINC01630                                    | Other        |       |                 |        |                                          |                                        |       |

(continued on next page)
| Expr | log ratio | ID | Flags | Symbol | Entrez gene name | Location | Type(s) | Drug(s) |
|------|-----------|----|-------|--------|-----------------|----------|---------|---------|
| -35.36 | 7.91E-03 | ENSG00000227958 | LINC01676 | Long intergenic non-protein coding RNA 1676 | Other | other |
| -30.00 | 4.38E-03 | ENSG000002279181 | LINC01688 | Long intergenic non-protein coding RNA 1688 | Other | other |
| -28.07 | 5.45E-03 | ENSG00000223496 | LINC01825 | Long intergenic non-protein coding RNA 1825 | Other | other |
| -28.07 | 5.45E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -25.63 | 1.04E-02 | ENSG000002251085 | LINC01944 | Long intergenic non-protein coding RNA 1944 | Other | other |
| -27.86 | 5.45E-03 | ENSG000002279313 | LINC02015 | Long intergenic non-protein coding RNA 2015 | Other | other |
| -29.89 | 4.38E-03 | ENSG00000229155 | LINC02308 | Uncharacterized LOC100506532 | Other | other |
| -30.00 | 4.38E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -28.23 | 5.52E-03 | ENSG00000228877 | LOC100996549 | Uncharacterized LOC100996549 | Other | other |
| -28.52 | 5.52E-03 | ENSG000002257056 | LINC02324 | Long intergenic non-protein coding RNA 2324 | Other | other |
| -28.54 | 5.52E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -29.77 | 4.38E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -30.00 | 4.38E-03 | ENSG000002279313 | LINC02015 | Long intergenic non-protein coding RNA 2015 | Other | other |
| -29.90 | 4.38E-03 | ENSG00000227958 | LINC01676 | Long intergenic non-protein coding RNA 1676 | Other | other |
| -28.36 | 1.04E-02 | ENSG000002251085 | LINC01944 | Long intergenic non-protein coding RNA 1944 | Other | other |
| -29.92 | 4.38E-03 | ENSG00000229155 | LINC02308 | Uncharacterized LOC100506532 | Other | other |
| -29.97 | 4.38E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -28.90 | 4.38E-03 | ENSG00000227958 | LINC01676 | Long intergenic non-protein coding RNA 1676 | Other | other |
| -28.23 | 5.52E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -29.96 | 4.38E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -28.23 | 5.52E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -29.96 | 4.38E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -28.23 | 5.52E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| -29.90 | 4.38E-03 | ENSG00000227958 | LINC01676 | Long intergenic non-protein coding RNA 1676 | Other | other |
| -28.23 | 5.52E-03 | ENSG000002254945 | LINC01894 | Long intergenic non-protein coding RNA 1894 | Other | other |
| Expr log ratio | ID Flags Symbol | Entrez gene name | Location | Type(s) Drug(s) |
|---------------|----------------|-----------------|----------|----------------|
| 26.50 7.91E-03 | ENSG00000120149 | MSX2 msh homeobox 2 | Nucleus | transcription regulator |
| 25.98 8.69E-03 | ENSG00000227035 | MTATP6P18 | Other | other |
| 27.58 5.67E-03 | ENSG00000237055 | MTCO1P48 | Other | other |
| 27.80 5.54E-03 | ENSG00000236211 | MTCO1P7 | Other | other |
| 19.32 5.83E-02 | ENSG0000023888 | MTCO2P17 | Other | other |
| 19.32 4.66E-02 | ENSG00000231576 | MTCO2P20 | Other | other |
| -26.36 7.91E-03 | ENSG00000254118 | MTCYBP20 | Other | other |
| -26.19 7.91E-03 | ENSG00000263241 | MTCYBP33 | Other | other |
| -28.80 5.52E-03 | ENSG00000271687 | MTND5P10 mitochondrially encoded NADH:ubiquinone oxidoreductase core subunit 5 pseudogene 10 | Other | other |
| -26.36 7.91E-03 | ENSG00000256045 | MTRNR2L10 MT-RNR2-like 10 | Other | other |
| -23.86 5.67E-03 | ENSG00000177034 | MTX3 metaxin 3 | Plasma Membrane | other |
| -30.00 4.30E-03 | ENSG00000169876 | MUC17 mucin 17, cell surface associated myogenic factor 6 | Nucleus | transcription regulator |
| -27.92 5.54E-03 | ENSG00000111046 | MYF6 myomaker, myoblast fusion factor | Plasma Membrane | other |
| -25.63 1.10E-02 | ENSG00000187616 | MYMK myomaker, myoblast fusion factor | Plasma Membrane | other |
| -26.36 7.91E-03 | ENSG00000225619 | MYT1L-AS1 MYT1L antisense RNA 1 | Other | other |
| -29.47 4.39E-03 | ENSG00000204272 | NBDY negative regulator of P-body association | Other | other |
| 26.13 8.21E-03 | ENSG00000124479 | NDP NDP, norrin cystine knot growth factor | Extracellular Space | growth factor |
| -29.85 4.30E-03 | ENSG0000016507 | NDST2 N-deacetylase and N-sulfotransferase 2 | Cytoplasm | enzyme |
| -29.94 4.30E-03 | ENSG00000242943 | NKA1P1 potassium transporting ATPase interacting 1 pseudogene 1 | Other | other |
| 26.83 7.14E-03 | ENSG00000248745 | NNNATP14 NNNAT pseudogene 4 | Other | other |
| -29.59 4.34E-03 | ENSG00000171596 | NMRI1 neuromedin U receptor 1 | Plasma Membrane | G-protein coupled receptor |
| -17.20 3.35E-02 | ENSG00000086891 | NOX4 NADPH oxidase 4 | Cytoplasm | enzyme |
| -28.00 5.54E-03 | ENSG00000112333 | NR2E1 nuclear receptor subfamily 2 group E member 1 | Nucleus | ligand-dependent nuclear receptor |
| -29.84 4.30E-03 | ENSG00000225964 | NRIR | Other | other |
| -15.04 4.30E-03 | ENSG00000101188 | NTSR1 neurotensin receptor 1 | Plasma Membrane | G-protein coupled receptor |
| -22.99 5.52E-03 | ENSG00000152463 | OLAH oleoyl-ACP hydrolase | Cytoplasm | G-protein coupled receptor |
| 27.58 5.67E-03 | ENSG00000125510 | OPR1L opioid related nociceptin receptor 1 | Plasma Membrane | G-protein coupled receptor |
| 27.83 5.54E-03 | ENSG00000171199 | OPRPN opiorphin prepropeptide | Extracellular Space | other |
| -28.53 5.52E-03 | ENSG00000180409 | OR1QA1P | Plasma Membrane | other |
| 26.85 7.20E-03 | ENSG00000130538 | OR1H12 (includes others) | Other | other |
| 26.50 7.91E-03 | ENSG00000257115 | OR1H12 (includes others) | Plasma Membrane | other |
| 26.50 7.91E-03 | ENSG00000203581 | OR1F2P | Other | other |
olfactory receptor family 1 subfamily F member 2 pseudogene
A member 41 pseudogene

Plasma Membrane G-protein coupled receptor

Other other

Plasma Membrane G-protein coupled receptor

Other other

Other other

Cytoplasm other

Cytoplasm enzyme

Cytoplasm enzyme

Cytoplasm other

Cytoplasm enzyme

Cytoplasm other

Cytoplasm other

Cytoplasm enzyme

Cytoplasm enzyme

Cytoplasm other

Cytoplasm enzyme

Other other
| Expr log ratio | Expr false discovery rate (q-value) | ID | Flags | Symbol | Entrez gene name | Location | Type(s) | Drug(s) |
|---------------|-----------------------------------|----|-------|--------|-----------------|----------|---------|---------|
| -28.52        | 5.52E-03                          | ENSG00000227462 | PSME2P6 | proteasome activator subunit 2 pseudogene 6 |
| -27.92        | 5.54E-03                          | ENSG00000244694 | PTCHD4 | patched domain containing 4 |
| -26.36        | 7.91E-03                          | ENSG00000171611 | PTCRA | pre-T-cell antigen receptor alpha |
| 26.50         | 7.91E-03                          | ENSG00000172733 | PURG | purine rich element binding protein G |
| 30.00         | 4.30E-03                          | ENSG00000159661 | RAB39B | RAB39B, member RAS oncogene family |
| 26.19         | 7.91E-03                          | ENSG00000198774 | RASSP9 | Ras association domain family member 9 |
| 27.58         | 5.67E-03                          | ENSG00000168411 | RFWD3 | ring finger and WD repeat domain 3 |
| 27.97         | 7.91E-03                          | ENSG00000102760 | RGCC | regulator of cell cycle |
| -29.62        | 4.37E-03                          | ENSG00000101883 | RHOX1F1 | RhoX homeobox family member 1 |
| 28.01         | 5.54E-03                          | ENSG00000234493 | RHOX1P1 | RhoX homeobox family member 1 pseudogene 1 |
| 28.49         | 5.52E-03                          | ENSG00000252490 | RN7SKP66 | RNA, 7SK small nuclear pseudogene 79 |
| 27.91         | 5.54E-03                          | ENSG00000199940 | RN7SKP75 | RNA, 7SL, cytoplasmic 123, pseudogene |
| 27.92         | 5.54E-03                          | ENSG00000200243 | RN7SKP79 | RNA, 7SL, cytoplasmic 184, pseudogene |
| 28.12         | 5.54E-03                          | ENSG00000266863 | RN7SL123P | RNA, 7SL, cytoplasmic 184, pseudogene |
| 29.55         | 4.77E-03                          | ENSG00000232979 | RN7SL184P | RNA, 7SL, cytoplasmic 184, pseudogene |
| 30.00         | 4.30E-03                          | ENSG00000265740 | RN7SL339P | RNA, 7SL, cytoplasmic 445, pseudogene |
| 28.09         | 5.54E-03                          | ENSG00000240577 | RN7SL445P | RNA, 7SL, cytoplasmic 583, pseudogene |
| 29.77         | 4.30E-03                          | ENSG00000202500 | RN7SL597P | RNA, 7SL, cytoplasmic 583, pseudogene |
| 29.14         | 4.77E-03                          | ENSG00000237444 | RN7SL63P | RNA, 55 ribosomal pseudogene 22 |
| 30.00         | 4.30E-03                          | ENSG00000239139 | RN7SL854P | RNA, 55 ribosomal pseudogene 240 |
| 29.77         | 4.30E-03                          | ENSG00000202263 | RN55P22 | RNA, 55 ribosomal pseudogene 240 |
| 26.19         | 7.91E-03                          | ENSG00000202225 | RN55P240 | RNA, 55 ribosomal pseudogene 240 |
| 27.92         | 5.54E-03                          | ENSG00000199554 | RN55P273 | RNA, 55 ribosomal pseudogene 273 |
| 26.83         | 7.14E-03                          | ENSG00000104889 | RNASEH2A | ribonuclease H2 subunit A |
| 26.36         | 7.91E-03                          | ENSG00000250596 | RNPS1P1 | RNA binding protein with serine rich domain 1 pseudogene 1 |
| 28.49         | 5.52E-03                          | ENSG00000202213 | RNU1-64P | RNA, U2 small nuclear 30, pseudogene |
| 25.48         | 1.15E-02                          | ENSG00000252018 | RNU2-30P | RNA, U4atac small nuclear 17, pseudogene |
| 28.55         | 5.52E-03                          | ENSG00000206931 | RNU4-1042P | RNA, U6 small nuclear 1042, pseudogene |
| 27.92         | 5.54E-03                          | ENSG00000201165 | RNU6-1229P | RNA, U6 small nuclear 1042, pseudogene |
| Accession        | Gene Name | Description                                                                 | Cell Type | Subcellular Location |
|------------------|-----------|------------------------------------------------------------------------------|-----------|----------------------|
| ENSG00000207312  | RNA, U6   | RNA, U6 small nuclear 129, pseudogene                                        | Other     | Other                |
| ENSG00000206983  | RNA, U6   | RNA, U6 small nuclear 49, pseudogene                                         | Other     | Other                |
| ENSG000002252860 | RNA, U6   | RNA, U6 small nuclear 570, pseudogene                                        | Other     | Other                |
| ENSG00000222972  | RNA, U6   | RNA, U6 small nuclear 429, pseudogene                                        | Other     | Other                |
| ENSG00000207333  | RNA, U6   | RNA, U6 small nuclear 784, pseudogene                                        | Other     | Other                |
| ENSG00000206960  | RNA, U6   | RNA, U6 small nuclear 793, pseudogene                                        | Other     | Other                |
| ENSG00000238788  | RNA, U7   | RNA, U7 small nuclear 182, pseudogene                                        | Other     | Other                |
| ENSG00000104237  | RP1       | RP1, axonemal microtubule associated                                           | Cytoplasm | Other                |
| ENSG00000230853  | RPL10P11  | ribosomal protein L10 pseudogene 11                                          | Other     | Other                |
| ENSG00000230559  | RPL11P12  | ribosomal protein L11 pseudogene 5                                            | Other     | Other                |
| ENSG00000243964  | RPL23AP65 | ribosomal protein L23a pseudogene 65                                          | Other     | Other                |
| ENSG00000230364  | RPL4P3    | ribosomal protein L4 pseudogene 3                                             | Other     | Other                |
| ENSG00000243914  | RPL5P14   | ribosomal protein L5 pseudogene 14                                            | Other     | Other                |
| ENSG00000235232  | RPL5P33   | ribosomal protein L5 pseudogene 33                                            | Other     | Other                |
| ENSG00000234415  | RPL5P7    | ribosomal protein L5 pseudogene 7                                             | Other     | Other                |
| ENSG00000234742  | RPLP0P2   | ribosomal protein lateral stalk subunit P0 pseudogene 2                       | Other     | Other                |
| ENSG00000180172  | RPS12P23  | ribosomal protein S12 pseudogene 23                                           | Other     | Other                |
| ENSG00000236862  | RPS20P24  | ribosomal protein S20 pseudogene 24                                           | Other     | Other                |
| ENSG00000231241  | RPS3AP3   | ribosomal protein S3A pseudogene 3                                            | Other     | Other                |
| ENSG00000226525  | RPS7P10   | ribosomal protein S7 pseudogene 10                                            | Cytoplasm | Other                |
| ENSG00000228820  | RPS5A1F   | ribosomal protein SA pseudogene 1                                             | Other     | Other                |
| ENSG00000227721  | RPS5A64   | ribosomal protein SA pseudogene 64                                            | Other     | Other                |
| ENSG00000235598  | RRM2M     | ribonucleotide reductase M2                                                   | Other     | Other                |
| ENSG00000166562  | SEC11C    | SEC11 homolog C, signal peptide peptidase complex subunit                    | Cytoplasm | Peptidase            |
| ENSG00000138623  | SEMA7A    | semaphorin 7A (John Milton Hagen blood group)                                 | Plasma Membrane | Transmembrane receptor |
| ENSG00000204089  | SEPT14    | SET pseudogene 14                                                             | Other     | Other                |
| ENSG00000090402  | SI        | sucrase-isomaltase                                                            | Cytoplasm | Enzyme               |
| ENSG00000225774  | SIRPA1F   | signal regulatory protein alpha                                               | Other     | Other                |
| ENSG00000179520  | SLC1A7    | solute carrier family 17 member 8                                             | Plasma Membrane | Transmembrane transporter |
| ENSG00000105143  | SLC1A6    | solute carrier family 1 member 6                                              | Plasma Membrane | Transmembrane transporter |
| ENSG00000183048  | SLC2A5    | solute carrier family 25 member 10                                            | Cytoplasm  | Other                |
| ENSG00000225347  | SLC2A5P8  | solute carrier family 25 member 5                                             | Other     | Other                |

(continued on next page)
| Expr log ratio | ID | Flags | Symbol | Entrez gene name | Location | Type(s) | Drug(s) |
|---------------|----|-------|--------|-----------------|----------|---------|---------|
| -27.92        | 5.54E-03 | ENSG00000251078 | SLC25A5P9 | solute carrier family 25 member 5 pseudogene 9 | Other | other |
| 30.00         | 4.30E-03 | ENSG00000124786 | SLC35B3 | solute carrier family 35 member B3 | Cytoplasm | transporter |
| -27.20        | 7.01E-03 | ENSG00000188338 | SLC38A3 | solute carrier family 38 member 3 | Plasma Membrane | transporter |
| -27.71        | 5.66E-03 | ENSG00000148482 | SLC39A12 | solute carrier family 39 member 12 | Plasma Membrane | transporter |
| -28.07        | 5.54E-03 | ENSG00000214329 | SLC9B1P2 | solute carrier family 9 member B1 pseudogene 2 | Other | other |
| -26.19        | 7.91E-03 | ENSG00000185985 | SLITRK2 | SLIT and NTRK like family member 2 | Plasma Membrane | other |
| 28.14         | 5.52E-03 | ENSG00000200354 | SNORD71D | small nucleolar RNA H/ACA box 71D | Other | other |
| 26.50         | 7.91E-03 | ENSG000002303043 | SNORD115-48 | small nucleolar RNA C/D box 115-48 | Other | other |
| 26.50         | 7.91E-03 | ENSG00000201330 | SNORD127 | small nucleolar RNA C/D box 127 | Other | other |
| 27.58         | 5.67E-03 | ENSG00000207215 | SNORD3H | small nucleolar RNA C/D box 3H | Other | other |
| 28.49         | 5.52E-03 | ENSG00000225642 | SNRPPF5 | small nuclear ribonucleoprotein polypeptide E pseudogene 5 | Other | other |
| 27.02         | 7.01E-03 | ENSG00000228741 | SPATA13 | spermatogenesis associated 13 | Plasma Membrane | other |
| 27.58         | 5.67E-03 | ENSG00000258916 | SPATA31E2P | SPATA31 subfamily E member 2, pseudogene | Other | other |
| 27.05         | 7.01E-03 | ENSG00000164299 | SPZ1 | spermatogenic leucine zipper 1 | Nucleus | transcription regulator |
| -23.05        | 9.68E-03 | ENSG00000138378 | STAT4 | signal transducer and activator of transcription 4 | Nucleus | transcription regulator |
| 30.00         | 4.30E-03 | ENSG00000165730 | STO5X1 | storkhead box 1 | Cytoplasm | other |
| 29.88         | 4.30E-03 | ENSG00000164744 | SUN3 | Sad1 and UNC84 domain containing 3 | Nucleus | other |
| 29.35         | 4.45E-03 | ENSG00000217442 | SYCE3 | synaptonemal complex central element protein 3 | Nucleus | other |
| 27.01         | 6.99E-03 | ENSG00000127362 | TAS2R3 | taste 2 receptor member 3 | Plasma Membrane | G-protein coupled receptor |
| -28.49        | 5.52E-03 | ENSG00000273513 | TBC1D3 (includes others) | TBC1 domain family member 3 | Extracellular Space | other |
| 20.61         | 9.19E-02 | ENSG00000274611 | TBC1D3 (includes others) | TBC1 domain family member 3 | Extracellular Space | other |
| -25.63        | 1.10E-02 | ENSG00000236567 | TCF3P1 | transcription factor 3 pseudogene 1 | Other | other |
| -26.69        | 7.65E-03 | ENSG00000167014 | TERB2 | telomere repeat binding bosquet formation protein 2 | Nucleus | other |
| -26.19        | 7.91E-03 | ENSG00000135426 | TESPA1 | thymocyte expressed, positive selection associated 1 | Cytoplasm | other |
| 26.85         | 7.20E-03 | ENSG00000237675 | TEX36-AS1 | TEX36 antisense RNA 1 | Other | other |
| 20.64         | 8.58E-02 | ENSG00000226674 | TEX41 | testis expressed 41 (non-protein coding) | Other | other |
| 27.58         | 5.67E-03 | ENSG0000008197 | TFAP2D | transcription factor AP-2 delta | Nucleus | transcription regulator |
| -26.19        | 7.91E-03 | ENSG00000243926 | TIPARP-AS1 | TIPARP antisense RNA 1 | Other | other |
| -26.19        | 7.91E-03 | ENSG00000151952 | TMEM132D | transmembrane protein 132D | Other | other |
| 27.72         | 5.66E-03 | ENSG00000178821 | TMEM52 | transmembrane protein 52 | Other | other |
| Gene ID               | Description                                      | Location        | Cell Component | Transcription Factor |
|----------------------|--------------------------------------------------|-----------------|----------------|----------------------|
| ENSG00000154646      | TMPRSS15 transmembrane protease, serine 15       | Extracellular    | peptidase      |                      |
| ENSG00000176040      | TMPRSS7 transmembrane protease, serine 7         | Plasma Membrane  | peptidase      |                      |
| ENSG00000235211      | TMSB10P2 thymosin beta 10 pseudogene 2           | Other            | other          |                      |
| ENSG00000188765      | TMSB4P2 thymosin beta 4, X-linked pseudogene 2   | Other            | other          |                      |
| ENSG00000223551      | TMSB4P4 thymosin beta 4, X-linked pseudogene 4   | Other            | other          |                      |
| ENSG00000248697      | TOX4P1 TOX high mobility group box family member 4 pseudogene 1 | Other            | other          |                      |
| ENSG00000139287      | TPH2 tryptophan hydroxylase 2                   | Plasma Membrane  | enzyme         |                      |
| ENSG00000234782      | TPT1P9 tumor protein, translationally-controlled 1 pseudogene 9 | Other            | other          |                      |
| ENSG00000211831      | TRA6I T cell receptor alpha joining 61 (non-functional) | Other            | other          |                      |
| ENSG00000211880      | TRA9 T cell receptor alpha joining 9            | Other            | other          |                      |
| ENSG00000211818      | TRAV39 T cell receptor alpha variable 39        | Other            | other          |                      |
| ENSG00000211710      | TRBV4-1 T cell receptor beta variable 4-1       | Other            | other          |                      |
| ENSG00000227550      | TRBV7-5 T cell receptor beta variable 7-5       | Other            | other          |                      |
| ENSG00000132109      | TRIM21 tripartite motif containing 21           | Nucleus          | enzyme         |                      |
| ENSG00000174173      | TRMT10C tRNA methyltransferase 10C               | Cytoplasm        | enzyme         |                      |
| ENSG00000134198      | TSPAN2 tetraspanin 2                            | Extracellular    | other          |                      |
| ENSG00000197763      | TXNRD3 thioredoxin reductase 3                  | Cytoplasm        | enzyme         |                      |
| ENSG00000215218      | UBEQQL1 ubiquitin conjugating enzyme E2 Q family like 1 | Nucleus          | enzyme         |                      |
| ENSG00000229667      | UBE2V1P9 ubiquitin conjugating enzyme E2 V1 pseudogene 9 | Other            | other          |                      |
| ENSG00000165623      | UCMA upper zone of growth plate and cartilage matrix associated | Extracellular    | other          |                      |
| ENSG00000260722      | VN1R67P vomenosanal 1 receptor 67 pseudogene    | Other            | other          |                      |
| ENSG00000251900      | VTRNA2-2P                                       | Other            | other          |                      |
| ENSG00000229932      | YWHAQP3 tyrosine 3-monoxygenase/tryptophan 5-monoxygenase activation protein zeta pseudogene 3 | Other            | other          |                      |
| ENSG00000155329      | ZCCHC10 zinc finger CCHC-type containing 10     | Other            | other          |                      |
| ENSG00000155256      | ZFVE27 zinc finger FYVE-type containing 27      | Plasma Membrane  | other          |                      |
| ENSG00000170631      | ZNF16 zinc finger protein 16                    | Nucleus          | other          |                      |
| ENSG00000204789      | ZNF204P zinc finger protein 204, pseudogene     | Other            | other          |                      |
| ENSG00000185947      | ZNF267 zinc finger protein 267                  | Nucleus          | other          |                      |
| ENSG00000186026      | ZNF284 zinc finger protein 284                  | Other            | other          |                      |
| ENSG00000180855      | ZNF443 zinc finger protein 443                  | Nucleus          | transcription regulator |                      |
| ENSG00000188668      | ZNF903 zinc finger protein 563                  | Nucleus          | other          |                      |
| ENSG00000198182      | ZNF906 zinc finger protein 607                  | Nucleus          | other          |                      |
| ENSG00000198807      | ZNF906 zinc finger protein 806                  | Other            | other          |                      |
| ENSG00000197933      | ZNF823 zinc finger protein 823                  | Nucleus          | other          |                      |
(the expression of that gene in the initial biopsy)] of that gene in the control subjects were significant. Thus, this data shows the genes in which mRNA expression was significantly changed by consumption of walnut compared to control and the direction of that change (increased or decreased).

The data in Table 2 contains all the loci which did not map to a gene but were identified as significantly altered in the breast tumor by consumption of walnut using the same calculations as for the data in Table 1. The meaning of changes in these loci has not been identified.

IPA analyses use the results shown in Table 1 to organize the genes into functional networks. This is important to identify the net effect of multiple changes on gene expression. The data in Table 3 lists all 25 significantly modified gene networks that were identified by IPA analyses, the genes in those networks and the top diseases and functions associated with the genes. The network ‘score’, the negative log of the overall statistical significance of the network, is shown. A network score of 41 means that in $10^{-41}$ experiments of a similar type one might encounter this pattern of mRNA expression changes by chance. The data in this table indicates the effect of walnut consumption on gene networks in the existing breast cancer and could indicate other diseases or functions in which dietary walnut may have benefit. Focused research would be needed to ascertain this benefit.

2. Experimental design, materials and methods

2.1. Experimental design

Women were recruited for this clinical trial when they came to the clinic for their first diagnostic biopsy, before it was known if the lump was cancer or not. Potential subjects must have had lumps large enough for the necessary biopsies for diagnosis and 1 or 2 extra research biopsies. After signing informed consent, subjects were randomized into walnut-consuming or control groups. Subjects in the walnut group immediately began to consume 2 ounces of walnuts per day until surgery. If a subject was later found to not have cancer or if the cancer was to be treated with chemotherapy or radiation prior to surgery, she was no longer included in the trial. Thirty-eight women were initially recruited. Twenty-four of 38 subjects were disqualified because the lump was benign, or the subject was to receive chemo- or radiation therapy prior to surgery. An additional 4 subjects were disqualified because the extracted mRNA of at least one specimen did not pass quality control. Remaining were 10 subjects; five in the walnut consuming and five in the control group. mRNA was extracted from each individual specimen then genome wide mRNA was determined in each specimen via next-generation sequencing. Gene expression ratios were calculated for each gene as: $(\text{walnut surgery/walnut biopsy})/(\text{control surgery/control biopsy})$ for further analyses [1].

2.2. IRB approval

The Marshall University Office of Research Integrity has an Institutional Review Board (IRB), which reviews and monitors all human subject research conducted at Marshall University, St. Mary’s Medical Center, Cabell Huntington Hospital and the Edwards Cancer Center. The research protocol and participant informed consent were approved by the IRB (protocol number 339384–3). This study was not listed at ClinicalTrials.gov. Potential study participants were identified from records review by the Research Study Nurse prior to their appointment for a diagnostic biopsy. At the appointment time, the potential participant was interviewed by the study nurse, the study was explained and informed consent was obtained. The physician obtained one or two additional biopsies for research use when the biopsy was obtained for pathology studies.

**Inclusion criteria:** All subjects: 1) were female and with a breast mass that, according to standard of care, was to be biopsied for diagnosis and was large enough to obtain the needed biopsies for pathology and research; 2) understood and were willing to sign the informed consent form; 3) had an ECOG (Eastern Cooperative Oncology Group) performance status of 0 or 1; (0 - Fully active, able to carry on all pre-disease performance without restriction. 1 - Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work.)
| Expr log ratio | Expr false discovery rate (q-value) | ID              |
|----------------|-----------------------------------|-----------------|
| −30            | 4.30E-03                          | ENSG00000206856 |
| −30            | 4.30E-03                          | ENSG00000222133 |
| 30             | 9.14E-04                          | ENSG00000248511 |
| −30            | 4.30E-03                          | ENSG00000249023 |
| −30            | 4.30E-03                          | ENSG00000249239 |
| 30             | 4.30E-03                          | ENSG00000249411 |
| 30             | 4.30E-03                          | ENSG00000249842 |
| −30            | 4.30E-03                          | ENSG00000250516 |
| 30             | 4.30E-03                          | ENSG00000250908 |
| −30            | 4.30E-03                          | ENSG00000251066 |
| −30            | 4.30E-03                          | ENSG00000254558 |
| −30            | 4.30E-03                          | ENSG00000256306 |
| −30            | 4.30E-03                          | ENSG00000259057 |
| 30             | 4.30E-03                          | ENSG00000260066 |
| 30             | 4.30E-03                          | ENSG00000264486 |
| −30            | 4.30E-03                          | ENSG00000265621 |
| 30             | 4.30E-03                          | ENSG00000269524 |
| −30            | 4.30E-03                          | ENSG00000272108 |
| 30             | 4.30E-03                          | ENSG00000277269 |
| 30             | 4.30E-03                          | ENSG00000279162 |
| −30            | 4.30E-03                          | ENSG00000279349 |
| 30             | 4.30E-03                          | ENSG00000279957 |
| 30             | 4.30E-03                          | ENSG00000280068 |
| −30            | 4.30E-03                          | ENSG00000281116 |
| 30             | 4.30E-03                          | ENSG00000254348 |
| −30            | 4.30E-03                          | ENSG00000278777 |
| −29.999        | 4.30E-03                          | ENSG00000251244 |
| −29.988        | 4.30E-03                          | ENSG00000274918 |
| −29.973        | 4.30E-03                          | ENSG00000273920 |
| −29.947        | 4.30E-03                          | ENSG00000255305 |
| −29.9896       | 4.30E-03                          | ENSG00000261334 |
| −29.878        | 4.30E-03                          | ENSG00000254242 |
| −29.86         | 4.30E-03                          | ENSG00000278126 |
| −29.818        | 4.30E-03                          | ENSG00000232306 |
| −29.801        | 4.30E-03                          | ENSG000002771627 |
| 29.732         | 4.30E-03                          | ENSG00000221210 |
| −29.718        | 4.30E-03                          | ENSG00000249818 |
| −29.634        | 4.45E-03                          | ENSG00000220349 |
| −29.58         | 4.37E-03                          | ENSG00000260317 |
| 29.547         | 4.30E-03                          | ENSG00000249189 |
| −29.495        | 4.37E-03                          | ENSG00000257654 |
| −29.495        | 4.37E-03                          | ENSG00000275228 |
| 29.495         | 4.37E-03                          | ENSG00000228935 |
| −29.474        | 4.32E-03                          | ENSG00000263713 |
| −29.465        | 4.37E-03                          | ENSG00000257863 |
| −29.437        | 4.45E-03                          | ENSG00000232328 |
| −29.424        | 4.45E-03                          | ENSG00000251448 |
| 29.4           | 4.37E-03                          | ENSG00000277598 |
| 29.354         | 4.45E-03                          | ENSG00000261835 |
| −29.347        | 4.45E-03                          | ENSG00000272940 |
| −29.287        | 4.62E-03                          | ENSG00000267286 |
| 29.239         | 4.62E-03                          | ENSG00000228438 |
| 29.172         | 4.70E-03                          | ENSG00000223738 |
| −29.143        | 4.77E-03                          | ENSG00000231916 |
| −29.143        | 4.77E-03                          | ENSG00000233703 |
| 29.134         | 4.77E-03                          | ENSG00000278192 |
| 29.068         | 4.71E-03                          | ENSG00000264642 |
| −28.843        | 5.52E-03                          | ENSG00000232887 |
| 28.841         | 5.08E-03                          | ENSG00000249061 |
| −28.802        | 5.52E-03                          | ENSG00000229370 |

(continued on next page)
| Expr log ratio | Expr false discovery rate (q-value) | ID               |
|----------------|-----------------------------------|------------------|
| −28.802        | 5.52E-03                          | ENSG00000233372  |
| −28.802        | 5.52E-03                          | ENSG00000235147  |
| −28.802        | 5.52E-03                          | ENSG00000258314  |
| 28.679         | 5.52E-03                          | ENSG00000274444  |
| 28.566         | 5.52E-03                          | ENSG00000264526  |
| −28.548        | 5.52E-03                          | ENSG00000256293  |
| −28.539        | 5.52E-03                          | ENSG00000229242  |
| −28.539        | 5.52E-03                          | ENSG00000240103  |
| −28.539        | 5.52E-03                          | ENSG00000257129  |
| −28.539        | 5.52E-03                          | ENSG00000269514  |
| −28.518        | 5.52E-03                          | ENSG00000276538  |
| −28.517        | 5.52E-03                          | ENSG00000281411  |
| −28.492        | 5.52E-03                          | ENSG00000232140  |
| −28.492        | 5.52E-03                          | ENSG00000234941  |
| −28.492        | 5.52E-03                          | ENSG00000237903  |
| −28.492        | 5.52E-03                          | ENSG00000248656  |
| −28.492        | 5.52E-03                          | ENSG00000260093  |
| −28.492        | 5.52E-03                          | ENSG00000274370  |
| −28.311        | 5.52E-03                          | ENSG00000273816  |
| −28.29         | 5.52E-03                          | ENSG00000281114  |
| 28.23          | 5.54E-03                          | ENSG00000202269  |
| 28.23          | 5.54E-03                          | ENSG00000223028  |
| 28.23          | 5.54E-03                          | ENSG00000239288  |
| 28.23          | 5.54E-03                          | ENSG00000261679  |
| 28.23          | 5.54E-03                          | ENSG00000270866  |
| 28.188         | 5.52E-03                          | ENSG00000232120  |
| 28.188         | 5.52E-03                          | ENSG00000234683  |
| 28.188         | 5.52E-03                          | ENSG00000282950  |
| 28.154         | 5.54E-03                          | ENSG00000255851  |
| 28.154         | 5.54E-03                          | ENSG00000281046  |
| 28.144         | 5.52E-03                          | ENSG00000261680  |
| 28.094         | 5.54E-03                          | ENSG00000233616  |
| −28.083        | 5.52E-03                          | ENSG00000278923  |
| 28.077         | 5.54E-03                          | ENSG00000244167  |
| −28.068        | 5.54E-03                          | ENSG0000029102   |
| −28.068        | 5.54E-03                          | ENSG00000263717  |
| 28.006         | 5.54E-03                          | ENSG00000251668  |
| 27.985         | 5.54E-03                          | ENSG00000256029  |
| 27.985         | 5.54E-03                          | ENSG00000280164  |
| −27.971        | 5.54E-03                          | ENSG00000249631  |
| −27.924        | 5.54E-03                          | ENSG00000225148  |
| −27.924        | 5.54E-03                          | ENSG00000255572  |
| −27.924        | 5.54E-03                          | ENSG00000260329  |
| −27.924        | 5.54E-03                          | ENSG00000270889  |
| −27.924        | 5.54E-03                          | ENSG00000272685  |
| 27.914         | 5.54E-03                          | ENSG00000279127  |
| 27.862         | 5.54E-03                          | ENSG00000283057  |
| −27.829        | 5.54E-03                          | ENSG00000271568  |
| −27.779        | 5.54E-03                          | ENSG00000254502  |
| −27.779        | 5.54E-03                          | ENSG00000263985  |
| −27.747        | 5.54E-03                          | ENSG00000254290  |
| 27.733         | 5.66E-03                          | ENSG00000227133  |
| 27.733         | 5.66E-03                          | ENSG00000243831  |
| 27.733         | 5.66E-03                          | ENSG00000259924  |
| 27.733         | 5.66E-03                          | ENSG00000273259  |
| 27.733         | 5.66E-03                          | ENSG00000279708  |
| 27.722         | 5.66E-03                          | ENSG00000241961  |
| 27.719         | 5.54E-03                          | ENSG00000258205  |
| −27.71         | 5.66E-03                          | ENSG00000260674  |
| 27.644         | 5.67E-03                          | ENSG00000254792  |
Table 2 (continued)

| Expr log ratio | Expr false discovery rate (q-value) | ID               |
|----------------|-------------------------------------|------------------|
| 27.644         | 5.67E-03                            | ENSG00000225720  |
| 27.579         | 5.67E-03                            | ENSG00000260261  |
| 27.579         | 5.67E-03                            | ENSG00000265819  |
| 27.579         | 5.67E-03                            | ENSG00000272512  |
| 27.579         | 5.67E-03                            | ENSG00000279485  |
| 27.579         | 5.67E-03                            | ENSG00000280023  |
| 27.579         | 5.67E-03                            | ENSG00000280188  |
| -27.496        | 5.66E-03                            | ENSG00000199285  |
| 27.477         | 5.67E-03                            | ENSG00000238009  |
| 27.477         | 5.67E-03                            | ENSG00000241168  |
| 27.477         | 5.67E-03                            | ENSG00000258271  |
| 27.477         | 5.67E-03                            | ENSG00000259450  |
| -27.477        | 6.04E-03                            | ENSG00000261379  |
| 27.407         | 6.04E-03                            | ENSG00000201535  |
| 27.357         | 6.18E-03                            | ENSG00000278269  |
| -27.323        | 6.26E-03                            | ENSG00000263938  |
| -27.058        | 6.99E-03                            | ENSG00000269981  |
| 27.051         | 7.01E-03                            | ENSG00000279122  |
| -27.022        | 7.01E-03                            | ENSG00000217512  |
| -27.022        | 7.01E-03                            | ENSG00000221376  |
| -27.022        | 7.01E-03                            | ENSG00000264855  |
| -27.022        | 7.01E-03                            | ENSG00000269974  |
| -27.022        | 7.01E-03                            | ENSG00000271118  |
| -27.018        | 7.01E-03                            | ENSG00000224661  |
| -27.018        | 7.01E-03                            | ENSG00000233645  |
| -27.018        | 7.01E-03                            | ENSG00000234622  |
| -27.018        | 7.01E-03                            | ENSG00000244259  |
| -27.018        | 7.01E-03                            | ENSG00000264715  |
| -27.018        | 7.01E-03                            | ENSG00000265445  |
| -27.018        | 7.01E-03                            | ENSG00000267004  |
| -27.018        | 7.01E-03                            | ENSG00000271253  |
| 27.005         | 6.99E-03                            | ENSG00000225591  |
| 27.005         | 6.99E-03                            | ENSG00000229791  |
| -26.96         | 7.09E-03                            | ENSG00000207027  |
| -26.96         | 7.09E-03                            | ENSG00000229878  |
| -26.96         | 7.09E-03                            | ENSG00000233778  |
| -26.96         | 7.09E-03                            | ENSG00000261620  |
| -26.96         | 7.09E-03                            | ENSG00000264222  |
| -26.91         | 7.01E-03                            | ENSG00000256783  |
| 26.854         | 7.20E-03                            | ENSG00000277930  |
| 26.854         | 7.20E-03                            | ENSG00000279173  |
| 26.826         | 7.14E-03                            | ENSG00000201370  |
| 26.826         | 7.14E-03                            | ENSG00000202410  |
| 26.826         | 7.14E-03                            | ENSG00000224904  |
| 26.826         | 7.14E-03                            | ENSG00000240159  |
| 26.761         | 7.20E-03                            | ENSG00000230687  |
| 26.761         | 7.20E-03                            | ENSG00000258773  |
| 26.761         | 7.20E-03                            | ENSG00000260702  |
| -26.688        | 7.65E-03                            | ENSG00000224945  |
| -26.688        | 7.65E-03                            | ENSG00000226986  |
| -26.688        | 7.65E-03                            | ENSG00000271993  |
| -26.688        | 7.65E-03                            | ENSG00000280395  |
| -26.688        | 7.65E-03                            | ENSG00000281304  |
| 26.498         | 7.91E-03                            | ENSG00000236209  |
| 26.498         | 7.91E-03                            | ENSG00000237555  |
| 26.469         | 7.91E-03                            | ENSG00000213184  |
| 26.469         | 7.91E-03                            | ENSG00000231297  |
| 26.469         | 7.91E-03                            | ENSG00000233428  |

(continued on next page)
| Expr log ratio | Expr false discovery rate (q-value) | ID              |
|---------------|------------------------------------|-----------------|
| 26.469        | 7.91E-03                           | ENSG00000253816 |
| 26.469        | 7.91E-03                           | ENSG00000262089 |
| 26.469        | 7.91E-03                           | ENSG00000267284 |
| 26.469        | 7.91E-03                           | ENSG00000273100 |
| 26.469        | 7.91E-03                           | ENSG00000274964 |
| 26.469        | 7.91E-03                           | ENSG00000277169 |
| 26.469        | 7.91E-03                           | ENSG00000277875 |
| 26.469        | 7.91E-03                           | ENSG00000279537 |
| 26.469        | 7.91E-03                           | ENSG00000280198 |
| -26.362       | 7.91E-03                           | ENSG00000199901 |
| -26.362       | 7.91E-03                           | ENSG00000206672 |
| -26.362       | 7.91E-03                           | ENSG00000206806 |
| -26.362       | 7.91E-03                           | ENSG00000213279 |
| -26.362       | 7.91E-03                           | ENSG00000254367 |
| -26.362       | 7.91E-03                           | ENSG00000259275 |
| -26.362       | 7.91E-03                           | ENSG00000262766 |
| -26.362       | 7.91E-03                           | ENSG00000265359 |
| -26.362       | 7.91E-03                           | ENSG00000267717 |
| -26.362       | 7.91E-03                           | ENSG00000269014 |
| -26.362       | 7.91E-03                           | ENSG00000271897 |
| -26.362       | 7.91E-03                           | ENSG00000271917 |
| -26.362       | 7.91E-03                           | ENSG00000277026 |
| -26.362       | 7.91E-03                           | ENSG00000279269 |
| -26.362       | 7.91E-03                           | ENSG00000279910 |
| -26.362       | 7.91E-03                           | ENSG00000280114 |
| -26.362       | 7.91E-03                           | ENSG00000280711 |
| -26.299       | 7.91E-03                           | ENSG00000236116 |
| -26.192       | 7.91E-03                           | ENSG00000204556 |
| -26.192       | 7.91E-03                           | ENSG00000207229 |
| -26.192       | 7.91E-03                           | ENSG00000221326 |
| -26.192       | 7.91E-03                           | ENSG00000227740 |
| -26.192       | 7.91E-03                           | ENSG00000228176 |
| -26.192       | 7.91E-03                           | ENSG00000228543 |
| -26.192       | 7.91E-03                           | ENSG00000233516 |
| -26.192       | 7.91E-03                           | ENSG00000233887 |
| -26.192       | 7.91E-03                           | ENSG00000235358 |
| -26.192       | 7.91E-03                           | ENSG00000248490 |
| -26.192       | 7.91E-03                           | ENSG00000249284 |
| -26.192       | 7.91E-03                           | ENSG00000254330 |
| -26.192       | 7.91E-03                           | ENSG00000254836 |
| -26.192       | 7.91E-03                           | ENSG00000255344 |
| -26.192       | 7.91E-03                           | ENSG00000260603 |
| -26.192       | 7.91E-03                           | ENSG00000261618 |
| -26.192       | 7.91E-03                           | ENSG00000265554 |
| -26.192       | 7.91E-03                           | ENSG00000268597 |
| -26.192       | 7.91E-03                           | ENSG00000271643 |
| -26.192       | 7.91E-03                           | ENSG00000274421 |
| -26.192       | 7.91E-03                           | ENSG00000276073 |
| -26.192       | 7.91E-03                           | ENSG00000278909 |
| -26.192       | 7.91E-03                           | ENSG00000280061 |
| -26.192       | 7.91E-03                           | ENSG00000281262 |
| 26.132        | 8.21E-03                           | ENSG00000217120 |
| 26.132        | 8.21E-03                           | ENSG00000231705 |
| 26.132        | 8.21E-03                           | ENSG00000237379 |
| 26.132        | 8.21E-03                           | ENSG00000243779 |
| 25.998        | 8.63E-03                           | ENSG00000265985 |
| 25.983        | 8.69E-03                           | ENSG00000223672 |
| 25.983        | 8.69E-03                           | ENSG00000225193 |
| 25.983        | 8.69E-03                           | ENSG00000254436 |
| 25.983        | 8.69E-03                           | ENSG00000256494 |
| 25.983        | 8.69E-03                           | ENSG00000261696 |
4) were between 18 and 90 years of age; 5) were recruited as available without regard to race or ethnicity.

Exclusion criteria: Excluded persons were: 1) those who do not like or who were allergic to walnuts or other tree nuts; 2) those with any metabolic disease that could be affected by walnut consumption; 3) those with a life expectancy less than 6 months; 4) those who were pregnant (to prevent confounding due to pregnancy hormonal factors).

2.3. Clinical protocol

Subjects were consented at their first visit and were randomized into treated (consume walnut) or control (no added walnuts) groups. Routine clinical data were recorded (age, weight, height, family history, etc.). A five ml blood specimen in EDTA was collected for the research laboratory. After the initial biopsy, the subject was asked to continue to consume the usual diet and to not change consumption of any medication or supplements. If she was randomized to the walnut group, the subject was given 30, one ounce packages of walnuts, was asked to consume two packages (two ounces) of walnuts daily and to return remaining packages for counting. If needed, due to extended time for the clinical workup, the subject was given additional packages of walnuts to allow for continued consumption of two ounces of walnuts per day until surgery (about two to three weeks). Control group subjects were asked to not intentionally consume walnuts. At the conclusion of the study, each subject

| Expr log ratio | Expr false discovery rate (q-value) | ID               |
|----------------|--------------------------------------|------------------|
| 25.983         | 8.69E-03                             | ENSG00000263606  |
| 25.983         | 8.69E-03                             | ENSG00000267027  |
| 25.983         | 8.69E-03                             | ENSG00000273348  |
| 25.983         | 8.69E-03                             | ENSG00000280245  |
| -25.71         | 9.87E-03                             | ENSG00000220076  |
| -25.71         | 9.87E-03                             | ENSG00000253960  |
| -25.71         | 9.87E-03                             | ENSG00000260244  |
| -25.71         | 9.87E-03                             | ENSG00000279077  |
| 25.687         | 9.93E-03                             | ENSG00000199635  |
| 25.687         | 9.93E-03                             | ENSG00000276337  |
| -25.633        | 1.10E-02                             | ENSG00000228035  |
| -25.633        | 1.10E-02                             | ENSG00000239036  |
| -25.633        | 1.10E-02                             | ENSG00000263489  |
| -25.484        | 1.15E-02                             | ENSG00000242953  |
| -25.484        | 1.15E-02                             | ENSG00000255774  |
| -22.956        | 1.33E-02                             | ENSG00000274522  |
| 22.792         | 3.30E-02                             | ENSG00000270019  |
| 22.383         | 3.50E-02                             | ENSG00000272461  |
| 22.266         | 1.01E-02                             | ENSG00000278233  |
| -21.352        | 7.91E-03                             | ENSG00000239381  |
| -20.711        | 8.68E-02                             | ENSG00000276668  |
| 20.55          | 9.19E-02                             | ENSG00000278824  |
| 19.815         | 7.91E-03                             | ENSG00000243429  |
| -19.642        | 7.91E-03                             | ENSG00000272366  |
| -19.632        | 2.85E-02                             | ENSG00000255740  |
| -19.491        | 5.52E-03                             | ENSG00000227777  |
| 18.824         | 4.75E-02                             | ENSG00000272763  |
| -18.033        | 6.99E-03                             | ENSG00000275188  |
| 17.984         | 8.53E-02                             | ENSG00000256757  |
| -17.983        | 1.03E-02                             | ENSG00000255871  |
| -16.819        | 5.84E-02                             | ENSG00000265129  |
| -16.575        | 9.30E-04                             | ENSG00000233875  |
| 16.457         | 5.88E-03                             | ENSG00000237158  |
| -16.035        | 4.59E-02                             | ENSG00000268906  |
| -15.501        | 5.14E-02                             | ENSG00000201892  |
| -2.414         | 3.36E-02                             | ENSG00000277089  |
| ID | Molecules in Network | Score | Focus Molecules | Top Diseases and Functions |
|----|----------------------|-------|----------------|---------------------------|
| 1  | ADGRC4,APAP1,AVPR1B,BDKRB1,CD3,CDH9,DAK,DDBX4,DPS3,EC1,EK, estrogen receptor,FAM49A,Ggr,Histone h3,HoxB5,Insulin,Jnk,MRP55, NMU1,NTR3,OPR1,PAK,PAIP2,P3K, (complex),Pcr(5),TLC,TLC4F1, PSEN1,SLC38A3,TCL1A,TFAP2D,TPAN2,ZCCHC10 | 41  | 23 | Reproductive System Development and Function, Carbohydrate Metabolism, Lipid Metabolism |
| 3  | ADY2,Ampk,BMP2,CLL14,CH18,Cg1,CRHM2,Collagen(s),Cre,DEFA6,GRA4, Growth hormone,GZMA,HTR7,KCN3,Mapk,MAPK4,miR-15,NDP,NOX4,NR2E1,PDGF BB,Pka,PPARb,Proinsulin, Ras,SEMA4A,Serine Protease,SLEC39A12,TMPRSS5, TMPRSS15,Tnf (family),trypsin, Vegf | 39  | 32 | Embryonic Development, Nervous System Development and Function, Organ Development |
| 4  | Ctg,CD1A,CLEC4A,CLEC4M,C2N2,CYP4A1,ERK1,2, Fcrla,GRF2,IAFP,JFN alpha,beta,JFN beta, Ifi44,lgf1,lgf2,lgf3,lgm,Il1,Il2,Il3,Il12,complex,JIL3,Immunglobulin, Interferon alpha,LDL,PE3,Pro-inflammtory Cytokine,PSMB9,RASHE1,A, SP21,STAT4,Tgf beta,TIRM21 | 27  | 17 | Endocrine System Disorders, Gastrointestinal Disease, Immunological Disease |
| 5  | ADAT1,AGPAT1,ARHGGE4F,CCDC134,CD200,CDF5, ELAV2,GAH4,IL18B3 (includes others),HIST1H2BO,JF44,JNGGJFN1,JIL5,Il6, ILK8,LCP2,LECT2,MAPK8,MGDA2,MOV10, MRPL22,NRNT,NSBP2,PAIP2B,P35,P38,PRKb,PRP1,SIRPB1, SLC35B3,SUN3,TESP11,TNFF13B2,FN443 | 25  | 16 | Cell-To-Cell Signaling and Interaction, Cellular Growth and Proliferation, Hematological System Development and Function |
| 6  | ACTA2,Actn3,AUH,C1orror8f,C1orf58,C1orf79,C1T127,A2,CD2F1,A2,FN1, HEATR5B,IL1K1,IMACEs,Mept4,MUC17,Mucin,NID2,OPRPN, OXL1,PD1,P38A,PSMG1,RA10,RAB33B,RA3B,RBBG,SECL1C, SLC1A6,SPE2F2,S1C13,CST31,T1V2,TRAPP5p,TRYP2,E27 | 23  | 15 | Cell-To-Cell Signaling and Interaction, Carbohydrate Metabolism, Drug Metabolism |
| 7  | APP,BNP1,C1orror2l,CA1M3,C2FT22,CCD140,CEC12A,D1T1, FOLR1,GOSR2,CTF2E1,HIST1H2BM,KCNIP4,KCNIP4-IT1,KN3, MED2,C3F2,B2CD2,B2POP1,FOP1,FOP2,FOP4,FOP7,GR,AD1C, RHOX5,FPR1,FPR2,FPR5,FPR25,FPR3,FPR4,FSP108,FSP1108B, SURF2,TCBD10C,TER822,YTN | 21  | 14 | RNA Post-Transcriptional Modification, Cell-To-Cell Signaling and Interaction, Skeletal and Muscular System Development and Function |
| 8  | ABHD10,AHRAXAS1,AHRAKXAS2,Adaptor protein 2, ADCPY1,ANKRD40,ATP2C1,BF2,CR1,B1,BUD13,CCBE1,CCN1, CHS5Y1,C15AS5A2A,C15AS5A5D2,CP37,ELAV1,FAM46C,FLYWCH1, GOLTB1,HCF1,HCHJ1,HXOX12,LMBD1,MLEC,MYADNM,NABP1, NAB2,PPTC7,PRM,SDFCP,SELENOT,SCL17A8,TIR13D1 (includes others), USP7,YPFL5 | 19  | 13 | Amino Acid Metabolism, Membrane Transport, Small Molecule Biochemistry |
| 9  | ABTP1,ANKRD30BP2,CCD153,CNBP,COX10,CST5,EMP3,ESPNL, FKTN,FOLH1,GAR1,HDGCC14,ME11,MED1,MED30,MED12,MED13L, NAV3,NID2,F17,FN3,OPR1,NR3C1,OLAH,PAR1,PAR4,PPARG, PPC,PJF1R145,SMACR54A,SPEN,SUNF6,TRAP | 19  | 13 | Cellular Assembly and Organization, Carbohydrate Metabolism, Gastrointestinal Disease |
| 10 | AK7,AQP3,AQP12,AQP28,ABT2N2,BLOC153,BLOC1S4,A, BLO C1S5,BMPPR,CCD134,CDH3,CLD12A1,COMP,DAND5,ER2, GALNT4,GCT,CMIP1,MAPK4,MTX3,MRSA2,PAH,B2,PDG, RASSF7,RASSF8,RB3,SCD2,SNBK,SOX2,SOX13,SPP2,STNF, TNXRD1,XPO1,ZP346L2,ZN5F27 | 17  | 12 | Cancer, Organismal Injury and Abnormalities, Reproductive System Disease |
| 11 | ANK3,AR,ATF13A4,AVK,BFC2AP06,CLDN3,CU2L1,CYC2L2,DDT, EDN2,EBB12,GCT,GECUY1A3,A3A,IL2-DQ,F2B,KIT2,LR212,SRC1, MARH4,Marx,MBP,MLKL,NUDT11,PD5,PPB2,PPPC4APR, PTCH4D,SCN1A,SNW1,YCE3,THM132D,TNFRSF10A,TP53, UCMA,ZNFSG3 | 17  | 12 | Organ Morphology, Reproductive System Development and Function, Tissue Morphology |
| No. | Gene(s)                                                                 | GO Terms                                                                                     |
|-----|-------------------------------------------------------------------------|----------------------------------------------------------------------------------------------|
| 12  | ADAM9, ADAM29, ADAM30, ADAMTS2, AHCTF1, CEACAM, C574, CYNMB, DACT2, DHH, EGF, FERD3, LIEG9, GRID1, KGL1, L1G1L5, L2RA, JQGAP2, JADE1, LNFG, MDL, Metalloresease, MFG, MYF5, PAPA2, PTCRA, RAB11, SLRC25A10, SPATA13, STX2, TCF3, TRMT10C, TSC22D1, ZNF607 | Cell-mediated Immune Response, Lymphoid Tissue Structure and Development, Hematopoiesis         |
| 13  | ACP5, ALPL, ARG1, CCNC, CXCXorf2, L1EOA, EXOS3C, GAD45, GTF2A1, GTF2A2, GTF2F2, GTF2F3, GTF2F4, GTF2F5, GTF2F6, GTF2F7, GTF2F8, GTF2F9, GTF2F10, HAS2, HMCGN1, MED13, MSX2, MTPN, PCHD12, POLR2G, POLR2J, RNA pol2-transcription factor, RNA polymerase II, S100A6, SRD5A2, SNX23, SPP1, TCEA1, TCEA2, TFR1, TFEB, TFP1, TFB1, TFB2 | Gene Expression, Dental Disease, Digestive System Development and Function                     |
| 14  | FAM9A1, FAM9A26 (includes others)                                      | Cancer, Neurological Disease, Organismal Injury and Abnormalities                            |
| 15  | CBLN2, mir-125b-5p (and other miRNAs w/seed CCCUGAG)                   | Cell Morphology, Cellular Function and Maintenance, Hematological System Development and Function |
| 16  | LHX2, OR8B8                                                            | Cellular Development, Cellular Growth and Proliferation, Digestive System Development and Function |
| 17  | mir-3146, mir-3146 (all miRNAs w/seed AUGCGAG)                         | Cancer, Neurological Injury and Abnormalities, Reproductive System Disease                   |
| 18  | mir-933, mir-933 (all miRNAs w/seed GUCCGCA)                           | Dermatological Diseases and Conditions, Developmental Disorder, Endocrine Development         |
| 19  | MIR-4737, mir-4737 (all miRNAs w/seed UGCCGAC)                         | Cell Morphology, Cell-To-Cell Signaling and Interaction, Nervous System Development and Function |
| 20  | ANKRD30B, HR                                                           | Behavioral, Cancer, Neurological Injury and Abnormalities, Organismal Injury and Abnormalities |
| 21  | mir-3118, mir-3118 (all miRNAs w/seed GUACAGC)                         | Cellular Growth and Proliferation, Developmental Disorder, Endocrine System Disorders        |
| 22  | T2R7, T52R3                                                            | Cell Morphology, Cell-To-Cell Signaling and Interaction, Nervous System Development and Function |
| 23  | ZNF221, ZNF233, ZNF284                                                | Behavior, Cancer, Organismal Injury and Abnormalities, Organismal Injury and Abnormalities   |
| 24  | MIR-6757, mic-6757 (miRNAs w/seed ACACUGG), mic-6757-5p (miRNAs w/seed AGGGAUG) | Cancer, Neurological Injury and Abnormalities, Organismal Injury and Abnormalities            |
| 25  | NVYJ, PTPRQ, PTTR5, JTRK2                                              | Cancer, Neurological Injury and Abnormalities, Organismal Injury and Abnormalities            |
was asked to identify whether any changes were made to the usual diet especially in the areas of fruits, vegetables, nuts or supplement consumption and fats used in cooking and whether walnuts were consumed (walnut group) or not (control group).

At the time that ultrasound guided core needle biopsies of the breast mass were obtained for diagnosis, one or two extra cores were taken for research use. In the procedure room, immediately upon removal, the biopsies for research were placed in Qiagen All-Protect tissue reagent (Qiagen.com) to preserve RNA, DNA and protein for up to 7 days at room temperature. Biopsies were delivered to the research laboratory for initial processing within 2 hours.

If the pathology report indicated that the lump was not cancer, no further tissue was collected and the subject was no longer part of the study. If the biopsied tissue was breast cancer and surgery was scheduled without intervening radiation or chemotherapy, another specimen of tumor tissue and blood was collected at surgery. A small section of macroscopically viable tumor, away from the clean margin, was excised then immediately placed in Qiagen All-Protect tissue reagent, as before. Any patient who, according to the clinical care plan, was to receive either chemotherapy or radiation prior to surgery was no longer part of the study so as to not confound analyses.

2.4. Laboratory protocols

Total RNA was extracted using RNeasy, Lipid Tissue kit (Qiagen.com). This micro-kit is suitable for less than five mg of tissue and for extracting up to 45 μg of total mRNA. mRNA was checked for quantity and sent to the Marshall University Genomics Core Facility for further processing. The Genomics Core is a full service facility and provided RNA quality assessment, RNA-Seq analysis on each specimen, and DESeq2 expression profiling analyses of the data.

2.5. RNA sequencing: next-generation sequencing

RNA sample quality was assessed on RNA Pico chips in using an Agilent 2100 Bioanalyzer (Agilent, Santa Clara, CA). RNA samples had RNA Integrity Numbers (RIN) ranging from 2.6 to 9.4. One microgram of total RNA was used to construct RNA-Seq libraries using a TruSeq stranded total RNA library prep kit with RiboZero(H \ M \ R) ribosomal RNA reduction (Illumina Inc., San Diego, CA) according to the kit’s instructions. RNA fragmentation times were modified based on RNA samples’ RIN value to generate inserts of equal size across all libraries.

Twenty RNA-Seq libraries were clustered on an Illumina cBot and sequenced on a HiSeq 1500 platform, in a 2 x 50 base paired end design yielding a minimum of 50 million reads per sample. Five matched pairs of samples (initial biopsy and subsequent surgery) were collected from each of the walnut consuming and control groups.

Reads were trimmed using Trimmomatic v 0.36 [2] to remove low-quality base calls and adapter sequences, and then aligned to the human reference genome GRCh38 using HISAT v2.1.0 [3]. Resulting bam files were sorted and indexed with SamTools v1.3.1 [3,4], and PCR and optical duplicate reads marked using Picard tools v2.6.0. The numbers of reads mapping to each gene for each sample were counted using the R/Bioconductor package GenomicAlignments, v1.12.2 [5] and the Ensembl gene database for GRCh38, build 84 [6]. Differential gene expression was computed using DESeq2 version 1.10.0 [7], with a statistical model comparing the ratio of expression between surgery and biopsy specimens for the walnut-consuming group to the ratio of expression between surgery and biopsy specimens for the control group, as described in “statistical analyses” below.

2.6. Statistical analyses

Differences between groups (walnut or control) in fractions of individual fatty acids as determined by gas chromatography or in clinical parameters were determined by T-test with a significance level of p ≤ 0.05.

It was expected that there would be large interpatient heterogeneity thus the baseline mRNA expression of individual genes would be highly variable between patients. The analyses of biopsy and surgical specimens allowed each patient to serve as her own control. Gene expressions for the sample
collected at initial biopsy and the sample collected at surgery were determined and the ratios of these expressions were calculated for each patient. Then the means of the ratio of expressions were compared between the walnut-consuming group and the control group. The comparison was performed using DESeq2, which models the read count per gene using a negative binomial distribution, and moderates the estimated expression changes to account for the dependence on overall read count [7]. Each patient was assigned a unique id within their treatment (walnut or control) group, and the statistical model (equation (1)):

\[
\text{extraction + treatment + patient’s group + extraction:treatment} \tag{1}
\]

was passed to DESeq2, with extraction taking values “biopsy” or “surgery”, and treatment taking values “walnut” or “control”. Genes that were significant for the extraction:treatment interaction parameter at a Benjamini-Hochberg (B-H) controlled false discovery rate of 10% were considered to be differentially expressed. The corresponding moderated fold change computed by DESeq2 is an estimate of this parameter, and can thus be considered to be an estimate of the quantities:

\[
\frac{g_w/s}{g_w/b} \quad \frac{g_c/s}{g_c/b} \tag{2}
\]

In Equation (2), ‘g’ represents the expression level of gene ‘g’, the subscripts ‘w’ and ‘c’ represent samples in the walnut and control groups, respectively, and the subscripts ‘s’ and ‘b’ represent samples from surgery and biopsy, respectively. Thus, the ratio of expression of gene ‘g’ from surgical specimens verses biopsy specimens of walnut patients was divided by the ratio of expression of gene ‘g’ from surgical specimens verses biopsy specimens of control patients. These analyses determined whether, across the group, there were significant and consistent changes in the mRNA expression of specific genes due to walnut consumption and provide the input for subsequent Ingenuity Pathway analyses.

2.7. Ingenuity Pathway analyses (IPA)

The complex data resulting from RNA seq expression profiling requires complex analyses. Data were analyzed by use of IPA [8]. Final downstream phenotypic effects are due to the balance of positive and negative influences on expression of genes in a pathway. The goal of the IPA Downstream Effects Analysis is to identify genes and the resulting functions that are expected to increase or decrease, given the observed gene expression changes in the experimental dataset [8]. Downstream Effects Analysis is based on expected causal effects between genes and functions; the expected causal effects are derived from the literature compiled in the Ingenuity® Knowledge Base [8]. The analysis examines genes in the dataset that are known to affect functions, compares the genes’ direction of change to expectations derived from the literature then issues a prediction for each function based on the direction of changes in the dataset [8]. IPA uses a z-score algorithm to make predictions which is designed to reduce the chance that random data will generate significant predictions [8]. A publication further describing Downstream Effects Analyses can be found at [9].

The p-values for networks were calculated using a Fisher exact test with B–H multiple testing corrections. The networks were generated through the use of IPA [8]. The network score is based on the hypergeometric distribution and is calculated with the right-tailed Fisher’s Exact Test with B–H multiple testing corrections. For example, for a network with a p-value of $1 \times 10^{-30}$, the network’s score $= [-\log(\text{Fisher’s Exact test result})] = 30$. Thus, a score of 30 can be interpreted as meaning that if there were no associations between walnut consumption and the gene expression changes seen in the network, an overlap between the network and the differentially expressed gene set would only occur 1 in $10^{30}$ times in similar experiments.

Files containing the raw reads, along with a shell script describing the complete data analysis pipeline, were deposited to the Gene Expression Omnibus (GEO) at the National Center for
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Transparency document

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