

**Nott et al., Supplemental Data**

**Table 1. ER $\alpha$ -mediated gene expression in response to E2**

| <b>Gene Name</b>   | <b>Symbol</b>   | <b>Process</b>                          | <b>Relative Change<sup>a</sup></b> |
|--|-----------------|---|------------------------------------|
| V-abl Abelson murine leukemia viral oncogene homolog 1   | <i>ABL1</i>     | Signal transduction, transcription      | 0.61                               |
| Actin binding LIM protein family, member 3               | <i>ABLIM3</i>   | Cytoskeleton biogenesis                 | 2.395                              |
| Acyl-coa synthetase long-chain family member 5           | <i>ACSL5</i>    | Metabolic processes                     | 1.626                              |
| Adrenomedullin   | <i>ADM</i>      | Signal transduction                     | 0.75                               |
| Adenosine A2b receptor                                   | <i>ADORA2B</i>  | Signal transduction                     | 0.398                              |
| Angiotensinogen  | <i>AGT</i>      | Signal transduction                     | 0.775                              |
| Aldehyde dehydrogenase 3 family, member B1               | <i>ALDH3B1</i>  | Metabolic processes                     | 2.78                               |
| Adhesion molecule with Ig-like domain 2                  | <i>AMIGO2</i>   | Cell adhesion                           | 0.447                              |
| Ankyrin repeat domain 1 (cardiac muscle)                 | <i>ANKRD1</i>   | Signal transduction                     | 1.461                              |
| Annexin A11  | <i>ANXA11</i>   | Immune processes                        | 2.45                               |
| Aquaporin 3  | <i>AQP3</i>     | Excretion, transport                    | 2.99                               |
| Rho gtpase activating protein 18                         | <i>ARHGAP18</i> | Signal transduction                     | 0.54                               |
| Rho gtpase activating protein 26                         | <i>ARHGAP26</i> | Signal transduction                     | 3.91                               |
| Rho/rac guanine nucleotide exchange factor (GEF) 2       | <i>ARHGEF2</i>  | Signal transduction                     | 0.73                               |
| AT rich interactive domain 4A (RBP1-like)                | <i>ARID4A</i>   | Transcription                           | 2.29                               |
| ADP-ribosylation factor-like 3                           | <i>ARL3</i>     | Signal transduction                     | 1.78                               |
| Aryl hydrocarbon receptor nuclear translocator-like      | <i>ARNTL</i>    | Signal transduction                     | 1.53                               |
| Adipocyte-specific adhesion molecule                     | <i>ASAM</i>     | Cell adhesion                           | 8.17                               |
| Ankyrin repeat and SOCS box-containing 13                | <i>ASB13</i>    | Protein degradation in cell             | 4.09                               |
| Brain abundant, membrane attached signal protein 1       | <i>BASP1</i>    | Unclear                                 | 0.8                                |
| Bridging integrator 1                                    | <i>BIN1</i>     | Cellular proliferation, differentiation | 2.01                               |
| Baculoviral IAP repeat-containing 2                      | <i>BIRC2</i>    | Signal transduction, apoptosis          | 0.625                              |
| Brain protein 44-like                                    | <i>BRP44L</i>   | Unclear                                 | 3.27                               |
| Complement component 3                                   | <i>C3</i>       | Signal transduction                     | 2.65                               |
| Cdk5 and Abl enzyme substrate 2                          | <i>CABLES2</i>  | Cell cycle regulation                   | 6.63                               |
| Centrosome-associated protein 350                        | <i>CAP350</i>   | Microtubule anchoring                   | 1.46                               |
| Caspase recruitment domain family, member 10             | <i>CARD10</i>   | Apoptosis regulation                    | 2.65                               |
| Caspase recruitment domain family, member 6              | <i>CARD6</i>    | Apoptosis regulation                    | 1.659                              |
| Caspase 7, apoptosis-related cysteine peptidase          | <i>CASP7</i>    | Apoptosis regulation                    | 2.07                               |
| Carbonyl reductase 3                                     | <i>CBR3</i>     | Metabolic processes                     | 0.498                              |
| Cyclin A1  | <i>CCNA1</i>    | Cell cycle regulation                   | 5.128                              |
| CD44 antigen   | <i>CD44</i>     | Cell adhesion, signal transduction      | 0.508                              |
| CD83 antigen   | <i>CD83</i>     | Signal transduction                     | 2.27                               |
| Cyclin-dependent kinase inhibitor 1A (p21, Cip1)         | <i>CDKN1A</i>   | Cell cycle regulation                   | 2.936                              |
| Cdon homolog (mouse)                                     | <i>CDON</i>     | Cell adhesion                           | 1.6                                |
| CCAAT/enhancer binding protein (C/EBP), delta            | <i>CEBPD</i>    | Transcription                           | 1.393                              |
| Creatine kinase, brain                                   | <i>CKB</i>      | Metabolic processes                     | 1.67                               |
| Cysteine-rich secretory protein LCCL domain containing 2 | <i>CRISPLD2</i> | Signal transduction                     | 8.754                              |
| Connective tissue growth factor                          | <i>CTGF</i>     | Proliferation, adhesion, motility       | 0.68                               |
| Cathepsin D (Lysosomal aspartyl peptidase)               | <i>CTSD</i>     | Proteolysis                             | 1.758                              |
| DAB2 interacting protein                                 | <i>DAB2IP</i>   | Signal transduction                     | 1.449                              |
| Development and differentiation enhancing factor 1       | <i>DDEF1</i>    | Regulation of GTPase ARF                | 0.669                              |
| DEAD (Asp-Glu-Ala-Asp) box polypeptide 47                | <i>DDX47</i>    | RNA metabolic process                   | 0.73                               |

<sup>a</sup> Gene expression regulated by E2-ER $\alpha$  compared to those mediated by the parent Ad5 in the presence of E2. The SEM, which was less than 10% of the mean, is not shown for simplicity.

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|---|------------------|--------------------------------------|-------|
| Dickkopf homolog 1 (Xenopus laevis)                       | <i>DKK1</i>      | Signal transduction                  | 0.455 |
| Desmuslin   | <i>DMN</i>       | Protein binding                      | 1.3   |
| Dnaj (Hsp40) homolog, subfamily B, member 1               | <i>DNAJB1</i>    | Protein folding                      | 0.645 |
| Dual specificity phosphatase 5                            | <i>DUSP5</i>     | Protein dephosphorylation            | 0.448 |
| Ectodermal-neural cortex (with BTB-like domain)           | <i>ENC1</i>      | System development                   | 0.529 |
| Epiplakin 1   | <i>EPPK1</i>     | Biological process                   | 1.26  |
| Family with sequence similarity 46, member A              | <i>FAM46A</i>    | Unclear                              | 3.19  |
| Family with sequence similarity 8, member A1              | <i>FAM8A1</i>    | Unclear                              | 1.85  |
| FK506 binding protein 4, 59kda                            | <i>FKBP4</i>     | Protein folding                      | 1.35  |
| FOS-like antigen 1  | <i>FOSL1</i>     | Cellular defense response            | 0.52  |
| Forkhead box O1A (rhabdomyosarcoma)                       | <i>FOXO1A</i>    | Transcription                        | 2.26  |
| Follicular lymphoma variant translocation 1               | <i>FVT1</i>      | Metabolic processes                  | 0.68  |
| Galnac-Transferase 1                                      | <i>GALNT1</i>    | Protein glycosylation                | 1.7   |
| GTP cyclohydrolase 1 (dopa-responsive dystonia)           | <i>GCH1</i>      | Metabolic and catabolic processes    | 2.28  |
| Gap junction protein, beta 2, 26kda (connexin 26)         | <i>GJB2</i>      | Cell-to-cell signaling               | 0.391 |
| G protein-coupled receptor, family C, group 5, member A   | <i>GPRC5A</i>    | Signal transduction                  | 0.64  |
| General transcription factor IIF, polypeptide 2, 30kda    | <i>GTF2F2</i>    | Transcription                        | 0.679 |
| H19, imprinted maternally expressed untranslated mrna     | <i>H19</i>       | Unclear                              | 1.28  |
| Hyaluronan synthase 2                                     | <i>HAS2</i>      | Matrix formation                     | 0.346 |
| Heparin-binding EGF-like growth factor                    | <i>HBEGF</i>     | Signal transduction                  | 0.379 |
| HEG homolog 1 (zebrafish)                                 | <i>HEG</i>       | Unclear                              | 1.68  |
| Hexokinase 1  | <i>HK1</i>       | Glycolysis                           | 2.03  |
| Heat shock 22kda protein 8                                | <i>HSPB8</i>     | Stress responses                     | 1.29  |
| Paraneoplastic antigen                                    | <i>HUMPPA</i>    | Unclear                              | 3.109 |
| Immediate early response 2                                | <i>IER2</i>      | Unclear                              | 0.623 |
| Immediate early response 5                                | <i>IER5</i>      | Unclear                              | 0.652 |
| Immediate early response 5-like                           | <i>IER5L</i>     | Unclear                              | 2.4   |
| Insulin-like growth factor binding protein 3              | <i>IGFBP3</i>    | Cell growth and apoptosis            | 2.04  |
| Insulin-like growth factor binding protein 4              | <i>IGFBP4</i>    | Signal Transduction, Cellular growth | 1.559 |
| Interleukin 18 (interferon-gamma-inducing factor)         | <i>IL18</i>      | Signal transduction                  | 0.533 |
| Inhibin, beta A (activin A, activin AB alpha polypeptide) | <i>INHBA</i>     | Multifunctional signaling processes  | 2.74  |
| Juxtaposed with another zinc finger gene 1                | <i>JAZF1</i>     | Transcription                        | 5.47  |
| Jumonji domain containing 2B                              | <i>JMJD2B</i>    | Transcription                        | 5.42  |
| Kiaa0247  | <i>KIAA0247</i>  | Unclear                              | 2.14  |
| KIAA0830 protein  | <i>KIAA0830</i>  | Unclear                              | 1.76  |
| Kiaa1553  | <i>KIAA1553</i>  | Unclear                              | 0.687 |
| KIAA1609 protein  | <i>KIAA1609</i>  | Unclear                              | 0.49  |
| KIAA1799 protein  | <i>KIAA1799</i>  | Unclear                              | 1.33  |
| Kinesin family member 21A                                 | <i>KIF21A</i>    | Microtubule based motility           | 1.8   |
| Kruppel-like factor 10                                    | <i>KLF10</i>     | Cell-to-cell signaling               | 2.26  |
| Lysosomal associated multispinning membrane protein 5     | <i>LAPTM5</i>    | Transport                            | 6.59  |
| Leukemia inhibitory factor receptor                       | <i>LIFR</i>      | Cellular proliferation               | 2.08  |
| Lipase, endothelial                                       | <i>LIPG</i>      | Lipid catabolism                     | 3.53  |
| Hypothetical protein LOC149832                            | <i>LOC149832</i> | Unclear                              | 1.47  |
| Hypothetical LOC201484                                    | <i>LOC201484</i> | Unclear                              | 1.47  |
| Hypothetical protein LOC283551                            | <i>LOC283551</i> | Unclear                              | 44.93 |
| Lysyl oxidase   | <i>LOX</i>       | Protein modification                 | 3.3   |
| Lysyl oxidase-like 4                                      | <i>LOXL4</i>     | Ion binding                          | 139.4 |
| Mitogen-activated protein kinase kinase 3                 | <i>MAP2K3</i>    | Signal transduction                  | 0.614 |

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| Mitogen-activated protein kinase kinase 5                 | <i>MAP2K5</i>   | Signal transduction                  | 4.39  |
| MARCKS-like 1   | <i>MARCKSL1</i> | Unclear                              | 2.9   |
| MADS box transcription enhancer factor 2, polypeptide A   | <i>MEF2A</i>    | Transcription                        | 2.24  |
| Likely ortholog of mouse schlafen 5                       | <i>MGC19764</i> | Cellular differentiation             | 2.48  |
| Microphthalmia-associated transcription factor            | <i>MITF</i>     | Transcription                        | 5.47  |
| MAP kinase interacting serine/threonine kinase 2          | <i>MKNK2</i>    | Signal Transduction, phosphorylation | 1.96  |
| Matrix metalloproteinase 1 (interstitial collagenase)     | <i>MMP1</i>     | Collagen catabolism, Proteolysis     | 0.22  |
| Matrix metalloproteinase 3 (stromelysin 1, progelatinase) | <i>MMP3</i>     | Collagen catabolism, Proteolysis     | 0.47  |
| Metallothionein 1X  | <i>MT1X</i>     | Responses to metal ions              | 2.02  |
| MAX dimerization protein 1                                | <i>MXD1</i>     | Transcription                        | 2.06  |
| Myeloid-associated differentiation marker                 | <i>MYADM</i>    | Unclear                              | 0.591 |
| Nanos homolog 1   | <i>NANOS1</i>   | Regulation of translation            | 4.9   |
| Neuron navigator 2  | <i>NAV2</i>     | Neural growth                        | 1.85  |
| Nuclear receptor coactivator 1                            | <i>NCOA1</i>    | Transcription                        | 3.13  |
| Neural precursor expr, develop down-reg 4-like            | <i>NEDD4L</i>   | Protein modification                 | 0.51  |
| Normal mucosa of esophagus specific 1                     | <i>NMES1</i>    | Unclear                              | 1.79  |
| Noggin  | <i>NOG</i>      | Tissue and organ development         | 0.72  |
| Neighbor of Punc E11                                      | <i>NOPE</i>     | Unclear                              | 0.65  |
| Neuregulin 1  | <i>NRG1</i>     | Cellular differentiation             | 0.5   |
| O-acyltransferase domain containing 1                     | <i>OACT1</i>    | Protein modification                 | 1.627 |
| Ornithine decarboxylase 1                                 | <i>ODC1</i>     | Polyamine biosynthetic process       | 0.649 |
| Olfactomedin-like 3                                       | <i>OLFML3</i>   | Matrix related function              | 8.62  |
| Oxysterol binding protein-like 3                          | <i>OSBPL3</i>   | Lipid transport, steroid metabolism  | 2.04  |
| OTU domain, ubiquitin aldehyde binding 2                  | <i>OTUB2</i>    | Amino acid metabolism                | 7.39  |
| 3'-phosphoadenosine 5'-phosphosulfate synthase 2          | <i>PAPSS2</i>   | Nucleic acid metabolism              | 2.82  |
| Pim-1 oncogene /// pim-1 oncogene                         | <i>PIM1</i>     | Cellular proliferation and apoptosis | 2.33  |
| Phosphatidylinositol-4-phosphate 5-kinase, type I, gamma  | <i>PIP5K1C</i>  | Phosphatidylinositol metabolism      | 3.2   |
| Plasminogen activator, tissue                             | <i>PLAT</i>     | Proteolysis                          | 0.639 |
| Plasminogen activator, urokinase                          | <i>PLAU</i>     | Proteolysis                          | 0.28  |
| Plasminogen activator, urokinase receptor                 | <i>PLAUR</i>    | Signal trans, motility, proteolysis  | 0.405 |
| POU domain, class 3, transcription factor 2               | <i>POU3F2</i>   | Transcription                        | 1.89  |
| Protein phosphatase 1, regulatory (inhibitor) subunit 13B | <i>PPP1R13B</i> | Apoptosis regulation                 | 1.9   |
| Prostaglandin-endoperoxide synthase 2                     | <i>PTGS2</i>    | Fatty acid biosynthetic process      | 9.67  |
| Ral GEF with PH domain and SH3 binding motif 2            | <i>RALGPS2</i>  | Signal transduction                  | 2.72  |
| RNA binding motif protein 24                              | <i>RBM24</i>    | Type I hypersensitivity              | 1.68  |
| REST corepressor 3  | <i>RCOR3</i>    | Transcription                        | 1.74  |
| Radixin   | <i>RDX</i>      | Cytoskeletal anchoring               | 1.77  |
| Regulator of nonsense transcripts 1                       | <i>RENT1</i>    | DNA and RNA processing               | 2.75  |
| RGM domain family, member B                               | <i>RGMB</i>     | Signal transduction                  | 0.66  |
| Regulator of G-protein signalling 10                      | <i>RGS10</i>    | Signal transduction                  | 1.73  |
| Regulator of G-protein signalling 19                      | <i>RGS19</i>    | Signal transduction                  | 3.63  |
| Rho-related BTB domain containing 3                       | <i>RHOBTB3</i>  | Biological process                   | 2.17  |
| Rhopilin, Rho gtpase binding protein 2                    | <i>RHPN2</i>    | Signal transduction                  | 0.599 |
| Ras and Rab interactor 2                                  | <i>RIN2</i>     | Signal transduction                  | 0.597 |
| RNA-binding region (RNP1, RRM) containing 1               | <i>RNPC1</i>    | DNA damage response                  | 0.614 |
| Ribonucleotide reductase M2 B (TP53 inducible)            | <i>RRM2B</i>    | DNA Repair and replication           | 1.49  |
| Retinoid X receptor, alpha                                | <i>RXRA</i>     | Signal transduction                  | 1.47  |
| Spermidine/spermine N1-acetyltransferase 2                | <i>SAT2</i>     | Metabolic processes                  | 1.82  |
| Sema domain, immunoglobulin domain,(semaphorin) 3B        | <i>SEMA3B</i>   | Cell-to-cell signaling               | 1.45  |

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| Sema domain (semaphorin) 6B                           | <i>SEMA6B</i>   | Cellular differentiation             | 2.21   |
| Serpin peptidase inhibitor, clade B, member 2         | <i>SERPINB2</i> | Apoptosis regulation                 | 0.154  |
| Serpin peptidase inhibitor, clade B, member 6         | <i>SERPINB6</i> | Endopeptidase inhibitor activity     | 1.54   |
| Serpin peptidase inhibitor, clade B, member 9         | <i>SERPINB9</i> | Apoptosis regulation                 | 17.92  |
| SERTA domain containing 2                             | <i>SERTAD2</i>  | Transcription                        | 0.72   |
| SERTA domain containing                               | <i>SERTAD4</i>  | Unclear                              | 0.48   |
| SH3-domain binding protein 5 (BTK-associated)         | <i>SH3BP5</i>   | Intracellular signaling cascade      | 1.77   |
| Solute carrier family 9, member 3 regulator 1         | <i>SLC9A3R1</i> | Protein complex assembly             | 2.64   |
| Slit-like 2 (Drosophila)                              | <i>SLITL2</i>   | Unclear                              | 1.67   |
| Cbl-interacting protein Sts-1                         | <i>STS-1</i>    | Endocytosis inhibition               | 0.436  |
| TBC1 domain family, member 4                          | <i>TBC1D4</i>   | Unclear                              | 0.685  |
| Thromboxane A2 receptor                               | <i>TBXA2R</i>   | Signal transduction                  | 5.65   |
| T-cell, immune regulator 1, atpase, H+ transporting   | <i>TCIRG1</i>   | Ion and proton transport             | 3.02   |
| Transforming growth factor, alpha                     | <i>TGFA</i>     | Cellular proliferation               | 2      |
| Transforming growth factor, beta 2                    | <i>TGFB2</i>    | Cellular proliferation, apoptosis    | 0.39   |
| Transmembrane protein 2                               | <i>TMEM2</i>    | Unclear                              | 2.61   |
| Tumor necrosis factor receptor superfamily, member 21 | <i>TNFRSF21</i> | Signal transduction                  | 0.66   |
| TNFAIP3 interacting protein 1                         | <i>TNIP1</i>    | Glycoprotein anabolism               | 2.02   |
| Transducer of ERBB2, 1                                | <i>TOB1</i>     | Cellular proliferation               | 3.298  |
| Tumor protein p53 inducible protein 3                 | <i>TP53I3</i>   | Apoptosis regulation                 | 2.05   |
| Trophoblast glycoprotein                              | <i>TPBG</i>     | Cell adhesion and motility           | 1.88   |
| Tumor protein D52-like 1                              | <i>TPD52L1</i>  | Apoptosis regulation                 | 12.549 |
| Translocation associated membrane protein 2           | <i>TRAM2</i>    | Protein transport                    | 0.53   |
| Tripartite motif-containing 47                        | <i>TRIM47</i>   | Ion binding                          | 1.67   |
| Twisted gastrulation homolog 1 (Drosophila)           | <i>TWSG1</i>    | Multicellular organismal development | 1.71   |
| Ubiquitin-conjugating enzyme E2Q (putative) 2         | <i>UBE2Q2</i>   | Regulation of protein metabolism     | 0.74   |
| UDP-glucose ceramide glucosyltransferase              | <i>UGCG</i>     | Glucosylceramide anabolism           | 0.64   |
| UDP-glucuronate decarboxylase 1                       | <i>UXS1</i>     | Metabolic processes                  | 1.71   |
| Vascular endothelial growth factor C                  | <i>VEGFC</i>    | Signaling, proliferation             | 0.52   |
| Wiskott-Aldrich syndrome protein interacting protein  | <i>WASPIP</i>   | Protein complex assembly             | 1.38   |
| Wingless-type MMTV integration site family, member 16 | <i>WNT16</i>    | Cell-to-cell signaling               | 151.1  |
| Wilms tumor   | <i>WT1</i>      | Transcription                        | 0.38   |
| Yippee-like 2 (Drosophila)                            | <i>YPEL2</i>    | Unclear                              | 44.73  |
| Zinc finger and BTB domain containing 38              | <i>ZBTB38</i>   | Transcription                        | 1.97   |
| Zinc finger protein 336                               | <i>ZNF336</i>   | Transcription                        | 2.46   |

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**Table 2. ER $\alpha_{\text{EBD}}$ -mediated gene expression in response to E2**

| <b>Gene Name</b>   | <b>Symbol</b>   | <b>Function</b>              | <b>Relative Change<sup>a</sup></b> |
|--|-----------------|------------------------------|------------------------------------|
| Ankyrin repeat domain 1 (cardiac muscle)                 | <i>ANKRD1</i>   | Signal transduction          | 1.556                              |
| Cysteine-rich secretory protein LCCL domain containing 2 | <i>CRISPLD2</i> | Signal transduction          | 1.47                               |
| Connective tissue growth factor                          | <i>CTGF</i>     | DNA replication, cell growth | 0.595                              |
| Dual specificity phosphatase 5                           | <i>DUSP5</i>    | Protein dephosphorylation    | 1.436                              |
| Follistatin  | <i>FST</i>      | Signal transduction          | 3.67                               |
| Gap junction protein, beta 2                             | <i>GJB2</i>     | Cell-cell signaling          | 1.797                              |
| G protein-coupled receptor, family C, group 5, member A  | <i>GPRC5A</i>   | Signal transduction          | 1.489                              |
| Hyaluronan synthase 2                                    | <i>HAS2</i>     | Matrix formation             | 0.695                              |
| Heparin-binding EGF-like growth factor                   | <i>HBEGF</i>    | Signal transduction          | 0.786                              |
| Insulin-like growth factor binding protein 4             | <i>IGFBP4</i>   | Signal transduction          | 1.262                              |
| Matrix metalloproteinase 1                               | <i>MMP1</i>     | Collagen catabolism          | 0.791                              |
| Matrix metalloproteinase 3                               | <i>MMP3</i>     | Collagen catabolism          | 3.83                               |
| Neuregulin 1   | <i>NRG1</i>     | Cellular differentiation     | 1.87                               |
| Plasminogen activator, tissue                            | <i>PLAT</i>     | Proteolysis                  | 2.211                              |
| Plasminogen activator, urokinase                         | <i>PLAU</i>     | Proteolysis                  | 2.404                              |
| Serpin peptidase inhibitor, clade B, member 2            | <i>SERPINB2</i> | Anti-apoptosis               | 2.686                              |

<sup>a</sup> Gene expression regulated by E2-ER $\alpha_{\text{EBD}}$  compared to those mediated by the parent Ad5 in the presence of E2. The SEM, which was less than 10% of the mean, is not shown for simplicity.