

Table S1. Targets of RPE components.

| Gene name | Protein name | Compounds |
|-----------------|--|--|
| <i>ACTA2</i> | Actin, aortic smooth muscle | Emodin |
| <i>ALR</i> | Aldose reductase | Aloe-emodin, Rhein |
| <i>BAX</i> | Apoptosis regulator BAX | Aloe-emodin |
| <i>BTX</i> | Tyrosine-protein kinase BTK | Emodin |
| <i>CALM</i> | Calmodulin | Chrysophanol, Emodin, Physcion |
| <i>CASP3</i> | Caspase-3 | Aloe-emodin, Emodin |
| <i>CCNB1</i> | G2/mitotic-specific cyclin-B1 | Aloe-emodin |
| <i>CDC2A</i> | Cell division control protein 2 homolog | Aloe-emodin |
| <i>CDKN1A</i> | Cyclin-dependent kinase inhibitor 1A | Aloe-emodin, Emodin |
| <i>CYP1A1</i> | Cytochrome P450 1A1 | Emodin |
| <i>EGF</i> | Pro-epidermal growth factor | Emodin |
| <i>EIF6</i> | Eukaryotic translation initiation factor 6 | Aloe-emodin |
| <i>F10</i> | Coagulation factor Xa | Emodin, Physcion |
| <i>F7</i> | Coagulation factor VII | Emodin, Physcion |
| <i>FASN</i> | Fatty acid synthase | Aloe-emodin |
| <i>GABRA1</i> | Gamma-aminobutyric acid receptor subunit alpha-1 | Chrysophanol |
| <i>GM-CSF</i> | Granulocyte-macrophage colony-stimulating factor | Emodin |
| <i>HSP90AA1</i> | Heat shock protein HSP 90 | Aloe-emodin, Chrysophanol, Emodin, Physcion, Rhein |
| <i>IGHG1</i> | Ig gamma-1 chain C region | Aloe-emodin, Chrysophanol, Emodin, Physcion |
| <i>IL1B</i> | Interleukin-1 beta | Aloe-emodin, Emodin |
| <i>JUN</i> | Transcription factor AP-1 | Rhein |
| <i>MAOB</i> | Amine oxidase [flavin-containing] B | Emodin |
| <i>MMP1</i> | Interstitial collagenase | Emodin |
| <i>MMP9</i> | Matrix metalloproteinase-9 | Emodin |

| | | |
|---------------|---|--|
| <i>MYC</i> | Myc proto-oncogene protein | Aloe-emodin, Emodin |
| <i>NCOA1</i> | Nuclear receptor coactivator 1 | Emodin, Physcion |
| <i>NCOA2</i> | Nuclear receptor coactivator 2 | Aloe-emodin, Chrysophanol, Emodin, Physcion, Rhein |
| <i>NOS3</i> | Nitric-oxide synthase, endothelial | Physcion |
| <i>PCNA</i> | Proliferating cell nuclear antigen | Aloe-emodin |
| <i>PDE3A</i> | CGMP-inhibited 3',5'-cyclic phosphodiesterase A | Chrysophanol |
| <i>PIK3CG</i> | Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit, gamma isoform | Aloe-emodin, Chrysophanol, Emodin, Physcion, Rhein |
| <i>PKIA</i> | cAMP-dependent protein kinase inhibitor alpha | Aloe-emodin, Chrysophanol, Physcion |
| <i>PPARG</i> | Peroxisome proliferator-activated receptor gamma | Emodin |
| <i>PRKACA</i> | mRNA of PKA Catalytic Subunit C-alpha | Aloe-emodin, Chrysophanol, Emodin, Physcion |
| <i>PRKCA</i> | Protein kinase C alpha type | Aloe-emodin |
| <i>PRKCD</i> | Protein kinase C delta type | Aloe-emodin, Emodin |
| <i>PRKCE</i> | Protein kinase C epsilon type | Aloe-emodin, Emodin |
| <i>PTGS1</i> | Prostaglandin G/H synthase 1 | Aloe-emodin, Chrysophanol, Emodin, Physcion, Rhein |
| <i>PTGS2</i> | Prostaglandin G/H synthase 2 | Aloe-emodin, Chrysophanol, Emodin, Physcion, Rhein |
| <i>RXRΒ</i> | Retinoic acid receptor RXR-alpha | Physcion |
| <i>SCN5A</i> | Sodium channel protein type 5 subunit alpha | Chrysophanol, Physcion |
| <i>SLC2A1</i> | Solute carrier family 2, facilitated glucose transporter member 1 | Emodin |
| <i>SLC2A4</i> | Solute carrier family 2, facilitated glucose transporter member 4 | Emodin |
| <i>TGFB1</i> | Transforming growth factor beta-1 | Emodin |
| <i>TNF</i> | Tumor necrosis factor | Aloe-emodin, Emodin |
| <i>TOP2A</i> | DNA topoisomerase II | Emodin, Physcion |
| <i>TP53</i> | Cellular tumor antigen p53 | Aloe-emodin, Emodin |
| <i>VEGFR1</i> | Vascular endothelial growth factor receptor 1 | Emodin |
| <i>VEGFR2</i> | Vascular endothelial growth factor receptor 2 | Emodin |
| <i>VEGFR3</i> | Vascular endothelial growth factor receptor 3 | Emodin |

Table S2. GO functional enrichment analysis on potential targets of RPE components.

| Category | GO term | Related genes |
|-----------------------|---|---|
| Biological Process | Positive regulation of pri-miRNA transcription by RNA polymerase II | <i>JUN, PPARG, TGFB1, TNF, TP53</i> |
| | Cellular response to cytokine stimulus | <i>CASP3, CDKN1A, HSP90AA1, IL1B, MMP9, PTGS2, TGFB1, TNF, TP53</i> |
| | Positive regulation of cellular metabolic process | <i>CCNB1, CDKN1A, EGF, PPARG, TGFB1, TP53</i> |
| | Regulation of pri-miRNA transcription by RNA polymerase II | <i>JUN, PPARG, TGFB1, TNF, TP53</i> |
| | Regulation of DNA binding | <i>EGF, JUN, MMP9, PPARG, TGFB1</i> |
| | Positive regulation of protein phosphorylation | <i>CDKN1A, EGF, HSP90AA1, IL1B, MMP9, TGFB1, TNF, TP53</i> |
| | Regulation of neuroinflammatory response | <i>IL1B, MMP9, PTGS2, TNF</i> |
| | Cytokine-mediated signaling pathway | <i>CASP3, CDKN1A, HSP90AA1, IL1B, MMP9, PTGS2, TGFB1, TNF, TP53</i> |
| | Regulation of fever generation | <i>IL1B, PTGS2, TNF</i> |
| | Positive regulation of heat generation | <i>IL1B, PTGS2, TNF</i> |
| Cellular Component | Cyclin-dependent protein kinase holoenzyme complex | <i>CCNB1, CDKN1A</i> |
| | Serine/threonine protein kinase complex | <i>CCNB1, CDKN1A</i> |
| | Intracellular organelle lumen | <i>CCNB1, HSP90AA1, MMP9, PTGS2, TGFB1</i> |
| | Platelet alpha granule lumen | <i>EGF, TGFB1</i> |
| | Actin-based cell projection | <i>ACTA2, TGFB1</i> |
| | Platelet alpha granule | <i>EGF, TGFB1</i> |
| | Secretory granule lumen | <i>EGF, HSP90AA1, TGFB1</i> |
| | Phosphatidylinositol 3-kinase complex, class I | <i>PIK3CG</i> |
| | Intracellular membrane-bounded organelle | <i>CASP3, CCNB1, CDKN1A, JUN, HSP90AA1, NOS3, PCNA, PPARG, PTGS1, TGFB1, TP53</i> |
| | Nucleus | <i>CASP3, CCNB1, CDKN1A, JUN, HSP90AA1, NOS3, PCNA, PPARG, TGFB1, TP53</i> |

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|-----------------------|--|---|
| Molecular Function | Ubiquitin-like protein ligase binding | <i>CCNB1, CDKN1A, JUN, HSP90AA1, TP53</i> |
| | Protein tyrosine kinase binding | <i>HSP90AA1, PCNA, TP53</i> |
| | Transcription regulatory region nucleic acid binding | <i>JUN, PPARG, TNF, TP53</i> |
| | Protein kinase binding | <i>ACTA2, CCNB1, CDKN1A, HSP90AA1, TP53</i> |
| | Ubiquitin protein ligase binding | <i>CDKN1A, HSP90AA1, JUN, TP53</i> |
| | DNA polymerase binding | <i>HSP90AA1, PCNA</i> |
| | Histone acetyltransferase binding | <i>PCNA, TP53</i> |
| | Receptor ligand activity | <i>EGF, IL1B, TGFB1, TNF</i> |
| | Disordered domain specific binding | <i>HSP90AA1, TP53</i> |
| | Cytokine activity | <i>IL1B, TGFB1, TNF</i> |

Table S3. KEGG enrichment analysis on potential targets of RPE components.

| KEGG pathway | Related genes |
|--|---|
| IL-17 signaling pathway | <i>CASP3, HSP90AA1, IL1B, JUN, MMP9, PTGS2, TNF</i> |
| TNF signaling pathway | <i>CASP3, IL1B, JUN, MMP9, PTGS2, TNF</i> |
| MAPK signaling pathway | <i>CASP3, EGF, IL1B, JUN, TGFB1, TNF, TP53</i> |
| Cell cycle | <i>CCNB1, CDKN1A, PCNA, TGFB1, TP53</i> |
| Th17 differentiation | <i>HSP90AA1, IL1B, JUN, TGFB1</i> |
| NF-kappa B signaling pathway | <i>IL1B, PTGS2, TNF</i> |
| VEGF signaling | <i>NOS3, PTGS2</i> |
| Cytokine-cytokine receptor interaction | <i>IL1B, TGFB1, TNF</i> |
| TGF-beta signaling pathway | <i>TGFB1, TNF</i> |
| JAK-STAT signaling pathway | <i>CDKN1A, EGF</i> |