## SUPPLEMENTARY TABLE 1

**Cell culture media.** Details of the cell culture media used for growth of ovarian cancer cell lines and normal ovarian cells. FBS, foetal bovine serum.

| Cell Line | Culture Media |
|---|---|
| Mesenchymal stem cells (MSCs) | Alpha MEM (Lonza), L-glutamine (Lonza), 16.5% Premium Select FBS (Atlanta Biologicals). |
| TERT immortalized normal ovarian fibroblasts (INOFs) | MCDB105:Medium 199 (1:1, both Sigma), L-glutamine, 15% Hyclone FBS (Pierce) |
| TERT immortalized normal ovarian epithelial cels (OSECs) | INOF medium + 10ng/ml epidermal growth factor, 34µg/ml bovine pituitary extract (Life Technologies), 500ng/ml hydrocortisone, 5µg/ml insulin (Sigma) |
| Hey.A8 | RPMI, L-glutamine, 10% FBS (PAA Laboratories) |
| OVCA429 | EMEM, L-glutamine, 1X non-essential amino acids, 1X sodium pyruvate (both Lonza), 10% FBS (PAA Laboratories) |
| 1847 | RPMI, L-glutamine, 10% FBS (PAA Laboratories) |
| COV318 | DMEM, L-glutamine, 10% FBS (PAA Laboratories) |
| FUOV1 | DMEM/F12, L-glutamine, 10% FBS (PAA Laboratories) |
| OVCAR8 | RPMI, L-glutamine, 10% FBS (PAA Laboratories) |
| CaOV3 | RPMI, L-glutamine, 10% FBS (PAA Laboratories) |

## SUPPLEMENTARY TABLE 2

**Patient characteristics in the tissue microarray.**

| | N (%) |
|---|---|
| ***Age*** | |
| <50 | 27 (18.6) |
| >50 | 118 (81.4) |
| ***Stage*** | |
| Stage 1 | 34 (23.4) |
| Stage 2 | 12 (8.3) |
| Stage 3 | 95 (65.5) |
| Stage 4 | 14 (9.7) |
| ***Grade*** | |
| Grade 1 | 14 (9.7) |
| Grade 2 | 44 (30.3) |
| Grade 3 | 87 (60.0) |
| ***Histology*** | |
| Serous | 98 (67.6) |
| Clear Cell | 24 (16.6) |
| Endometrioid | 12 (8.3) |
| Mucinous | 9 (6.2) |
| Other | 2 (1.4) |

## SUPPLEMENTARY TABLE 3

**Gene ontology (GO) analyses of gene differentially expressed in co-cultured stromal cells.** DAVID was used to test for enrichment of Biological Processes, Cellular Compartments and Molecular Function GO terms. Genes differentially expressed by EOC-co-cultured stromal cells were enriched for pathways involved in female pregnancy, and tended to be associated with the extracellular milieu. Statistically significant terms are shown (P<0.05, adjusted).

| | | P Value | | |
|---|---|---|---|---|
| **Term** | **Count** | **Unadjusted** | **Benjamini** | **Fold Enrichment** |
| ***BIOLOGICAL PROCESSES*** | | | | |
| GO:0007155~cell adhesion | 62 | 1.36E-06 | 0.004 | 1.90 |
| GO:0022610~biological adhesion | 62 | 1.43E-06 | 0.002 | 1.90 |
| GO:0051270~regulation of cell motion | 26 | 3.24E-06 | 0.003 | 2.90 |
| GO:0030198~extracellular matrix organization | 18 | 5.48E-06 | 0.004 | 3.72 |
| GO:0040012~regulation of locomotion | 25 | 9.44E-06 | 0.006 | 2.80 |
| GO:0030334~regulation of cell migration | 23 | 1.15E-05 | 0.006 | 2.93 |
| GO:0007565~female pregnancy | 18 | 1.19E-05 | 0.005 | 3.52 |
| GO:0007229~integrin-mediated signaling pathway | 14 | 1.69E-05 | 0.007 | 4.30 |
| GO:0043062~extracellular structure organization | 22 | 2.13E-05 | 0.007 | 2.90 |
| GO:0001568~blood vessel development | 28 | 2.74E-05 | 0.008 | 2.46 |
| GO:0009611~response to wounding | 47 | 3.18E-05 | 0.009 | 1.91 |
| GO:0001944~vasculature development | 28 | 4.21E-05 | 0.011 | 2.40 |
| GO:0042127~regulation of cell proliferation | 62 | 5.17E-05 | 0.012 | 1.69 |
| GO:0010033~response to organic substance | 58 | 5.36E-05 | 0.012 | 1.73 |
| GO:0030155~regulation of cell adhesion | 19 | 6.28E-05 | 0.013 | 2.98 |
| GO:0035150~regulation of tube size | 11 | 1.38E-04 | 0.026 | 4.46 |
| GO:0050880~regulation of blood vessel size | 11 | 1.38E-04 | 0.026 | 4.46 |
| GO:0003013~circulatory system process | 22 | 1.49E-04 | 0.027 | 2.54 |
| GO:0008015~blood circulation | 22 | 1.49E-04 | 0.027 | 2.54 |
| GO:0006928~cell motion | 41 | 1.95E-04 | 0.033 | 1.86 |
| | | | | |
| ***CELLULAR COMPARTMENT*** | | | | |
| GO:0044421~extracellular region part | 94 | 1.50E-11 | 2.11E-08 | 2.06 |
| GO:0005576~extracellular region | 156 | 1.05E-10 | 1.48E-07 | 1.63 |
| GO:0031012~extracellular matrix | 42 | 5.08E-08 | 7.15E-05 | 2.56 |

| | | | | |
|---|---|---|---|---|
| GO:0005578~proteinaceous extracellular matrix | 38 | 4.64E-07 | 6.53E-04 | 2.50 |
| GO:0005615~extracellular space | 60 | 5.57E-06 | 0.008 | 1.84 |
| GO:0044420~extracellular matrix part | 19 | 9.36E-06 | 0.013 | 3.42 |
| GO:0000267~cell fraction | 81 | 3.82E-05 | 0.054 | 1.57 |
| GO:0005794~Golgi apparatus | 67 | 9.48E-05 | 0.133 | 1.62 |
| GO:0005626~insoluble fraction | 65 | 9.88E-05 | 0.139 | 1.63 |
| GO:0005624~membrane fraction | 63 | 1.11E-04 | 0.155 | 1.64 |
| GO:0015629~actin cytoskeleton | 28 | 1.92E-04 | 0.270 | 2.19 |
| GO:0044459~plasma membrane part | 139 | 2.11E-04 | 0.296 | 1.33 |
| GO:0031252~cell leading edge | 18 | 2.82E-04 | 0.395 | 2.75 |
| GO:0005604~basement membrane | 13 | 2.85E-04 | 0.400 | 3.51 |
| GO:0031226~intrinsic to plasma membrane | 84 | 3.79E-04 | 0.532 | 1.46 |
| GO:0005887~integral to plasma membrane | 82 | 4.71E-04 | 0.661 | 1.45 |
| GO:0005605~basal lamina | 6 | 9.06E-04 | 1.267 | 7.43 |
| GO:0009986~cell surface | 31 | 0.001 | 1.590 | 1.88 |
| GO:0005886~plasma membrane | 212 | 0.002 | 3.339 | 1.18 |
| GO:0005912~adherens junction | 17 | 0.003 | 3.871 | 2.31 |
| | | | | |
| ***MOLECULAR FUNCTION*** | | | | |
| GO:0005178~integrin binding | 15 | 3.24E-07 | 2.81E-04 | 5.51 |
| GO:0005509~calcium ion binding | 73 | 5.24E-06 | 0.002 | 1.72 |
| GO:0008289~lipid binding | 42 | 2.32E-05 | 0.007 | 2.02 |
| GO:0008092~cytoskeletal protein binding | 45 | 3.33E-05 | 0.007 | 1.94 |
| GO:0032403~protein complex binding | 23 | 1.01E-04 | 0.017 | 2.54 |
| GO:0003779~actin binding | 30 | 5.36E-04 | 0.075 | 1.99 |
| GO:0005201~extracellular matrix structural constituent | 13 | 5.51E-04 | 0.066 | 3.28 |
| GO:0005520~insulin-like growth factor binding | 7 | 7.78E-04 | 0.081 | 6.07 |
| GO:0019838~growth factor binding | 14 | 0.001 | 0.096 | 2.89 |
| GO:0005543~phospholipid binding | 19 | 0.001 | 0.111 | 2.33 |
| GO:0016717~oxidoreductase activity, acting on paired donors | 4 | 0.002 | 0.129 | 14.45 |
| GO:0050840~extracellular matrix binding | 6 | 0.007 | 0.402 | 4.82 |
| GO:0008083~growth factor activity | 16 | 0.007 | 0.392 | 2.15 |
| GO:0015082~di-, tri-valent inorganic cation transmembrane transporter activity | 7 | 0.008 | 0.404 | 3.89 |
| GO:0034185~apolipoprotein binding | 4 | 0.009 | 0.413 | 8.67 |
| GO:0001871~pattern binding | 15 | 0.012 | 0.471 | 2.11 |
| GO:0030247~polysaccharide binding | 15 | 0.012 | 0.471 | 2.11 |
| GO:0005539~glycosaminoglycan binding | 14 | 0.013 | 0.475 | 2.17 |
| GO:0005507~copper ion binding | 9 | 0.014 | 0.484 | 2.83 |
| GO:0004065~arylsulfatase activity | 4 | 0.016 | 0.514 | 7.22 |

## SUPPLEMENTARY TABLE 4

**Gene ontology (GO) analyses of gene differentially expressed in co-cultured stromal cells.** DAVID was used to test for enrichment of KEGG pathway analysis terms. Statistically significant terms are shown (P<0.05, unadjusted).

| | | P Value | | |
|---|---|---|---|---|
| **Term** | **Count** | **Unadjusted** | **Benjamini** | **Fold Enrichment** |
| hsa04512:ECM-receptor interaction | 16 | 5.38E-05 | 0.009 | 3.37 |
| hsa05200:Pathways in cancer | 33 | 0.001 | 0.105 | 1.78 |
| hsa04010:MAPK signaling pathway | 28 | 0.002 | 0.099 | 1.86 |
| hsa04510:Focal adhesion | 22 | 0.004 | 0.155 | 1.94 |
| hsa04115:p53 signaling pathway | 11 | 0.004 | 0.132 | 2.87 |
| hsa05222:Small cell lung cancer | 12 | 0.007 | 0.173 | 2.53 |
| hsa04640:Hematopoietic cell lineage | 12 | 0.008 | 0.176 | 2.47 |
| hsa05412:Arrhythmogenic right ventricular cardiomyopathy (ARVC) | 11 | 0.010 | 0.178 | 2.56 |
| hsa05416:Viral myocarditis | 10 | 0.017 | 0.270 | 2.50 |
| hsa04270:Vascular smooth muscle contraction | 13 | 0.023 | 0.313 | 2.06 |
| hsa04810:Regulation of actin cytoskeleton | 20 | 0.032 | 0.386 | 1.65 |
| hsa05414:Dilated cardiomyopathy | 11 | 0.033 | 0.366 | 2.12 |
| hsa05410:Hypertrophic cardiomyopathy (HCM) | 10 | 0.048 | 0.462 | 2.08 |

ovarian cancer. NT-proBNP is elevated in 4/8 EOC patients independently of cardiac failure. Dashed line = cutoff for elevated NT-proBNP (100pg/ml).

**Table 1. Differentially expressed genes in co-cultured stromal cells.** This table shows the top 20 up- and downregulated genes in INOFs and MSCs co-cultured with Hey.A8 ovarian cancer cells compared to INOFs/MSCs co-cultured with normal ovarian surface epithelial cells. Genes are ranked by pooled fold change.

**Table 2. Immunohistochemical staining of NPPB in EOC specimens.** 145 tumours were stained for NPPB. Patient characteristics can be found in Supplementary Table 2. P-values indicate the results of Fisher's Exact tests. Statistically significant associations are shown in bold.

## SUPPLEMENTARY DATA

**Supplementary Table 1. Cell culture media.** Details of the cell culture media used for growth of ovarian cancer cell lines and normal ovarian cells. FBS, foetal bovine serum.

**Supplementary Table 2. Patient characteristics in the tissue microarray.**

**Supplementary Table 3. Gene ontology (GO) analyses of gene differentially expressed in co-cultured stromal cells.** DAVID was used to test for enrichment of Biological Processes, Cellular Compartments and Molecular Function GO terms. Genes differentially expressed by EOC-co-cultured stromal cells were enriched for pathways involved in female pregnancy, and tended to be associated with the extracellular milieu. Statistically significant terms are shown ($P<0.05$, adjusted).

**Supplementary Table 4. Gene ontology (GO) analyses of gene differentially expressed in co-cultured stromal cells.** DAVID was used to test for enrichment of KEGG pathway analysis terms. Statistically significant terms are shown ($P<0.05$, unadjusted).