

Inflammatory Factors Mediate Vulnerability to a Social Stress-Induced Depressive-Like Phenotype in Passive Coping Rats***Supplemental Information*****Table S1.** Stress-induced changes in gene expression in the locus coeruleus relative to control

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|-----------------------------|---|-----------|-------------|---------------|-------------|---|
| Short Latency | | | | | | |
| <i>Downregulated</i> | | | | | | |
| ADRB1 | Adrenoceptor beta 1 | Rn.87064 | â-4.759 | PM | GPCR | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| NOS2 | Nitric oxide synthase 2, inducible | Rn.10400 | â-3.355 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| GRM5 | Glutamate receptor, metabotropic 5 | Rn.29972 | â-3.345 | PM | GPCR | Nutri, CVD, Metab, Neuro, Psych |
| AGTR2 | Angiotensin II receptor, type 2 | Rn.162367 | â-3.016 | PM | GPCR | GI, CVD, Nutri, Neuro, Renal |
| CYP19A1 | Cytochrome P450, family 19, subfamily A, polypeptide 1 | Rn.21402 | â-2.335 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| MMP9 | Matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase) | Rn.10209 | â-2.326 | Extracellular | Peptidase | Nutri, Inflam, Immun, CVD, Metab, GI, Neuro, Renal |
| VCAM1 | Vascular cell adhesion molecule 1 | Rn.11267 | â-2.208 | PM | TM receptor | Inflam, Immun, CVD, Metab, GI, Endo, Neuro, Renal |
| GRM7 | Glutamate receptor, metabotropic 7 | Rn.10409 | â-2.068 | PM | GPCR | GI, Neuro, Psych |
| ICAM1 | Intercellular adhesion molecule 1 | Rn.12 | â-1.995 | PM | TM receptor | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|-----------------------------|---|----------------|--------------------|-----------------|----------------|---|
| <i>COL1A1</i> | Collagen, type I, alpha 1 | Rn.2953 |  -1.786 | Extracellular | Other | GI, Inflam, CVD, Neuro |
| <i>IL1R1</i> | Interleukin 1 receptor, type I | Rn.9758 |  -1.636 | PM | TM receptor | GI, Inflam, CVD, Nutri, Neuro, Renal, Immun, Endo, Metab |
| <i>Upregulated</i> | | | | | | |
| <i>IL1R2</i> | Interleukin 1 receptor, type II | Rn.10758 |  7.976 | PM | TM receptor | GI, Inflam, Immun, Endo, Metab |
| <i>IL1B</i> | Interleukin 1, beta | Rn.9869 |  3.993 | Extracellular | Cytokine | GI, Inflam, CVD, Nutri, Neuro, Psych, Immun, Endo, Metab |
| <i>LHCGR</i> | Luteinizing hormone/choriogonadotropin receptor | Rn.11216 |  2.418 | PM | GPCR | CVD, Nutri, Endo |
| <i>NPY1R</i> | Neuropeptide Y receptor Y1 | Rn.11642 |  2.198 | PM | GPCR | Nutri, Immun, CVD, Metab |
| <i>Long Latency</i> | | | | | | |
| <i>Downregulated</i> | | | | | | |
| <i>NOS2</i> | Nitric oxide synthase 2, inducible | Rn.10400 |  -3.932 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>NPY2R</i> | Neuropeptide Y receptor Y2 | Rn.64505 |  -3.664 | PM | GPCR | N/A* |
| <i>IL1B</i> | Interleukin 1, beta | Rn.9869 |  -3.199 | Extracellular | Cytokine | GI, Inflam, CVD, Nutri, Neuro, Psych, Immun, Endo, Metab |
| <i>EDN1</i> | Endothelin 1 | Rn.10918 |  -2.794 | Extracellular | Cytokine | GI, Inflam, CVD, Neuro, Renal |
| <i>GRM5</i> | Glutamate receptor, metabotropic 5 | Rn.29972 |  -2.727 | PM | GPCR | Nutri, CVD, Metab, Neuro, Psych |
| <i>ICAM1</i> | Intercellular adhesion molecule 1 | Rn.12 |  -2.571 | PM | TM receptor | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>DRD1</i> | Dopamine receptor D1 | Rn.24039 |  -2.321 | PM | GPCR | Nutri, CVD, Metab, GI, Endo, Neuro, Renal, Psych |
| <i>TNF</i> | Tumor necrosis factor | Rn.2275 |  -2.089 | Extracellular | Cytokine | Nutri, Inflam, Immun, CVD, Metab, GI, Endo, Neuro, Renal, Psych |

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|--------------------|--|----------|-------------|-----------|-------------------------|---|
| <i>EGR1</i> | Early growth response 1 | Rn.9096 | â-2.028 | Nucleus | Transcription regulator | Infam, Immun, CVD, GI, Neuro |
| <i>SOCS1</i> | Suppressor of cytokine signaling 1 | Rn.82754 | â-1.815 | Cytoplasm | Other | Inflam, Immun, CVD, Metab, GI, Endo, Renal |
| <i>KCNH8</i> | Potassium voltage-gated channel, subfamily H (eag-related), member 8 | Rn.30029 | â-1.686 | PM | Ion channel | N/A* |
| <i>BCL2L1</i> | BCL2-like 1 | Rn.10323 | â-1.681 | Cytoplasm | Other | Inflam, Immun, CVD, GI, Neuro |
| <i>OPRK1</i> | Opioid receptor, kappa 1 | Rn.89571 | â-1.533 | PM | GPCR | Nutri, Inflam, Immun, CVD, GI, Neuro, Psych |
| Upregulated | | | | | | |
| <i>IL1R2</i> | Interleukin 1 receptor, type II | Rn.10758 | â4.31 | PM | TM receptor | GI, Inflam, Immun, Endo, Metab |
| <i>NPY1R</i> | Neuropeptide Y receptor Y1 | Rn.11642 | â1.745 | PM | GPCR | Nutri, Immun, CVD, Metab |
| <i>UCP1</i> | Uncoupling protein 1 (mitochondrial, proton carrier) | Rn.10281 | â1.615 | Cytoplasm | Transporter | Metab |
| <i>LHCGR</i> | Luteinizing hormone/choriogonadotropin receptor | Rn.11216 | â1.550 | PM | GPCR | CVD, Nutri, Endo |

Genes >1.5 fold differentially expressed vs. controls.

CVD, cardiovascular disease; Endo, endocrine system disorders; GI, gastrointestinal disease; GPCR, G-protein coupled receptor signaling; Immun, immunological disease; Inflam, inflammatory disease; Metab, metabolic disease; Neuro, neurological disease; Nutri, nutritional disease; PM, plasma membrane; Psych, psychological disorders; Renal, renal and urological disease; TM, transmembrane; *N/A, no disease association was provided by IPA.

Table S2. Stress-induced changes in gene expression in the dorsal raphe relative to control

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|----------------------|--|----------|-------------|---------------|-------------------------|---|
| Short Latency | | | | | | |
| Downregulated | | | | | | |
| <i>COL1A1</i> | Collagen, type I, alpha 1 | Rn.2953 |  -7.234 | Extracellular | Other | GI, Inflam, CVD, Neuro |
| <i>CYP19A1</i> | Cytochrome P450, family 19, subfamily A, polypeptide 1 | Rn.21402 |  -4.319 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>IL1R2</i> | Interleukin 1 receptor, type II | Rn.10758 |  -3.766 | PM | TM receptor | GI, Inflam, Immun, Endo, Metab |
| <i>TACR1</i> | Tachykinin receptor 1 | Rn.89609 |  -3.423 | PM | GPCR | GI, Inflam, Nutri, Psych |
| <i>AKT1</i> | V-akt murine thymoma viral oncogene homolog 1 | Rn.11422 |  -3.231 | Cytoplasm | Kinase | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>EDN1</i> | Endothelin 1 | Rn.10918 |  -2.783 | Extracellular | Cytokine | GI, Inflam, CVD, Neuro, Renal |
| <i>NPY2R</i> | Neuropeptide Y receptor Y2 | Rn.64505 |  -2.616 | PM | GPCR | N/A* |
| <i>IL1R1</i> | Interleukin 1 receptor, type I | Rn.9758 |  -2.412 | PM | TM receptor | GI, Inflam, CVD, Nutri, Neuro, Renal, Immun, Endo, Metab |
| <i>LHCGR</i> | Luteinizing hormone/choriogonadotropin receptor | Rn.11216 |  -2.310 | PM | GPCR | CVD, Nutri, Endo |
| <i>CCNE1</i> | Cyclin E1 | Rn.15455 |  -2.284 | Nucleus | Transcription regulator | CVD |
| <i>GALR2</i> | Galanin receptor 2 | Rn.9789 |  -2.142 | PM | GPCR | GI |
| <i>GRM1</i> | Glutamate receptor, metabotropic 1 | Rn.87787 |  -2.123 | PM | GPCR | GI, Neuro, Psych |
| <i>S1PR2</i> | Sphingosine-1-phosphate receptor 2 | Rn.2491 |  -2.104 | PM | GPCR | Neuro, Immun |
| <i>ADORA2A</i> | Adenosine A2a receptor | Rn.11180 |  -2.027 | PM | GPCR | GI, Inflam, CVD, Nutri, Neuro, Renal, Immun |
| <i>JUN</i> | Jun proto-oncogene | Rn.93714 |  -1.975 | Nucleus | Transcription regulator | GI, Inflam, CVD, Neuro, Psych, Renal, Immun, Endo, Metab |

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|--------------|---|-----------|-------------|---------------|-------------------------|---|
| <i>GRM7</i> | Glutamate receptor, metabotropic 7 | Rn.10409 |   -1.929 | PM | GPCR | GI, Neuro, Psych |
| <i>AGTR2</i> | Angiotensin II receptor, type 2 | Rn.162367 |   -1.873 | PM | GPCR | GI, CVD, Nutri, Neuro, Renal |
| <i>NOS2</i> | Nitric oxide synthase 2, inducible | Rn.10400 |   -1.802 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>CASR</i> | Calcium-sensing receptor | Rn.10019 |   -1.755 | PM | GPCR | GI, Inflam, CVD, Neuro, Renal, Endo |
| <i>ADRB1</i> | Adrenoceptor beta 1 | Rn.87064 |   -1.724 | PM | GPCR | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>GRM2</i> | Glutamate receptor, metabotropic 2 | Rn.9681 |   -1.715 | PM | GPCR | Neuro, Psych |
| <i>CTGF</i> | Connective tissue growth factor | Rn.17145 |   -1.702 | Extracellular | Growth factor | GI, CVD, Neuro, Psych, Renal, Metab |
| <i>S1PR1</i> | Sphingosine-1-phosphate receptor 1 | Rn.109455 |   -1.696 | PM | GPCR | GI, Inflam, Neuro, Immun |
| <i>LPAR1</i> | Lysophosphatidic acid receptor 1 | Rn.11200 |   -1.680 | PM | GPCR | GI, Neuro |
| <i>ICAM1</i> | Intercellular adhesion molecule 1 | Rn.12 |   -1.631 | PM | TM receptor | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>OPRK1</i> | Opioid receptor, kappa 1 | Rn.89571 |   -1.623 | PM | GPCR | GI, Inflam, CVD, Neuro, Psych, Renal, Immun |
| <i>PTGS2</i> | Prostaglandin-endoperoxide synthase 2 (prostaglandin G/H synthase and cyclooxygenase) | Rn.44369 |   -1.585 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>ELK4</i> | ELK4, ETS-domain protein (SRF accessory protein 1) | Rn.204345 |   -1.575 | Nucleus | Transcription regulator | GI |
| <i>AGT</i> | Angiotensinogen (serpin peptidase inhibitor, clade A, member 8) | Rn.6319 |   -1.527 | Extracellular | Growth factor | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|----------------------|---|-----------|-------------|---------------|---------------|---|
| <i>DRD2</i> | Dopamine receptor D2 | Rn.87299 |   -1.500 | PM | GPCR | N/A* |
| Upregulated | | | | | | |
| <i>PTGDR</i> | Prostaglandin D2 receptor (DP) | Rn.220703 |   2.707 | PM | GPCR | GI, Inflam, CVD, Neuro |
| <i>IL1B</i> | Interleukin 1, beta | Rn.9869 |   1.932 | Extracellular | Cytokine | GI, Inflam, CVD, Nutri, Neuro, Psych, Immun, Endo, Metab |
| Long Latency | | | | | | |
| Downregulated | | | | | | |
| <i>NOS2</i> | Nitric oxide synthase 2, inducible | Rn.10400 |   -6.868 | Cytoplasm | Enzyme | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>DRD2</i> | Dopamine receptor D2 | Rn.87299 |   -2.914 | PM | GPCR | N/A* |
| <i>AGT</i> | Angiotensinogen (serpin peptidase inhibitor, clade A, member 8) | Rn.6319 |   -2.826 | Extracellular | Growth factor | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| <i>AGTR2</i> | Angiotensin II receptor, type 2 | Rn.162367 |   -2.490 | PM | GPCR | GI, CVD, Nutri, Neuro, Renal |
| <i>IL1B</i> | Interleukin 1, beta | Rn.9869 |   -2.475 | Extracellular | Cytokine | GI, Inflam, CVD, Nutri, Neuro, Psych, Immun, Endo, Metab |
| <i>GRM7</i> | Glutamate receptor, metabotropic 7 | Rn.10409 |   -2.392 | PM | GPCR | GI, Neuro, Psych |
| <i>OPRD1</i> | Opioid receptor, delta 1 | Rn.10310 |   -1.952 | PM | GPCR | GI, Inflam, CVD, Nutri, Neuro, Psych, Immun |
| <i>S1PR1</i> | Sphingosine-1-phosphate receptor 1 | Rn.109455 |   -1.662 | PM | GPCR | GI, Inflam, Neuro, Immun |
| <i>LHCGR</i> | Luteinizing hormone/choriogonadotropin receptor | Rn.11216 |   -1.524 | PM | GPCR | CVD, Nutri, Endo |

| Symbol | Entrez Gene Name | UniGene | Fold Change | Location | Type(s) | Disease Involvement |
|---------------------------|---------------------------------|-----------|-------------|----------|-------------|---|
| <i>Upregulated</i> | | | | | | |
| PTGDR | Prostaglandin D2 receptor (DP) | Rn.220703 | é4.392 | PM | GPCR | GI, Inflam, CVD, Neuro |
| IL1R2 | Interleukin 1 receptor, type II | Rn.10758 | é2.767 | PM | TM receptor | GI, Inflam, Immun, Endo, Metab |
| ADRB2 | Adrenoceptor beta 2, surface | Rn.10206 | é1.987 | PM | GPCR | GI, Inflam, CVD, Nutri, Neuro, Psych, Renal, Immun, Endo, Metab |
| CASR | Calcium-sensing receptor | Rn.10019 | é1.793 | PM | GPCR | GI, Inflam, CVD, Neuro, Renal, Endo |

Genes >1.5 fold differentially expressed vs. controls.

CVD, cardiovascular disease; Endo, endocrine system disorders; GI, gastrointestinal disease; GPCR, G-protein coupled receptor signaling; Immun, immunological disease; Inflam, inflammatory disease; Metab, metabolic disease; Neuro, neurological disease; Nutri, nutritional disease; PM, plasma membrane; Psych, psychological disorders; Renal, renal and urological disease; TM, transmembrane; *N/A, no disease association was provided by IPA.