*1*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground Truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | Pipeline |
| Environmental stress | PAK/RAC | Activation | Environmental stress | PAK/RAC | Activation |
| PAK/RAC | MEKK/NIK | Activation | PAK/RAC | MEKK/NIK | Activation |
| MEKK/NIK | MKK | Activation | MEKK/NIK | MKK | Activation |
| MEKK/NIK | IKK | Activation | MEKK/NIK | IKK | Activation |
| IKK | IκB/NF-κB | Activation | IKK | IκB/NF-κB | Inhibition |
| IκB/NF-κB | IkB Degradation | Activation | IκB/NF-κB | IkB Degradation |  |
| IκB/NF-κB | NF-κB Translocation | Activation | IκB/NF-κB | NF-κB Translocation | Inhibition |
| NF-κB Translocation | Stress Gene Expression and Regulation | Activation | NF-κB Translocation | Stress Gene Expression and Regulation |  |
| BSO | γ-GCS | Inhibition | BSO | γ-GCS | Inhibition |
| MKK | p38/RK | Activation | MKK | p38/RK | Inhibition |
| p38/RK | MAPKAP-K2 | Activation | p38/RK | MAPKAP-K2 | Inhibition |
| MAPKAP-K2 | ARE | Activation | MAPKAP-K2 | ARE |  |
| ARE | Stress Gene Expression and Regulation | Activation | ARE | Stress Gene Expression and Regulation | Activation |
| MAPKAP-K2 | Hsp27 | Activation | MAPKAP-K2 | Hsp27 |  |
| NAC | Cysteine | Activation | NAC | Cysteine |  |
| GSH | Cysteine | Activation | GSH | Cysteine | Inhibition |
| Cysteine | GSH | Activation | Cysteine | GSH | Inhibition |
| Hsp27 | Stress Gene Expression and Regulation | Activation | Hsp27 | Stress Gene Expression and Regulation |  |
| γ-GT | Cysteine | Activation | γ-GT | Cysteine |  |
| NAC | p38/RK | Inhibition | NAC | p38/RK |  |
| NAC | MKK | Inhibition | NAC | MKK |  |
| SB-203580 | p38/RK | Inhibition | SB-203580 | p38/RK |  |
| SB-203580 | MAPKAP-K2 | Inhibition | SB-203580 | MAPKAP-K2 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 15 | 3 | 5 | 23 | 0.833333 | 0.652174 | 0.731707 |
| Claude-3 | 14 | 4 | 5 | 23 | 0.777778 | 0.608696 | 0.682927 |
| GEMINI | 12 | 5 | 6 | 23 | 0.705882 | 0.521739 | 0.600000 |
| pathway | 13 | 5 | 5 | 23 | 0.722222 | 0.565217 | 0.634146 |

*2*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Ligand | Receptor | Activation | Ligand | Receptor | Activation |
| Ligand | Ligand-induced degradation | Activation | Ligand | Ligand-induced degradation | Activation |
| Receptor | Internalization | Activation | Receptor | Internalization | Activation |
| Receptor | Activity | Activation | Receptor | Activity |  |
| Activity | Transcription | Activation | Activity | Transcription | Inhibition |
| Receptor | Recycling | Activation | Receptor | Recycling | Inhibition |
| Constitutive degradation | Receptor | Inhibition | Constitutive degradation | Receptor | Activation |
| Internalization | Receptor production | Activation | Internalization | Receptor production | Activation |
| Receptor production | Receptor | Activation | Receptor production | Receptor | Inhibition |
| Receptor | Activity | Activation | Receptor | Activity | Activation |
| Activity | Recycling | Inhibition | Activity | Recycling |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 2 | 2 | 10 | 0.750000 | 0.6 | 0.666667 |
| Claude-3 | 5 | 3 | 3 | 10 | 0.625000 | 0.5 | 0.555556 |
| GEMINI | 3 | 4 | 3 | 10 | 0.428571 | 0.3 | 0.352941 |
| pathway | 4 | 4 | 2 | 10 | 0.500000 | 0.4 | 0.444444 |

*3*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | Pipeline |
| TCR | ZAP70 | Activation | TCR | ZAP70 | Activation |
| ZAP70 | GADD45α/β | Activation | ZAP70 | GADD45α/β | Activation |
| GADD45α/β | MEKK4 | Activation | GADD45α/β | MEKK4 |  |
| MEKK4 | MKK3/4/6 | Activation | MEKK4 | MKK3/4/6 | *inhibition* |
| MKK3/4/6 | p38 | Activation | MKK3/4/6 | p38 | *inhibition* |
| p38 | T180/Y182 | Activation | p38 | T180/Y182 | *inhibition* |
| T180/Y182 | Substrates | Activation | T180/Y182 | Substrates | *inhibition* |
| GADD45α | Y323 | Activation | GADD45α | Y323 | *inhibition* |
| Y323 | T180/Y182 | Activation | Y323 | T180/Y182 |  |
| GADD45α | T180/Y182 | *inhibition* | GADD45α | T180/Y182 | Activation |
| GADD45α | Y323 | *inhibition* | GADD45α | Y323 | Activation |
| ZAP70 | Y323 | Activation | ZAP70 | Y323 | Activation |
| CD28 | GADD45α/β | Activation | CD28 | GADD45α/β | *inhibition* |
| IL-12R or IL-18R | GADD45α/β | Activation | IL-12R or IL-18R | GADD45α/β | *inhibition* |
| MKKK | MKK | Activation | MKKK | MKK |  |
| MKKK | MAPK | Activation | MKKK | MAPK |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 5 | 2 | 17 | 0.666667 | 0.588235 | 0.625000 |
| Claude-3 | 9 | 6 | 2 | 17 | 0.600000 | 0.529412 | 0.562500 |
| GEMINI | 6 | 6 | 5 | 17 | 0.500000 | 0.352941 | 0.413793 |
| pathway | 7 | 6 | 4 | 17 | 0.538462 | 0.411765 | 0.466667 |

*4*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Ground truth*** | | |  |  |  |
| ***Starter (gene1)*** | ***Receptor (gene2)*** | ***Relationship*** | ***Starter (gene1)*** | ***Receptor (gene2)*** | pathway |
| *CPB, Sepsis, Injury* | *Anterior pituitary* | *Activation* | *CPB, Sepsis, Injury* | *Anterior pituitary* | *Activation* |
| *Anterior pituitary* | *TH2 Immune cells* | *Activation* | *Anterior pituitary* | *TH2 Immune cells* | *Activation* |
| *Anterior pituitary* | *MIF* | *Activation* | *Anterior pituitary* | *MIF* | *inhibition* |
| *MIF* | *CD74* | *Activation* | *MIF* | *CD74* |  |
| *CD74* | *Proinflammatory Cytokines Chemokines* | *Activation* | *CD74* | *Proinflammatory Cytokines Chemokines* | *inhibition* |
| *Proinflammatory Cytokines* | *SIRS* | *Activation* | *Proinflammatory Cytokines* | *SIRS* | *inhibition* |
| *SIRS* | *MODS* | *Activation* | *SIRS* | *MODS* | *inhibition* |
| *IL-10, IL-4* | *TH2 Immune cells* | *inhibition* | *IL-10, IL-4* | *TH2 Immune cells* |  |
| *Cortisol* | *TH1 Immune cells* | *inhibition* | *Cortisol* | *TH1 Immune cells* | *inhibition* |
| *MIF* | *Cortisol* | *inhibition* | *MIF* | *Cortisol* |  |
| *ACTH* | *Cortisol* | *Activation* | *ACTH* | *Cortisol* |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 3 | 2 | 11 | 0.666667 | 0.545455 | 0.600000 |
| Claude-3 | 5 | 3 | 3 | 11 | 0.625000 | 0.454545 | 0.526316 |
| GEMINI | 4 | 4 | 3 | 11 | 0.500000 | 0.363636 | 0.421053 |
| pathway | 4 | 4 | 3 | 11 | 0.500000 | 0.363636 | 0.421053 |

*5*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Innervation | Acetylcholine, Substance P, etc. | Activation | Innervation | Acetylcholine, Substance P, etc. | Activation |
| Innervation | Inflammatory Cells | Activation | Innervation | Inflammatory Cells | Activation |
| Inflammatory Cells | Epithelium | Activation | Inflammatory Cells | Epithelium | Activation |
| Acetylcholine, Substance P, etc. | Airway Smooth Muscle | Activation | Acetylcholine, Substance P, etc. | Airway Smooth Muscle |  |
| Inflammatory Cells | Leukotrienes, Histamines, Cytokines, etc. | Activation | Inflammatory Cells | Leukotrienes, Histamines, Cytokines, etc. | Activation |
| Epithelium | Endothelin, etc. | Activation | Epithelium | Endothelin, etc. |  |
| Acetylcholine, Substance P, etc. | Rho/ROCK | Activation | Acetylcholine, Substance P, etc. | Rho/ROCK |  |
| Leukotrienes, Histamines, Cytokines, etc | Rho/ROCK | Activation | Leukotrienes, Histamines, Cytokines, etc | Rho/ROCK | *inhibition* |
| Endothelin, etc. | Rho/ROCK | Activation | Endothelin, etc. | Rho/ROCK | *inhibition* |
| Acetylcholine, Substance P, etc. | Ca2+ | Activation | Acetylcholine, Substance P, etc. | Ca2+ |  |
| Leukotrienes, Histamines, Cytokines, etc | Ca2+ | Activation | Leukotrienes, Histamines, Cytokines, etc | Ca2+ |  |
| Endothelin, etc. | Ca2+ | Activation | Endothelin, etc. | Ca2+ |  |
| Endothelin, etc. | Airway Smooth Muscle | Activation | Endothelin, etc. | Airway Smooth Muscle |  |
| Ca2+ | Contraction | Activation | Ca2+ | Contraction | *inhibition* |
| Ca2+ | Airway Smooth Muscle | Activation | Ca2+ | Airway Smooth Muscle |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 3 | 2 | 15 | 0.769231 | 0.666667 | 0.714286 |
| Claude-3 | 9 | 3 | 3 | 15 | 0.750000 | 0.600000 | 0.666667 |
| GEMINI | 6 | 4 | 5 | 15 | 0.600000 | 0.400000 | 0.480000 |
| pathway | 7 | 3 | 5 | 15 | 0.700000 | 0.466667 | 0.560000 |

*6*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| IGF-I | IGF-I-R | Activation | IGF-I | IGF-I-R | Activation |
| IGF-I-R | PI3-kinase | Activation | IGF-I-R | PI3-kinase | Activation |
| PI3-kinase | PKB (Akt) | Activation | PI3-kinase | PKB (Akt) | Activation |
| PKB (Akt) | Transcription or Splicing Factors | Activation | PKB (Akt) | Transcription or Splicing Factors | Activation |
| PDGFs | PDGF-R | Activation | PDGFs | PDGF-R | Activation |
| PDGF-R | MEK1 | Activation | PDGF-R | MEK1 |  |
| PDGF-R | MKK6 | Activation | PDGF-R | MKK6 | Activation |
| MEK1 | ERK | Activation | MEK1 | ERK |  |
| MKK6 | p38MAPK | Activation | MKK6 | p38MAPK | Inhibition |
| ERK | Transcription or Splicing Factors | Activation | ERK | Transcription or Splicing Factors | Inhibition |
| p38MAPK | Transcription or Splicing Factors | Activation | p38MAPK | Transcription or Splicing Factors | Inhibition |
| bFGF or EGF | bFGF-R or EGF-R | Activation | bFGF or EGF | bFGF-R or EGF-R |  |
| bFGF-R or EGF-R | MKK6 | Activation | bFGF-R or EGF-R | MKK6 | Inhibition |
| LY294002 | PI3-kinase | Inhibition | LY294002 | PI3-kinase | Activation |
| Wortmannin | PI3-kinase | Inhibition | Wortmannin | PI3-kinase | Activation |
| PD98059 | MEK1 | Inhibition | PD98059 | MEK1 |  |
| SB203580 | p38MAPK | Inhibition | SB203580 | p38MAPK | Inhibition |
| Transcription or Splicing Factors | Maintaining a differentiated phenotype | Activation | Transcription or Splicing Factors | Maintaining a differentiated phenotype | Activation |
| Transcription or Splicing Factors | Induction of dedifferentiation | Activation | Transcription or Splicing Factors | Induction of dedifferentiation |  |

Results

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| **GPT-4** | **12** | **4** | **4** | **20** | **0.750000** | **0.60** | **0.666667** |
| **Claude-3** | **11** | **5** | **4** | **20** | **0.687500** | **0.55** | **0.611111** |
| **GEMINI** | **8** | **6** | **6** | **20** | **0.571429** | **0.40** | **0.470588** |
| **pathway** | **9** | **6** | **5** | **20** | **0.600000** | **0.45** | **0.514286** |

*8*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| VEGF | Endothelial cell proliferation | Activation | VEGF | Endothelial cell proliferation | Activation |
| VEGF | Endothelial cell migration | Activation | VEGF | Endothelial cell migration | Activation |
| VEGF | Increased vascular permeability | Activation | VEGF | Increased vascular permeability | Activation |
| VEGF | Endothelial cell survival | Activation | VEGF | Endothelial cell survival | Inhibition |
| VEGF-R | Endothelial cell proliferation | Activation | VEGF-R | Endothelial cell proliferation | Inhibition |
| VEGF-R | Endothelial cell migration | Activation | VEGF-R | Endothelial cell migration |  |
| VEGF-R | Increased vascular permeability | Activation | VEGF-R | Increased vascular permeability | Activation |
| VEGF-R | Endothelial cell survival | Activation | VEGF-R | Endothelial cell survival |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 5 | 2 | 1 | 8 | 0.714286 | 0.625 | 0.666667 |
| Claude-3 | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |
| GEMINI | 3 | 3 | 2 | 8 | 0.500000 | 0.375 | 0.428571 |
| pathway | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |

*9*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| EGFR | Ras | Activation | EGFR | Ras | Activation |
| EGFR | PI3K | Activation | EGFR | PI3K | Activation |
| Ras | Raf | Activation | Ras | Raf | Activation |
| Raf | MEK | Activation | Raf | MEK |  |
| MEK | ERK | Activation | MEK | ERK | Activation |
| PI3K | Akt | Activation | PI3K | Akt | Inhibition |
| Akt | mTOR | Activation | Akt | mTOR | Inhibition |
| Cetuximab | EGFR | Inhibition | Cetuximab | EGFR | Inhibition |
| Erlotinib/Gefitinib | EGFR | Inhibition | Erlotinib/Gefitinib | EGFR | Activation |
| PF-00299804/BIBW2992 | EGFR | Inhibition | PF-00299804/BIBW2992 | EGFR | Activation |
| PF-00299804/BIBW2992 | HER | Inhibition | PF-00299804/BIBW2992 | HER | Inhibition |
| Salirasib | Ras | Inhibition | Salirasib | Ras |  |
| LY294002 | PI3K | Inhibition | LY294002 | PI3K | Activation |
| BEZ235 | PI3K | Inhibition | BEZ235 | PI3K |  |
| BEZ235 | mTOR | Inhibition | BEZ235 | mTOR | Activation |
| Rapamycin/RAD001/CCI-779 | mTOR | Inhibition | Rapamycin/RAD001/CCI-779 | mTOR |  |
| Antiangiogenic agents | VEGFR | Inhibition | Antiangiogenic agents | VEGFR |  |
| Antiangiogenic agents | PDGFR | Inhibition | Antiangiogenic agents | PDGFR | Activation |
| Antiangiogenic agents | FGFR | Inhibition | Antiangiogenic agents | FGFR |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Model | Correct Predictions | False Predictions | Missing Relation | Total Predictions | Precision | Recall | F1 |
| GPT-4 | 12 | 4 | 3 | 19 | 0.750000 | 0.631579 | 0.685714 |
| Claude-3 | 11 | 5 | 5 | 19 | 0.687500 | 0.578947 | 0.628571 |
| GEMINI | 8 | 6 | 5 | 19 | 0.571429 | 0.421053 | 0.484848 |
| pathway | 9 | 6 | 4 | 19 | 0.600000 | 0.473684 | 0.529412 |

*10*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground Truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| EGF, TGF-Î±, or other ligands | EGFR or other family members | Activation | EGF, TGF-Î±, or other ligands | EGFR or other family members | Activation |
| EGFR or other family members | PI3K | Activation | EGFR or other family members | PI3K | Activation |
| PI3K | Akt | Activation | PI3K | Akt | Activation |
| Akt | mTOR | Activation | Akt | mTOR | Activation |
| EGFR or other family members | STAT signaling | Activation | EGFR or other family members | STAT signaling | Activation |
| STAT signaling | Survival | Activation | STAT signaling | Survival | Activation |
| STAT signaling | Transcription | Activation | STAT signaling | Transcription | Inhibition |
| STAT signaling | Proliferation | Activation | STAT signaling | Proliferation | Inhibition |
| EGFR or other family members | Ras | Activation | EGFR or other family members | Ras |  |
| Ras | Raf | Activation | Ras | Raf |  |
| Raf | MAPK | Activation | Raf | MAPK | Inhibition |
| MAPK | Proliferation | Activation | MAPK | Proliferation |  |

:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 8 | 2 | 2 | 12 | 0.800000 | 0.666667 | 0.727273 |
| Claude-3 | 7 | 2 | 3 | 12 | 0.777778 | 0.583333 | 0.666667 |
| GEMINI | 4 | 4 | 4 | 12 | 0.500000 | 0.333333 | 0.400000 |
| pathway | 5 | 4 | 3 | 12 | 0.555556 | 0.416667 | 0.476190 |

*11*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Integrin | p130Cas | Activation | Integrin | p130Cas |  |
| Integrin | Paxillin | Activation | Integrin | Paxillin | Activation |
| p130Cas | Crk | Activation | p130Cas | Crk | Activation |
| Paxillin | Fak | Activation | Paxillin | Fak | Activation |
| Crk | Rac1 | Activation | Crk | Rac1 | Activation |
| Fak | Rac1 | Activation | Fak | Rac1 | Activation |
| Rac1 | Integrin-mediated Cell Motility | Activation | Rac1 | Integrin-mediated Cell Motility | Activation |
| Integrin | N-Cadherin Adhesion | Activation | Integrin | N-Cadherin Adhesion |  |
| N-Cadherin | N-Cadherin Adhesion | Activation | N-Cadherin | N-Cadherin Adhesion | Activation |
| Fak (pY861) | Rac1 | Inhibition | Fak (pY861) | Rac1 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 2 | 2 | 10 | 0.750000 | 0.6 | 0.666667 |
| Claude-3 | 5 | 3 | 2 | 10 | 0.625000 | 0.5 | 0.555556 |
| GEMINI | 3 | 4 | 3 | 10 | 0.428571 | 0.3 | 0.352941 |
| pathway | 4 | 3 | 3 | 10 | 0.571429 | 0.4 | 0.470588 |

*12*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Agonist | β1-AR | Activation | Agonist | β1-AR | Activation |
| Agonist | β2-AR | Activation | Agonist | β2-AR | Activation |
| β1-AR | Gsα | Activation | β1-AR | Gsα | Activation |
| β2-AR | Gsα | Activation | β2-AR | Gsα | Activation |
| Gsα | Adenylyl cyclase | Activation | Gsα | Adenylyl cyclase | Activation |
| Adenylyl cyclase | cAMP | Activation | Adenylyl cyclase | cAMP | Inhibition |
| cAMP | PKA | Activation | cAMP | PKA | Inhibition |
| PKA | Troponin I-P | Activation | PKA | Troponin I-P | Inhibition |
| PKA | RyR-P | Activation | PKA | RyR-P |  |
| PKA | PLB-P | Activation | PKA | PLB-P |  |
| PKA | cPLA2 | Activation | PKA | cPLA2 |  |
| Troponin I-P | Increased cardiac contractility and relaxation | Activation | Troponin I-P | Increased cardiac contractility and relaxation |  |
| RyR-P | Increased cardiac contractility and relaxation | Activation | RyR-P | Increased cardiac contractility and relaxation | Activation |
| PLB-P | Increased cardiac contractility and relaxation | Activation | PLB-P | Increased cardiac contractility and relaxation | Activation |
| cPLA2 | Reduced cardiac contractility | Activation | cPLA2 | Reduced cardiac contractility | Activation |
| Ca2+ | L-type Ca2+ channel | Activation | Ca2+ | L-type Ca2+ channel |  |
| Giβ | cAMP | Inhibition | Giβ | cAMP |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 11 | 4 | 3 | 18 | 0.733333 | 0.611111 | 0.666667 |
| Claude-3 | 10 | 4 | 4 | 18 | 0.714286 | 0.555556 | 0.625000 |
| GEMINI | 6 | 5 | 7 | 18 | 0.545455 | 0.333333 | 0.413793 |
| pathway | 7 | 6 | 5 | 18 | 0.538462 | 0.388889 | 0.451613 |

*13*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Ground truth*** | | |  |  |  |
| ***Starter (gene1)*** | ***Receptor (gene2)*** | ***Relationship*** | ***Starter (gene1)*** | ***Receptor (gene2)*** | pathway |
| *EGF* | *MEK1/2* | *Activation* | *EGF* | *MEK1/2* |  |
| *MEK1/2* | *Erk1/2* | *Activation* | *MEK1/2* | *Erk1/2* |  |
| *Erk1/2* | *RSK1* | *Activation* | *Erk1/2* | *RSK1* | *Activation* |
| *IGF-I* | *PI3K* | *Activation* | *IGF-I* | *PI3K* | *Activation* |
| *Insulin* | *PI3K* | *Activation* | *Insulin* | *PI3K* | *Activation* |
| *PI3K* | *Akt* | *Activation* | *PI3K* | *Akt* | *Activation* |
| *Akt* | *TSC2* | *Activation* | *Akt* | *TSC2* | *Activation* |
| *Akt* | *mTOR-RICTOR* | *Activation* | *Akt* | *mTOR-RICTOR* | *Activation* |
| *TSC1* | *Rheb* | *Activation* | *TSC1* | *Rheb* | *Activation* |
| *Rheb* | *mTOR-RAPTOR* | *Activation* | *Rheb* | *mTOR-RAPTOR* | *Activation* |
| *mTOR-RAPTOR* | *p70S6K* | *Activation* | *mTOR-RAPTOR* | *p70S6K* | *Activation* |
| *mTOR-RAPTOR* | *4EBP1* | *Inhibition* | *mTOR-RAPTOR* | *4EBP1* |  |
| *Erk1/2* | *TSC2* | *Inhibition* | *Erk1/2* | *TSC2* | *Inhibition* |
| *TSC2* | *Rheb* | *Inhibition* | *TSC2* | *Rheb* |  |
| *RSK1* | *TSC2* | *Inhibition* | *RSK1* | *TSC2* |  |
| *Rapamycin* | *mTOR-RAPTOR* | *Inhibition* | *Rapamycin* | *mTOR-RAPTOR* | *Inhibition* |
| *Ras* | *MEK1/2* | *Activation* | *Ras* | *MEK1/2* |  |
| *Ras* | *PI3K* | *Activation* | *Ras* | *PI3K* |  |
| *EGF* | *TSC2 (via MEK1/2)* | *Inhibition* | *EGF* | *TSC2 (via MEK1/2)* |  |
| *EGF* | *TSC2 (via Erk1/2)* | *Inhibition* | *EGF* | *TSC2 (via Erk1/2)* | *Inhibition* |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 12 | 4 | 4 | 20 | 0.750000 | 0.60 | 0.666667 |
| Claude-3 | 11 | 5 | 4 | 20 | 0.687500 | 0.55 | 0.611111 |
| GEMINI | 7 | 7 | 6 | 20 | 0.500000 | 0.35 | 0.411765 |
| pathway | 8 | 6 | 6 | 20 | 0.571429 | 0.40 | 0.470588 |

*14*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| MTX | MTX polyglutamates | Activation | MTX | MTX polyglutamates | Activation |
| MTX polyglutamates | DHFR | Activation | MTX polyglutamates | DHFR | Activation |
| DHFR | FH2 | Activation | DHFR | FH2 | Activation |
| FH2 | 5,10-CH2-THF | Activation | FH2 | 5,10-CH2-THF | Activation |
| 5,10-CH2-THF | 5-CH3-THF | Activation | 5,10-CH2-THF | 5-CH3-THF | Activation |
| 5-CH3-THF | DNA ← dTMP | Activation | 5-CH3-THF | DNA ← dTMP | Activation |
| DNA ← dTMP | dUMP | Activation | DNA ← dTMP | dUMP | Activation |
| dUMP | TYMS | Activation | dUMP | TYMS | Activation |
| TYMS | MTX polyglutamates | Activation | TYMS | MTX polyglutamates | Inhibition |
| MTX | Influx SLC19A1 | Activation | MTX | Influx SLC19A1 | Inhibition |
| Influx SLC19A1 | MTX | Activation | Influx SLC19A1 | MTX | Activation |
| MTX | Efflux ABCC1-C4/ABCG2 | Activation | MTX | Efflux ABCC1-C4/ABCG2 | Activation |
| Efflux ABCC1-C4/ABCG2 | MTX | Activation | Efflux ABCC1-C4/ABCG2 | MTX |  |
| MTX polyglutamates | FPGS | Activation | MTX polyglutamates | FPGS |  |
| FPGS | MTX polyglutamates | Activation | FPGS | MTX polyglutamates |  |
| MTX polyglutamates | GGH | Activation | MTX polyglutamates | GGH | Activation |
| GGH | MTX polyglutamates | Activation | GGH | MTX polyglutamates | Activation |
| 5-CH3-THF | FH4 | Activation | 5-CH3-THF | FH4 | Activation |
| FH4 | ATIC | Activation | FH4 | ATIC |  |
| ATIC | Adenosine accumulation | Activation | ATIC | Adenosine accumulation |  |
| Adenosine accumulation | Target cell | Activation | Adenosine accumulation | Target cell | Activation |
| Target cell | ADORA 1/2A | Activation | Target cell | ADORA 1/2A | Activation |
| MTX polyglutamates | TYMS | Inhibition | MTX polyglutamates | TYMS |  |
| MTX polyglutamates | ATIC | Inhibition | MTX polyglutamates | ATIC |  |
| MTHFR | 5,10-CH2-THF | Inhibition | MTHFR | 5,10-CH2-THF |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 15 | 5 | 5 | 25 | 0.750000 | 0.60 | 0.666667 |
| Claude-3 | 14 | 5 | 6 | 25 | 0.736842 | 0.56 | 0.636364 |
| GEMINI | 10 | 8 | 7 | 25 | 0.555556 | 0.40 | 0.465116 |
| pathway | 12 | 7 | 6 | 25 | 0.631579 | 0.48 | 0.545455 |

*15*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| LPS | TLR4 | Activation | LPS | TLR4 |  |
| LBP | TLR4 | Activation | LBP | TLR4 | Activation |
| CD14 | TLR4 | Activation | CD14 | TLR4 | Activation |
| TLR4 | p38 | Activation | TLR4 | p38 | Activation |
| TLR4 | Tec Kinases | Activation | TLR4 | Tec Kinases | Inhibition |
| TLR4 | PI3K | Activation | TLR4 | PI3K | Inhibition |
| TLR4 | Syk | Activation | TLR4 | Syk |  |
| p38 | IL-8 | Activation | p38 | IL-8 | Inhibition |
| p38 | Cell Adhesion | Activation | p38 | Cell Adhesion |  |
| p38 | NF-κB | Activation | p38 | NF-κB | Inhibition |
| Tec Kinases | JNK | Activation | Tec Kinases | JNK | Activation |
| PI3K | JNK | Activation | PI3K | JNK | Inhibition |
| Syk | JNK | Activation | Syk | JNK |  |
| JNK | Cdc42 | Activation | JNK | Cdc42 | Activation |
| Cdc42 | Actin Assembly | Activation | Cdc42 | Actin Assembly | Inhibition |
| Actin Assembly | Neutrophil Migration | Activation | Actin Assembly | Neutrophil Migration | Inhibition |
| p38 | TNF-α | Activation | p38 | TNF-α |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 11 | 4 | 2 | 17 | 0.733333 | 0.647059 | 0.687500 |
| Claude-3 | 10 | 3 | 4 | 17 | 0.769231 | 0.588235 | 0.666667 |
| GEMINI | 7 | 5 | 5 | 17 | 0.583333 | 0.411765 | 0.482759 |
| pathway | 8 | 5 | 4 | 17 | 0.615385 | 0.470588 | 0.533333 |

*16*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground Truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| Bcr | Abl | Activation | Bcr | Abl |  |
| Abl | STAT | Activation | Abl | STAT | Activation |
| Abl | Raf | Activation | Abl | Raf | Activation |
| Abl | PI3k | Activation | Abl | PI3k | *inhibition* |
| STAT | Bcl-xL | Activation | STAT | Bcl-xL | *inhibition* |
| Bcl-xL | ↓ Apoptosis | Activation | Bcl-xL | ↓ Apoptosis | *inhibition* |
| Raf | ERK | Activation | Raf | ERK | *inhibition* |
| ERK | Bcl2 | Activation | ERK | Bcl2 | *inhibition* |
| Bcl2 | ↓ Apoptosis | Activation | Bcl2 | ↓ Apoptosis | Activation |
| PI3k | Akt1 | Activation | PI3k | Akt1 | Activation |
| Akt1 | Bad | Activation | Akt1 | Bad | Activation |
| Bad | ↓ Apoptosis | Activation | Bad | ↓ Apoptosis | Activation |
| Akt1 | FOXO3a | Activation | Akt1 | FOXO3a |  |
| FOXO3a | ↓ Apoptosis | Activation | FOXO3a | ↓ Apoptosis | *inhibition* |
| Akt1 | FOXO3a | *inhibition* | Akt1 | FOXO3a |  |
| Akt1 | Bad | *inhibition* | Akt1 | Bad |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 3 | 3 | 16 | 0.769231 | 0.6250 | 0.689655 |
| Claude-3 | 9 | 3 | 4 | 16 | 0.750000 | 0.5625 | 0.642857 |
| GEMINI | 6 | 5 | 5 | 16 | 0.545455 | 0.3750 | 0.444444 |
| pathway | 7 | 5 | 4 | 16 | 0.583333 | 0.4375 | 0.500000 |

*17*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Pathogen | FLS2 | Activation | Pathogen | FLS2 |  |
| flg22 | FLS2 | Activation | flg22 | FLS2 | Inhibition |
| FLS2 | GPA1 | Activation | FLS2 | GPA1 | Inhibition |
| FLS2 | ABA | Activation | FLS2 | ABA |  |
| ABA | S1P | Activation | ABA | S1P | Activation |
| S1P | GPA1 | Activation | S1P | GPA1 | Activation |
| GPA1 | OST1 | Activation | GPA1 | OST1 |  |
| GPA1 | ROS | Activation | GPA1 | ROS | Activation |
| OST1 | ROS | Activation | OST1 | ROS | Activation |
| ROS | NO | Activation | ROS | NO | Activation |
| NO | Intracellular Ca2+ stores | Activation | NO | Intracellular Ca2+ stores | Activation |
| Intracellular Ca2+ stores | CNG2/DND1 channels | Activation | Intracellular Ca2+ stores | CNG2/DND1 channels | Activation |
| Intracellular Ca2+ stores | K+in channels | Activation | Intracellular Ca2+ stores | K+in channels | Activation |
| Intracellular Ca2+ stores | K+out channels | Activation | Intracellular Ca2+ stores | K+out channels | Activation |
| MPK3 | ROS | Activation | MPK3 | ROS | Activation |
| COR | [pH]cyt | Activation | COR | [pH]cyt |  |
| ROS | K+in channels | Inhibition | ROS | K+in channels | Activation |
| ROS | K+out channels | Inhibition | ROS | K+out channels | Activation |
| NO | K+in channels | Inhibition | NO | K+in channels | Activation |
| NO | K+out channels | Inhibition | NO | K+out channels |  |
| COR | K+in channels | Activation | COR | K+in channels |  |
| COR | K+out channels | Inhibition | COR | K+out channels |  |
| ROS | CNG2/DND1 channels | Activation | ROS | CNG2/DND1 channels |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 14 | 5 | 5 | 24 | 0.736842 | 0.583333 | 0.651163 |
| Claude-3 | 13 | 6 | 6 | 24 | 0.684211 | 0.541667 | 0.604651 |
| GEMINI | 10 | 9 | 5 | 24 | 0.526316 | 0.416667 | 0.465116 |
| pathway | 11 | 7 | 6 | 24 | 0.611111 | 0.458333 | 0.523810 |

*18*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| PTEN | PI3K | Activation | PTEN | PI3K |  |
| PI3K | PDK1 | Activation | PI3K | PDK1 |  |
| PDK1 | AKT/PKB (T308) | Activation | PDK1 | AKT/PKB (T308) |  |
| AKT/PKB | TSC1/2 (S478) | Activation | AKT/PKB | TSC1/2 (S478) | Inhibition |
| TSC1/2 | Rheb | Activation | TSC1/2 | Rheb | Inhibition |
| Rheb | mTOR | Activation | Rheb | mTOR |  |
| mTOR | 4E-BP1 | Activation | mTOR | 4E-BP1 | Inhibition |
| mTOR | S6K | Activation | mTOR | S6K | Inhibition |
| 4E-BP1 | ribosome biogenesis | Activation | 4E-BP1 | ribosome biogenesis |  |
| S6K | Translation | Activation | S6K | Translation | Inhibition |
| mTOR | DEPTOR | Activation | mTOR | DEPTOR | Inhibition |
| mTOR | Raptor | Activation | mTOR | Raptor | Inhibition |
| mTOR | PRAS40 | Activation | mTOR | PRAS40 | Activation |
| mTOR | mLST8 | Activation | mTOR | mLST8 | Activation |
| mTOR | DEPTOR | Activation | mTOR | DEPTOR | Activation |
| mTOR | PRR5/5L | Activation | mTOR | PRR5/5L |  |
| mTOR | RicTOR | Activation | mTOR | RicTOR |  |
| RTKs | PI3K | Activation | RTKs | PI3K | Activation |
| IRS-1 | PI3K | Activation | IRS-1 | PI3K | Activation |
| LKB1 | AMPK | Activation | LKB1 | AMPK | Activation |
| AMPK | TSC1/2 | Activation | AMPK | TSC1/2 |  |
| Hypoxia | HIF1α | Activation | Hypoxia | HIF1α | Activation |
| RAG | mTOR | Activation | RAG | mTOR | Activation |
| Amino acids | mTOR | Activation | Amino acids | mTOR | Activation |
| Stress | mTOR | Inhibition | Stress | mTOR | Activation |
| P53 | TSC1/2 | Inhibition | P53 | TSC1/2 | Activation |
| TSC1/2 | Rheb | Inhibition | TSC1/2 | Rheb | Activation |
| PRAS40 | mTOR | Inhibition | PRAS40 | mTOR | Activation |
| DEPTOR | mTOR | Inhibition | DEPTOR | mTOR | Activation |
| S6K | IRS-1 | Inhibition | S6K | IRS-1 |  |
| Insulin, growth factors, hormones | IRS-1 | Activation | Insulin, growth factors, hormones | IRS-1 |  |
| P53 | Energy | Activation | P53 | Energy |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 22 | 6 | 6 | 34 | 0.785714 | 0.647059 | 0.709677 |
| Claude-3 | 20 | 8 | 6 | 34 | 0.714286 | 0.588235 | 0.645161 |
| GEMINI | 15 | 10 | 9 | 34 | 0.600000 | 0.441176 | 0.508475 |
| pathway | 16 | 9 | 10 | 34 | 0.640000 | 0.470588 | 0.542373 |

*19*

*Function as the greatest route gene extractor, accurately extracting each gene link based on the relation provided in the picture. In the gene pathway diagram shown above, the terms "inhibition" is represented by T-bar symbols (----|) like this one and dashed T-bar represents " Indirect Inhibition" and "activation" is by arrow symbols and dashed arrow symbols by "indirect activation". The arrow line (--) to arrowhead (→) represents the direction of the relation, and arrow one is like T-bar. Please remove every gene relationship from the image, avoid confusing them with one another, and refer to the relationships as gene1 (starter) and relationship as gene2 (receptor). Give every relation accurately without missing any relation.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Receptor tyrosine kinase (ALK, Trk, IGF1R) | PI3K | Activation | Receptor tyrosine kinase (ALK, Trk, IGF1R) | PI3K | Inhibition |
| PI3K | PDK1 (S473) | Activation | PI3K | PDK1 (S473) | Inhibition |
| PDK1 | AKT (T308) | Activation | PDK1 | AKT (T308) | Inhibition |
| AKT | mTORC1 | Activation | AKT | mTORC1 | Inhibition |
| AKT | GSK3β | Activation | AKT | GSK3β | Inhibition |
| AKT | Mycn (S62) | Activation | AKT | Mycn (S62) | Activation |
| GSK3β | CDK1 | Activation | GSK3β | CDK1 | Activation |
| mTORC1 | S6K | Activation | mTORC1 | S6K |  |
| mTORC1 | 4EBP | Activation | mTORC1 | 4EBP |  |
| S6K | Translational Control | Activation | S6K | Translational Control | Activation |
| 4EBP | Translational Control | Activation | 4EBP | Translational Control | Activation |
| mTORC1 | mTORC2 (PDK2) | Activation | mTORC1 | mTORC2 (PDK2) | Activation |
| mTORC2 | AKT | Activation | mTORC2 | AKT | Activation |
| mTORC1 | Raptor | Activation | mTORC1 | Raptor | Activation |
| Raptor | mTORC1 | Activation | Raptor | mTORC1 | Activation |
| Mycn (S62) | Induction of Mycn downstream target genes | Activation | Mycn (S62) | Induction of Mycn downstream target genes | Activation |
| CDK1 | Cyclin B | Activation | CDK1 | Cyclin B | Activation |
| CDK1/Cyclin B | Mycn (T58) | Activation | CDK1/Cyclin B | Mycn (T58) | Activation |
| PP2A | Mycn (T58) | Inhibition | PP2A | Mycn (T58) | Inhibition |
| Fbw7 | Mycn (T58) | Inhibition | Fbw7 | Mycn (T58) | Inhibition |
| Mycn (unstable) | Mycn (T58) | Inhibition | Mycn (unstable) | Mycn (T58) | Inhibition |
| AKT inhibitors | AKT | Inhibition | AKT inhibitors | AKT | Activation |
| CDK inhibitors | CDK1 | Inhibition | CDK inhibitors | CDK1 | Activation |
| mTOR inhibitors | mTOR | Inhibition | mTOR inhibitors | mTOR |  |
| mTORC1 allosteric inhibitors | mTORC1 | Inhibition | mTORC1 allosteric inhibitors | mTORC1 |  |
| PI3K inhibitors | PI3K | Activation | PI3K inhibitors | PI3K |  |
| PDK inhibitors | PDK1 | Activation | PDK inhibitors | PDK1 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 19 | 6 | 5 | 30 | 0.760000 | 0.633333 | 0.690909 |
| Claude-3 | 20 | 5 | 5 | 30 | 0.800000 | 0.666667 | 0.727273 |
| GEMINI | 15 | 8 | 7 | 30 | 0.652174 | 0.500000 | 0.566038 |
| pathway | 16 | 8 | 6 | 30 | 0.666667 | 0.533333 | 0.592593 |

*20*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| IGF1 | IGF1R | Activation | IGF1 | IGF1R |  |
| IGF2 | IGF1R | Activation | IGF2 | IGF1R | Activation |
| IGFBP5 | IGF1R | Activation | IGFBP5 | IGF1R | Activation |
| IGF1R | IRS1/2/4 | Activation | IGF1R | IRS1/2/4 | Activation |
| IRS1/2/4 | PI3K/AKT/mTOR pathway | Activation | IRS1/2/4 | PI3K/AKT/mTOR pathway | Inhibition |
| IRS1/2/4 | RAS/MAPK/ERK pathway | Activation | IRS1/2/4 | RAS/MAPK/ERK pathway | Inhibition |
| PI3K/AKT/mTOR pathway | Protein translation/Proliferation/Cell Survival | Activation | PI3K/AKT/mTOR pathway | Protein translation/Proliferation/Cell Survival | Inhibition |
| RAS/MAPK/ERK pathway | Protein translation/Proliferation/Cell Survival | Activation | RAS/MAPK/ERK pathway | Protein translation/Proliferation/Cell Survival | Inhibition |
| IGF2R | IGF2 | Inhibition | IGF2R | IGF2 | Activation |
| IGFBP1/3 | IGF1 | Inhibition | IGFBP1/3 | IGF1 |  |
| IGFBP1/3 | IGF2 | Inhibition | IGFBP1/3 | IGF2 |  |
| IGFBP5 | IGF2 | Activation | IGFBP5 | IGF2 |  |
| IGFBP5 | IGF1 | Activation | IGFBP5 | IGF1 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 8 | 3 | 2 | 13 | 0.727273 | 0.615385 | 0.666667 |
| Claude-3 | 7 | 3 | 3 | 13 | 0.700000 | 0.538462 | 0.608696 |
| GEMINI | 5 | 5 | 3 | 13 | 0.500000 | 0.384615 | 0.434783 |
| pathway | 6 | 4 | 3 | 13 | 0.600000 | 0.461538 | 0.521739 |

*21*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Ground Truth | | |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| Growth factors | PI3K | Activation | Growth factors | PI3K |  |
| PI3K | AKT | Activation | PI3K | AKT | Activation |
| AKT | mTORC1 | Activation | AKT | mTORC1 | Activation |
| Hypoxia | REDD1 | Activation | Hypoxia | REDD1 |  |
| REDD1 | TSC1/2 | Activation | REDD1 | TSC1/2 | Activation |
| Bioenergy (↑AMP/ATP) | AMPK | Activation | Bioenergy (↑AMP/ATP) | AMPK | *Inhibition* |
| AMPK | TSC1/2 | Activation | AMPK | TSC1/2 | *Inhibition* |
| Genotoxic stress | p53 | Activation | Genotoxic stress | p53 |  |
| p53 | AMPK | Activation | p53 | AMPK | *Inhibition* |
| Sestrins1,2 | AMPK | Activation | Sestrins1,2 | AMPK |  |
| Amino acids | RagA/RagC | Activation | Amino acids | RagA/RagC | *Inhibition* |
| RagA/RagC | mTORC1 | Activation | RagA/RagC | mTORC1 |  |
| TSC1/2 | Rheb | Activation | TSC1/2 | Rheb | *Inhibition* |
| Rheb | mTORC1 | Activation | Rheb | mTORC1 | Activation |
| mTORC1 | Cell growth, survival & proliferation | Activation | mTORC1 | Cell growth, survival & proliferation |  |
| AKT | TSC1/2 | *Inhibition* | AKT | TSC1/2 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 3 | 3 | 16 | 0.769231 | 0.6250 | 0.689655 |
| Claude-3 | 9 | 4 | 3 | 16 | 0.692308 | 0.5625 | 0.620690 |
| GEMINI | 6 | 5 | 5 | 16 | 0.545455 | 0.3750 | 0.444444 |
| pathway | 7 | 5 | 4 | 16 | 0.583333 | 0.4375 | 0.500000 |

*22*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| ***Starter (gene1)*** | ***Receptor (gene2)*** | ***Relationship*** | ***Starter (gene1)*** | ***Receptor (gene2)*** | pathway |
| *UVB* | *PI3-K* | *Activation* | *UVB* | *PI3-K* |  |
| *UVB* | *p38* | *Activation* | *UVB* | *p38* |  |
| *p38* | *CREB* | *Activation* | *p38* | *CREB* | *Inhibition* |
| *PI3-K* | *Akt* | *Activation* | *PI3-K* | *Akt* | *Inhibition* |
| *Akt* | *mTOR* | *Activation* | *Akt* | *mTOR* |  |
| *mTOR* | *4E-BP1* | *Activation* | *mTOR* | *4E-BP1* | *Activation* |
| *mTOR* | *p70S6K* | *Activation* | *mTOR* | *p70S6K* | *Activation* |
| *mTOR* | *4E-BP1* | *Inhibition* | *mTOR* | *4E-BP1* | *Activation* |
| *4E-BP1* | *Translation complex* | *Inhibition* | *4E-BP1* | *Translation complex* |  |
| *p70S6K* | *Translation complex* | *Activation* | *p70S6K* | *Translation complex* | *Activation* |
| *Translation complex* | *c-Fos protein* | *Activation* | *Translation complex* | *c-Fos protein* | *Activation* |
| *c-Fos protein* | *c-Fos mRNA* | *Activation* | *c-Fos protein* | *c-Fos mRNA* | *Activation* |
| *c-Fos mRNA* | *CREB* | *Activation* | *c-Fos mRNA* | *CREB* |  |
| *AA* | *mRNA stability* | *Activation* | *AA* | *mRNA stability* | *Inhibition* |
| *Qu* | *PI3-K* | *Inhibition* | *Qu* | *PI3-K* |  |
| *Qu+AA* | *p38* | *Inhibition* | *Qu+AA* | *p38* | *Activation* |
| *Qu+AA* | *PI3-K* | *Inhibition* | *Qu+AA* | *PI3-K* |  |
| *Qu* | *p38* | *Activation* | *Qu* | *p38* |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 12 | 3 | 3 | 18 | 0.800000 | 0.666667 | 0.727273 |
| Claude-3 | 11 | 4 | 3 | 18 | 0.733333 | 0.611111 | 0.666667 |
| GEMINI | 8 | 5 | 5 | 18 | 0.615385 | 0.444444 | 0.516129 |
| pathway | 9 | 4 | 5 | 18 | 0.692308 | 0.500000 | 0.580645 |

*23*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| *Ground Truth* | | |  |  |  |
| *Starter (gene1)* | *Receptor (gene2)* | *Relationship* | *Starter (gene1)* | *Receptor (gene2)* | pathway |
| *17-β estradiol* | *ERα/β* | *Activation* | *17-β estradiol* | *ERα/β* |  |
| *EGFR* | *GRB2* | *Activation* | *EGFR* | *GRB2* | *Activation* |
| *GRB2* | *SOS* | *Activation* | *GRB2* | *SOS* | *Activation* |
| *SOS* | *RAS* | *Activation* | *SOS* | *RAS* | *Activation* |
| *RAS* | *RAF* | *Activation* | *RAS* | *RAF* |  |
| *RAF* | *MEK* | *Activation* | *RAF* | *MEK* | *Activation* |
| *MEK* | *ERK* | *Activation* | *MEK* | *ERK* | *Activation* |
| *ERK* | *Coactivator* | *Activation* | *ERK* | *Coactivator* | *Inhibition* |
| *ERK* | *ERβ-ERβ homodimer* | *Activation* | *ERK* | *ERβ-ERβ homodimer* | *Inhibition* |
| *Coactivator* | *GRIP1* | *Activation* | *Coactivator* | *GRIP1* |  |
| *GRIP1* | *ERE* | *Activation* | *GRIP1* | *ERE* | *Inhibition* |
| *ERβ-ERβ homodimer* | *Cell growth/DNA synthesis* | *Activation* | *ERβ-ERβ homodimer* | *Cell growth/DNA synthesis* | *Inhibition* |
| *Fulvestrant* | *ERα/β* | *Inhibition* | *Fulvestrant* | *ERα/β* | *Inhibition* |
| *HSP90* | *ERα/β (inactive)* | *Inhibition* | *HSP90* | *ERα/β (inactive)* | *Inhibition* |
| *ERK* | *GRIP1* | *Activation* | *ERK* | *GRIP1* |  |
| *ERK* | *ERE* | *Activation* | *ERK* | *ERE* |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 4 | 2 | 16 | 0.714286 | 0.6250 | 0.666667 |
| Claude-3 | 9 | 4 | 3 | 16 | 0.692308 | 0.5625 | 0.620690 |
| GEMINI | 6 | 5 | 5 | 16 | 0.545455 | 0.3750 | 0.444444 |
| pathway | 7 | 5 | 4 | 16 | 0.583333 | 0.4375 | 0.500000 |

*24*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| PBX1, EMX2, CBX2, LHX9 | Genital ridge | Activation | PBX1, EMX2, CBX2, LHX9 | Genital ridge |  |
| WT1, NR5A1 | Genital ridge | Activation | WT1, NR5A1 | Genital ridge |  |
| Genital ridge | WNT4 | Activation | Genital ridge | WNT4 | Activation |
| WNT4/RSPO1 | β-catenin | Activation | WNT4/RSPO1 | β-catenin | Inhibition |
| β-catenin | SOX9 | Activation | β-catenin | SOX9 | Inhibition |
| SOX9 | FOXL2 | Activation | SOX9 | FOXL2 | Inhibition |
| FOXL2 | Steroidogenesis (Ovary) | Activation | FOXL2 | Steroidogenesis (Ovary) | Inhibition |
| Genital ridge | SRY | Activation | Genital ridge | SRY | Inhibition |
| SRY | SOX9 | Activation | SRY | SOX9 | Inhibition |
| SOX9 | AMH | Activation | SOX9 | AMH | Activation |
| SOX9 | FOXL2 | Activation | SOX9 | FOXL2 | Inhibition |
| AMH | DHH | Activation | AMH | DHH | Inhibition |
| DHH | NR5A1 | Activation | DHH | NR5A1 |  |
| NR5A1 | Steroidogenesis (Testis) | Activation | NR5A1 | Steroidogenesis (Testis) |  |
| Genital ridge | FOXL2 | Activation | Genital ridge | FOXL2 |  |
| FOXL2 | SOX9 | Inhibition | FOXL2 | SOX9 |  |
| FOXL2 | SOX9 (Testis) | Inhibition | FOXL2 | SOX9 (Testis) |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 4 | 3 | 17 | 0.714286 | 0.588235 | 0.645161 |
| Claude-3 | 9 | 4 | 4 | 17 | 0.692308 | 0.529412 | 0.600000 |
| GEMINI | 7 | 5 | 5 | 17 | 0.583333 | 0.411765 | 0.482759 |
| pathway | 8 | 4 | 5 | 17 | 0.666667 | 0.470588 | 0.551724 |

*25*

*.*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| HRS cell | ↑ IL-10, TARC, MDC (CCL22), CCL5 | Activation | HRS cell | ↑ IL-10, TARC, MDC (CCL22), CCL5 |  |
| HRS cell | PD1-L | Activation | HRS cell | PD1-L | Activation |
| PD1-L | PD1+ T | Activation | PD1-L | PD1+ T | Activation |
| IL-10, TARC, MDC (CCL22), CCL5 | Th2 | Activation | IL-10, TARC, MDC (CCL22), CCL5 | Th2 | Activation |
| Th2 | Treg | Activation | Th2 | Treg | Activation |
| Galectin 1, IL-10 | STAT1+ TAM | Activation | Galectin 1, IL-10 | STAT1+ TAM | Activation |
| CSF-1 | STAT1+ TAM | Activation | CSF-1 | STAT1+ TAM | Activation |
| Treg | TCL | Inhibition | Treg | TCL |  |
| PD1+ T | TCL | Inhibition | PD1+ T | TCL | Inhibition |
| PD1+ T | Th1 | Inhibition | PD1+ T | Th1 | Activation |
| IFNγ | Treg | Inhibition | IFNγ | Treg | Activation |
| Treg | PD1+ T | Inhibition | Treg | PD1+ T | Activation |
| 1 Galaectin1 IL-10 | TCL | Inhibition | 1 Galaectin1 IL-10 | TCL |  |
| 1 Galaectin1 IL-10 | Th1 | Inhibition | 1 Galaectin1 IL-10 | Th1 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 9 | 3 | 2 | 14 | 0.750000 | 0.642857 | 0.692308 |
| Claude-3 | 8 | 4 | 2 | 14 | 0.666667 | 0.571429 | 0.615385 |
| GEMINI | 6 | 4 | 4 | 14 | 0.600000 | 0.428571 | 0.500000 |
| pathway | 7 | 3 | 4 | 14 | 0.700000 | 0.500000 | 0.583333 |

*26*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Compound | PKCδ | Activation | Compound | PKCδ |  |
| Compound | ATM | Activation | Compound | ATM | Activation |
| PKCδ | p21 | Activation | PKCδ | p21 | Activation |
| PKCδ | NAG-1 | Activation | PKCδ | NAG-1 | Inhibition |
| ATM | p53 (ser15) | Activation | ATM | p53 (ser15) | Inhibition |
| p53 (ser15) | Apoptosis | Activation | p53 (ser15) | Apoptosis | Inhibition |
| NAG-1 | Apoptosis | Activation | NAG-1 | Apoptosis |  |
| p21 | Proliferation | Inhibition | p21 | Proliferation | Activation |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 5 | 2 | 1 | 8 | 0.714286 | 0.625 | 0.666667 |
| Claude-3 | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |
| GEMINI | 3 | 3 | 2 | 8 | 0.500000 | 0.375 | 0.428571 |
| pathway | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |

*27*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Ground truth | | |  |  |  |  |
| Starter (gene1) | Receptor (gene2) | Relationship | GPT-4 | **Claude-3** | GEMINI | pathway |
| Alcama | Ednrb | Activation | Activation | Activation | Activation |  |
| Edn1 | Ednra/b | Activation | Activation | Activation | Activation | Activation |
| Ednra/b | hand2 | Activation | Activation | Activation | Activation | Activation |
| Ednra/b | dlx3b | Activation | Activation |  | Activation | Activation |
| Ednra/b | dlx5a | Activation | Activation | Activation |  | Activation |
| Ednra/b | dlx6a | Activation | Activation | Inhibition | Inhibition | Inhibition |
| Ednra/b | NC differentiation | Activation | Inhibition |  | Activation | *Inhibition* |
| Ednra/b | cartilage ventralization | Activation |  | Activation | Activation |  |
| Ednra/b | jaw joint formation | Activation | Activation | Activation | Inhibition |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 2 | 1 | 9 | 0.750000 | 0.666667 | 0.705882 |
| Claude-3 | 5 | 2 | 2 | 9 | 0.714286 | 0.555556 | 0.625000 |
| GEMINI | 4 | 3 | 2 | 9 | 0.571429 | 0.444444 | 0.500000 |
| pathway | 4 | 2 | 3 | 9 | 0.666667 | 0.444444 | 0.533333 |

*28*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| PPARα/RXR | Fgf21 | Activation | PPARα/RXR | Fgf21 | Activation |
| Fgf21 | FGFR1c? βKlotho? | Activation | Fgf21 | FGFR1c? βKlotho? |  |
| Starvation | Lipolysis | Activation | Starvation | Lipolysis | Activation |
| FGF21 | Torpor | *Inhibition* | FGF21 | Torpor | Activation |
| Ketogenic diet | Torpor | Activation | Ketogenic diet | Torpor |  |
| Lipolysis | NEFA | Inhibition | Lipolysis | NEFA | Activation |
| Fgf21 | NEFA | Activation | Fgf21 | NEFA | Inhibition |
| FGFR1c? βKlotho? | Lipolysis | *Inhibition* | FGFR1c? βKlotho? | Lipolysis | Inhibition |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 1 | 1 | 8 | 0.857143 | 0.750 | 0.800000 |
| Claude-3 | 5 | 2 | 1 | 8 | 0.714286 | 0.625 | 0.666667 |
| GEMINI | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |
| pathway | 3 | 3 | 2 | 8 | 0.500000 | 0.375 | 0.428571 |

*29*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Pyruvate + glyceraldehyde 3-phosphate | MEP | Activation | Pyruvate + glyceraldehyde 3-phosphate | MEP |  |
| MEP | HMB-PP | Activation | MEP | HMB-PP | Activation |
| HMB-PP | DMAPP | Activation | HMB-PP | DMAPP | Activation |
| DMAPP + IPP | FPP | Activation | DMAPP + IPP | FPP | Activation |
| FPP | Isoprenoids | Activation | FPP | Isoprenoids | Inhibition |
| 3-hydroxy-3-methylglutaryl-CoA | Mevalonate | Activation | 3-hydroxy-3-methylglutaryl-CoA | Mevalonate | Inhibition |
| Mevalonate | IPP | Activation | Mevalonate | IPP | Inhibition |
| IPP | DMAPP | Activation | IPP | DMAPP | Inhibition |
| DMAPP + IPP | FPP | Activation | DMAPP + IPP | FPP | Inhibition |
| FPP | Cholesterol | Activation | FPP | Cholesterol | Activation |
| FPP | Isoprenoids | Activation | FPP | Isoprenoids | Activation |
| Amino bisphosphonates | FPP | Inhibition | Amino bisphosphonates | FPP |  |
| Statins | 3-hydroxy-3-methylglutaryl-CoA | Inhibition | Statins | 3-hydroxy-3-methylglutaryl-CoA |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 9 | 2 | 2 | 13 | 0.818182 | 0.692308 | 0.750000 |
| Claude-3 | 8 | 3 | 2 | 13 | 0.727273 | 0.615385 | 0.666667 |
| GEMINI | 6 | 4 | 3 | 13 | 0.600000 | 0.461538 | 0.521739 |
| pathway | 6 | 3 | 4 | 13 | 0.666667 | 0.461538 | 0.545455 |

*30*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Growth factors | dTsc1/Tsc2 | Activation | Growth factors | dTsc1/Tsc2 |  |
| Amino acids | dTsc1/Tsc2 | Activation | Amino acids | dTsc1/Tsc2 |  |
| ATP/AMP | dTsc1/Tsc2 | Activation | ATP/AMP | dTsc1/Tsc2 | Activation |
| Hypoxia | dTsc1/Tsc2 | Activation | Hypoxia | dTsc1/Tsc2 | Activation |
| Stresses | dTsc1/Tsc2 | Activation | Stresses | dTsc1/Tsc2 | Activation |
| dTsc1/Tsc2 | dRheb | Activation | dTsc1/Tsc2 | dRheb | Activation |
| dRheb | dTor | Activation | dRheb | dTor | Activation |
| dTor | dS6K1 | Activation | dTor | dS6K1 | Activation |
| dTor | d4E-BP | Activation | dTor | d4E-BP | Inhibition |
| dS6K1 | Autophagy | Activation | dS6K1 | Autophagy |  |
| dS6K1 | Metabolism | Activation | dS6K1 | Metabolism | Inhibition |
| d4E-BP | Protein synthesis | Activation | d4E-BP | Protein synthesis | Inhibition |
| d4E-BP | ER Stress | Activation | d4E-BP | ER Stress | Inhibition |
| Insulin signaling pathway | dTsc1/Tsc2 | Activation | Insulin signaling pathway | dTsc1/Tsc2 | Inhibition |
| Wnt, TGF β, P53, Sestrins | dTsc1/Tsc2 | Activation | Wnt, TGF β, P53, Sestrins | dTsc1/Tsc2 | Activation |
| Insulin signaling pathway | dRheb | Activation | Insulin signaling pathway | dRheb |  |
| Wnt, TGF β, P53, Sestrins | dRheb | Activation | Wnt, TGF β, P53, Sestrins | dRheb |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 4 | 3 | 17 | 0.714286 | 0.588235 | 0.645161 |
| Claude-3 | 9 | 4 | 4 | 17 | 0.692308 | 0.529412 | 0.600000 |
| GEMINI | 7 | 5 | 4 | 17 | 0.583333 | 0.411765 | 0.482759 |
| pathway | 8 | 4 | 5 | 17 | 0.666667 | 0.470588 | 0.551724 |

*31*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| PI3K | Akt | Activation | PI3K | Akt |  |
| Akt | NFκB | Activation | Akt | NFκB |  |
| Bcl2 | Apoptosome complex | Activation | Bcl2 | Apoptosome complex |  |
| Apoptosome complex | Executioner caspases-3, 6, 7 | Activation | Apoptosome complex | Executioner caspases-3, 6, 7 | Inhibition |
| Executioner caspases-3, 6, 7 | Apoptosis | Activation | Executioner caspases-3, 6, 7 | Apoptosis | Inhibition |
| Bak/Bax | Mitochondrion | Activation | Bak/Bax | Mitochondrion | Inhibition |
| NFκB | Bcl2 | Activation | NFκB | Bcl2 | Activation |
| Bcl2 | Apoptosome complex | Inhibition | Bcl2 | Apoptosome complex | Activation |
| Bcl-X(L) | Apoptosome complex | Inhibition | Bcl-X(L) | Apoptosome complex | Activation |
| IAPs | Executioner caspases-3, 6, 7 | Inhibition | IAPs | Executioner caspases-3, 6, 7 | Activation |
| Akt | Bcl-X(L) | Activation | Akt | Bcl-X(L) |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 8 | 2 | 1 | 11 | 0.800000 | 0.727273 | 0.761905 |
| Claude-3 | 7 | 2 | 2 | 11 | 0.777778 | 0.636364 | 0.700000 |
| GEMINI | 5 | 3 | 3 | 11 | 0.625000 | 0.454545 | 0.526316 |
| pathway | 6 | 3 | 2 | 11 | 0.666667 | 0.545455 | 0.600000 |

*32*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| IFNAR | JAK1 | Activation | IFNAR | JAK1 |  |
| JAK1 | TYK2 | Activation | JAK1 | TYK2 | Activation |
| TYK2 | STAT1 (P) | Activation | TYK2 | STAT1 (P) | Activation |
| dsRNA | RIG-I | Activation | dsRNA | RIG-I | Activation |
| RIG-I | MAVS | Activation | RIG-I | MAVS | Activation |
| MAVS | NEMO | Activation | MAVS | NEMO | Activation |
| NEMO | IKKα | Activation | NEMO | IKKα | Activation |
| IKKα | NFκB | Activation | IKKα | NFκB | Activation |
| NEMO | TBK1 | Activation | NEMO | TBK1 | Activation |
| TBK1 | IRF3 | Activation | TBK1 | IRF3 | Activation |
| IRF3 | IFN-β | Activation | IRF3 | IFN-β | Activation |
| NFκB | IFN-β | Activation | NFκB | IFN-β | Inhibition |
| IFN-β | IKKα | Activation | IFN-β | IKKα | Inhibition |
| IKKα | STAT1 (P) | Activation | IKKα | STAT1 (P) | Inhibition |
| cytokine receptor | STAT1 (P) | Activation | cytokine receptor | STAT1 (P) | Inhibition |
| cytokine (e.g., IL6) | cytokine receptor | Activation | cytokine (e.g., IL6) | cytokine receptor | Activation |
| IKKα | cytokine (e.g., IL6) | Inhibition | IKKα | cytokine (e.g., IL6) |  |
| IFNAR | STAT1 (P) | Activation | IFNAR | STAT1 (P) |  |
| cytokine (e.g., IL6) | STAT1 (P) | Activation | cytokine (e.g., IL6) | STAT1 (P) |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 14 | 3 | 2 | 19 | 0.823529 | 0.736842 | 0.777778 |
| Claude-3 | 13 | 3 | 3 | 19 | 0.812500 | 0.684211 | 0.742857 |
| GEMINI | 10 | 4 | 5 | 19 | 0.714286 | 0.526316 | 0.606061 |
| pathway | 11 | 4 | 4 | 19 | 0.733333 | 0.578947 | 0.647059 |

*33*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Gln | ASCT2 (SLC1A5) | Activation | Gln | ASCT2 (SLC1A5) |  |
| ASCT2 (SLC1A5) | Gln | Activation | ASCT2 (SLC1A5) | Gln |  |
| Gln | LAT1 (SLC7A5) | Activation | Gln | LAT1 (SLC7A5) | Activation |
| LAT1 (SLC7A5) | Gln | Activation | LAT1 (SLC7A5) | Gln | Activation |
| Gln | Glutamate | Activation | Gln | Glutamate | Activation |
| Glutamate | α-KG | Activation | Glutamate | α-KG | Activation |
| α-KG | TCA | Activation | α-KG | TCA | Activation |
| TCA | Malate | Activation | TCA | Malate | Activation |
| TCA | Fumarate | Activation | TCA | Fumarate | Activation |
| TCA | Succinate | Activation | TCA | Succinate | Activation |
| TCA | Citrate | Activation | TCA | Citrate | Activation |
| Citrate | CoA | Activation | Citrate | CoA | Activation |
| GOT2/GPT2 | Glutamate | Activation | GOT2/GPT2 | Glutamate | Inhibition |
| GDH1 | Glutamate | Activation | GDH1 | Glutamate | Inhibition |
| mTOR | Myc | Activation | mTOR | Myc | Inhibition |
| Myc | mTOR | Activation | Myc | mTOR | Inhibition |
| BCH | LAT1 (SLC7A5) | Inhibition | BCH | LAT1 (SLC7A5) | Activation |
| DON Azaserine Acivicin | Gln | Inhibition | DON Azaserine Acivicin | Gln | Activation |
| GPNA | ASCT2 (SLC1A5) | Inhibition | GPNA | ASCT2 (SLC1A5) | Activation |
| BPTES/CB-839 | GLS | Inhibition | BPTES/CB-839 | GLS | Activation |
| Compound 968 | GLS | Inhibition | Compound 968 | GLS |  |
| Purpurin/R162 | GDH1 | Inhibition | Purpurin/R162 | GDH1 |  |
| EGCG | GDH1 | Inhibition | EGCG | GDH1 |  |
| AOA | GOT2/GPT2 | Inhibition | AOA | GOT2/GPT2 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 16 | 4 | 5 | 25 | 0.800000 | 0.64 | 0.711111 |
| Claude-3 | 15 | 5 | 5 | 25 | 0.750000 | 0.60 | 0.666667 |
| GEMINI | 13 | 6 | 6 | 25 | 0.684211 | 0.52 | 0.590909 |
| pathway | 14 | 6 | 5 | 25 | 0.700000 | 0.56 | 0.622222 |

*34*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| Growth signals | D-cyclins | Activation | Growth signals | D-cyclins | Activation |
| D-cyclins | CDKs 4/6 | Activation | D-cyclins | CDKs 4/6 | Activation |
| CDKs 4/6 | RB | Inhibition | CDKs 4/6 | RB |  |
| RB | E2F | Inhibition | RB | E2F | Inhibition |
| E2F | Cell cycle | Activation | E2F | Cell cycle | Inhibition |
| Damage signals | p53 | Activation | Damage signals | p53 | Inhibition |
| p53 | CDKN1s p21 | Activation | p53 | CDKN1s p21 | Inhibition |
| CDKN2s p16 | CDKs 4/6 | Inhibition | CDKN2s p16 | CDKs 4/6 | Activation |
| CDKN1s p21 | CDKs 4/6 | Inhibition | CDKN1s p21 | CDKs 4/6 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 2 | 1 | 9 | 0.750000 | 0.666667 | 0.705882 |
| Claude-3 | 5 | 2 | 2 | 9 | 0.714286 | 0.555556 | 0.625000 |
| GEMINI | 4 | 3 | 2 | 9 | 0.571429 | 0.444444 | 0.500000 |
| pathway | 5 | 2 | 2 | 9 | 0.714286 | 0.555556 | 0.625000 |

*35*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Myocardial Damage | AT1R/p38 MAPK | Activation | Myocardial Damage | AT1R/p38 MAPK | Activation |
| AT1R/p38 MAPK | ACE | Activation | AT1R/p38 MAPK | ACE | Activation |
| PFD | AT1R/p38 MAPK | Inhibition | PFD | AT1R/p38 MAPK | Activation |
| ACE | Ang II | Activation | ACE | Ang II | Inhibition |
| ACE2 | Ang(1-7) | Activation | ACE2 | Ang(1-7) | Inhibition |
| Ang(1-7) | MAS | Activation | Ang(1-7) | MAS | Inhibition |
| Ang II | AT1R | Activation | Ang II | AT1R | Inhibition |
| LXR-α | ACE | Activation | LXR-α | ACE | Activation |
| LXR-α | AT1R/p38 MAPK | Activation | LXR-α | AT1R/p38 MAPK | Activation |
| PFD | LXR-α | Activation | PFD | LXR-α | Activation |
| PFD | Inhibition of Cardiac fibrosis | Activation | PFD | Inhibition of Cardiac fibrosis | Inhibition |
| ACE2 | Ang(1-7) | Inhibition | ACE2 | Ang(1-7) | Inhibition |
| MAS | Cardiac fibrosis | Inhibition | MAS | Cardiac fibrosis | Inhibition |
| Ang(1-7) | Cardiac fibrosis | Activation | Ang(1-7) | Cardiac fibrosis | Activation |
| AT1R/p38 MAPK | ACE2 | Inhibition | AT1R/p38 MAPK | ACE2 |  |
| ACE2 | Ang(1-7) | Inhibition | ACE2 | Ang(1-7) |  |
| Ang(1-7) | MAS | Inhibition | Ang(1-7) | MAS |  |
| PFD | Cardiac fibrosis | Inhibition | PFD | Cardiac fibrosis |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 14 | 2 | 2 | 18 | 0.875000 | 0.777778 | 0.823529 |
| Claude-3 | 14 | 3 | 1 | 18 | 0.823529 | 0.777778 | 0.800000 |
| GEMINI | 10 | 4 | 2 | 18 | 0.714286 | 0.555556 | 0.625000 |
| pathway | 11 | 3 | 4 | 18 | 0.785714 | 0.611111 | 0.687500 |

*36*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Syx | RhoA | Activation | Syx | RhoA |  |
| RhoA | SIRT1 | Activation | RhoA | SIRT1 |  |
| SIRT1 | RARγ | Activation | SIRT1 | RARγ | Inhibition |
| RARγ | Noggin | Activation | RARγ | Noggin | Inhibition |
| Noggin | Neural differentiation | Activation | Noggin | Neural differentiation | Activation |
| F-actin | Rab3d | Inhibition | F-actin | Rab3d | Activation |
| RARγ | RHPN2 | Inhibition | RARγ | RHPN2 | Activation |
| Noggin | BMP4 | Inhibition | Noggin | BMP4 | Activation |
| BMP4 | pSmad1 | Activation | BMP4 | pSmad1 | Activation |
| pSmad1 | Neural differentiation | Inhibition | pSmad1 | Neural differentiation |  |
| RhoA | Neural differentiation | Activation | RhoA | Neural differentiation | Inhibition |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 7 | 2 | 2 | 11 | 0.777778 | 0.636364 | 0.700000 |
| Claude-3 | 6 | 2 | 3 | 11 | 0.750000 | 0.545455 | 0.631579 |
| GEMINI | 5 | 3 | 3 | 11 | 0.625000 | 0.454545 | 0.526316 |
| pathway | 6 | 2 | 3 | 11 | 0.750000 | 0.545455 | 0.631579 |

*37*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| KAR | GA3oxs | Activation | KAR | GA3oxs |  |
| GA3oxs | GA | Activation | GA3oxs | GA |  |
| GA | GID1 | Activation | GA | GID1 |  |
| GID1 | SCFSLY/GID1 | Activation | GID1 | SCFSLY/GID1 | Activation |
| SCFSLY/GID1 | DELLA | Inhibition | SCFSLY/GID1 | DELLA | Activation |
| DELLA | GAMYB | Inhibition | DELLA | GAMYB | Activation |
| GAMYB | EXP2 | Activation | GAMYB | EXP2 | Activation |
| EXP2 | Germination | Activation | EXP2 | Germination | Activation |
| EXP2 | Hypocotyl elongation | Activation | EXP2 | Hypocotyl elongation | Activation |
| KAR | ABA2 | Activation | KAR | ABA2 | Activation |
| ABA2 | ABA | Activation | ABA2 | ABA | Activation |
| ABA | PYR/PYL/RCAR | Activation | ABA | PYR/PYL/RCAR | Activation |
| PYR/PYL/RCAR | PP2Cs | Inhibition | PYR/PYL/RCAR | PP2Cs | Inhibition |
| PP2Cs | SnRK2s | Inhibition | PP2Cs | SnRK2s | Inhibition |
| SnRK2s | TFs | Inhibition | SnRK2s | TFs | Inhibition |
| TFs | ABI3 | Activation | TFs | ABI3 | Inhibition |
| ABI3 | Germination | Inhibition | ABI3 | Germination | Inhibition |
| ABI3 | Hypocotyl elongation | Activation | ABI3 | Hypocotyl elongation | Inhibition |
| KAR | YUCCAs | Activation | KAR | YUCCAs | Inhibition |
| YUCCAs | Auxin | Activation | YUCCAs | Auxin | Activation |
| Auxin | TIR1/AFB | Activation | Auxin | TIR1/AFB | Activation |
| TIR1/AFB | SCFTIR1 | Activation | TIR1/AFB | SCFTIR1 | Activation |
| SCFTIR1 | AUX/IAA | Inhibition | SCFTIR1 | AUX/IAA | Activation |
| AUX/IAA | ARFs | Inhibition | AUX/IAA | ARFs | Activation |
| ARFs | IAA1 | Activation | ARFs | IAA1 | Activation |
| IAA1 | Germination | Inhibition | IAA1 | Germination | Inhibition |
| IAA1 | Hypocotyl elongation | Activation | IAA1 | Hypocotyl elongation | Activation |
| RHPN2 | RARγ | Inhibition | RHPN2 | RARγ |  |
| KAR | Auxin | Activation | KAR | Auxin |  |
| Biosynthesis | Phytohormone | Activation | Biosynthesis | Phytohormone |  |
| Phytohormone | Receptor | Activation | Phytohormone | Receptor |  |
| Receptor | E3 liges | Activation | Receptor | E3 liges |  |
| E3 liges | Repressor | Inhibition | E3 liges | Repressor |  |
| Repressor | Transcription factor | Inhibition | Repressor | Transcription factor |  |
| Transcription factor | Response gene | Activation | Transcription factor | Response gene |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 25 | 6 | 7 | 38 | 0.806452 | 0.657895 | 0.724638 |
| Claude-3 | 23 | 7 | 8 | 38 | 0.766667 | 0.605263 | 0.676471 |
| GEMINI | 18 | 10 | 10 | 38 | 0.642857 | 0.473684 | 0.545455 |
| pathway | 20 | 8 | 10 | 38 | 0.714286 | 0.526316 | 0.606061 |

*38*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Ground Truth** | | |  |  |  |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| FLT-3 | PRKD1 | Activation | FLT-3 | PRKD1 |  |
| PRKD1 | AKT | Activation | PRKD1 | AKT |  |
| AKT | mTOR | Activation | AKT | mTOR | Activation |
| mTOR | Cell Survival Signaling | Activation | mTOR | Cell Survival Signaling | Activation |
| NOTCH4 | PI3K | Activation | NOTCH4 | PI3K | Activation |
| PI3K | PRKD1 | Activation | PI3K | PRKD1 | Activation |
| MAS1 | CDC42 | Activation | MAS1 | CDC42 | Activation |
| CDC42 | RHO | Activation | CDC42 | RHO | Activation |
| RHO | GAP/GEF | Activation | RHO | GAP/GEF | *Inhibition* |
| GAP/GEF | MAPK | Activation | GAP/GEF | MAPK | *Inhibition* |
| MAPK | ERK1/2 | Activation | MAPK | ERK1/2 | *Inhibition* |
| ERK1/2 | NFATC1/4 | Activation | ERK1/2 | NFATC1/4 | *Inhibition* |
| NFATC1/4 | VEGFR1 | Activation | NFATC1/4 | VEGFR1 | *Inhibition* |
| NFATC1/4 | VEGFR2 | Activation | NFATC1/4 | VEGFR2 | *Inhibition* |
| VEGF | VEGFR1 | Activation | VEGF | VEGFR1 |  |
| VEGF | VEGFR2 | Activation | VEGF | VEGFR2 |  |
| NFATC1/4 | Angiogenesis and Vasoreactivity | Activation | NFATC1/4 | Angiogenesis and Vasoreactivity | Activation |
| AT1R | RAS/RAF | Activation | AT1R | RAS/RAF |  |
| RAS/RAF | MAPK | Activation | RAS/RAF | MAPK | Activation |
| RAS/RAF | p38MAPK | Activation | RAS/RAF | p38MAPK |  |
| p38MAPK | ERK1/2 | Activation | p38MAPK | ERK1/2 |  |
| VEGFR1 | VEGF | Activation | VEGFR1 | VEGF |  |
| VEGFR2 | VEGF | Indirect Activation | VEGFR2 | VEGF |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 16 | 4 | 4 | 24 | 0.800000 | 0.666667 | 0.727273 |
| Claude-3 | 15 | 4 | 5 | 24 | 0.789474 | 0.625000 | 0.697674 |
| GEMINI | 13 | 6 | 5 | 24 | 0.684211 | 0.541667 | 0.604651 |
| pathway | 14 | 9 | 5 | 24 | 0.608696 | 0.583333 | 0.595745 |

*39*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| HIF-1β | HIF-1α | Activation | HIF-1β | HIF-1α |  |
| HIF-1α | PHDs | Activation | HIF-1α | PHDs |  |
| PHDs | VHL E3 | Activation | PHDs | VHL E3 | Activation |
| VHL E3 | Ub ubiquitin | Activation | VHL E3 | Ub ubiquitin | Activation |
| Ub ubiquitin | HIF-1α proteasomal degradation | Activation | Ub ubiquitin | HIF-1α proteasomal degradation | Activation |
| HIF-1α | Nucleus | Activation | HIF-1α | Nucleus | Activation |
| HIF-1β | Nucleus | Activation | HIF-1β | Nucleus |  |
| HIF-1α | HRES | Activation | HIF-1α | HRES |  |
| HIF-1β | HRES | Activation | HIF-1β | HRES |  |
| HRES | NCGTG | Activation | HRES | NCGTG |  |
| NCGTG | Proliferation, Anti-apoptosis, Anti-inflammation, Angiogenesis | Activation | NCGTG | Proliferation, Anti-apoptosis, Anti-inflammation, Angiogenesis |  |
| Angiogenesis | Caspase-3 | Activation | Angiogenesis | Caspase-3 | Inhibition |
| Caspase-3 | MEK-1/2 | Activation | Caspase-3 | MEK-1/2 |  |
| MEK-1/2 | ERK-1/2 | Activation | MEK-1/2 | ERK-1/2 |  |
| ERK-1/2 | Akt | Activation | ERK-1/2 | Akt | Inhibition |
| EPO | EPO-R | Activation | EPO | EPO-R | Inhibition |
| EPO-R | VEGF | Activation | EPO-R | VEGF | Activation |
| VEGF | VEGFR | Activation | VEGF | VEGFR | Activation |
| ADM | Vasomotor regulation | Activation | ADM | Vasomotor regulation |  |
| Glut-1 | Energy metabolism | Activation | Glut-1 | Energy metabolism | Activation |
| HO-1 | ROS | Activation | HO-1 | ROS | Activation |
| ROS | IRS1/PI3K/Akt2 | Activation | ROS | IRS1/PI3K/Akt2 | Activation |
| IRS1/PI3K/Akt2 | Keap1/Nrf2/ERK | Activation | IRS1/PI3K/Akt2 | Keap1/Nrf2/ERK | Activation |
| HIF-1α | Maintain mitochondrial membrane potential | Activation | HIF-1α | Maintain mitochondrial membrane potential | Activation |
| PHDs | HIF-1α | Inhibition | PHDs | HIF-1α | Inhibition |
| Ub ubiquitin | HIF-1α | Inhibition | Ub ubiquitin | HIF-1α |  |
| HIF-1α proteasomal degradation | HIF-1α | Inhibition | HIF-1α proteasomal degradation | HIF-1α | Activation |
| HO-1 | ROS | Inhibition | HO-1 | ROS | Activation |
| EPO-R | Hormone effect | Activation | EPO-R | Hormone effect | Activation |
| VEGF | Proliferation, Anti-apoptosis, Anti-inflammation, Angiogenesis | Activation | VEGF | Proliferation, Anti-apoptosis, Anti-inflammation, Angiogenesis | Activation |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 25 | 5 | 5 | 35 | 0.833333 | 0.714286 | 0.769231 |
| Claude-3 | 24 | 6 | 5 | 35 | 0.800000 | 0.685714 | 0.738462 |
| GEMINI | 20 | 8 | 7 | 35 | 0.714286 | 0.571429 | 0.634921 |
| pathway | 22 | 7 | 6 | 35 | 0.758621 | 0.628571 | 0.687500 |

*40*

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| Starter (gene1) | Receptor (gene2) | Relationship | GPT-4 | Starter (gene1) | Receptor (gene2) | pathway |
| Egr-1 | PDGFC | Activation | Activation | Egr-1 | PDGFC | Inhibition |
| Sp1 | PDGFC | Activation | Activation | Sp1 | PDGFC | Inhibition |
| PDGFC | PDGF-CC | Activation | Activation | PDGFC | PDGF-CC | Inhibition |
| tPA | inactive PDGF-CC | Activation | Activation | tPA | inactive PDGF-CC | Inhibition |
| inactive PDGF-CC | active PDGF-CC | Activation |  | inactive PDGF-CC | active PDGF-CC |  |
| active PDGF-CC | PDGFR-α | Activation | Activation | active PDGF-CC | PDGFR-α | Inhibition |
| PDGFR-α | PI3K | Activation | Activation | PDGFR-α | PI3K | Inhibition |
| PDGFR-α | Ras MAPK | Activation | Activation | PDGFR-α | Ras MAPK | Activation |
| PDGFR-α | p38 MAPK | Activation | Activation | PDGFR-α | p38 MAPK | Activation |
| PDGFR-α | PLC-γ | Activation | Activation | PDGFR-α | PLC-γ | Activation |
| PAI-1 | tPA | Inhibition | Activation | PAI-1 | tPA |  |
| Neuroserpin | tPA | Inhibition | Activation | Neuroserpin | tPA |  |
| LRP1 | PDGFR-α | Activation | Activation | LRP1 | PDGFR-α |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 10 | 2 | 1 | 13 | 0.833333 | 0.769231 | 0.800000 |
| Claude-3 | 9 | 2 | 2 | 13 | 0.818182 | 0.692308 | 0.750000 |
| GEMINI | 7 | 3 | 3 | 13 | 0.700000 | 0.538462 | 0.608696 |
| pathway | 8 | 2 | 3 | 13 | 0.800000 | 0.615385 | 0.695652 |

*41*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Growth factor | Growth factor receptor | Activation | Growth factor | Growth factor receptor | Activation |
| Growth factor receptor | IRS | Activation | Growth factor receptor | IRS | Activation |
| IRS | PIP2 | Activation | IRS | PIP2 | Activation |
| PIP2 | PI3K | Activation | PIP2 | PI3K | Activation |
| PIP2 | PTEN | Activation | PIP2 | PTEN | Activation |
| PI3K | PIP3 | Activation | PI3K | PIP3 | Inhibition |
| PIP3 | PDK1 | Activation | PIP3 | PDK1 | Inhibition |
| PDK1 | AKT (Thr308) | Activation | PDK1 | AKT (Thr308) | Activation |
| mTORC2 | AKT (Ser473) | Activation | mTORC2 | AKT (Ser473) | Activation |
| AKT | mTORC1 | Activation | AKT | mTORC1 |  |
| mTORC1 | S6K1/2 | Activation | mTORC1 | S6K1/2 | Activation |
| mTORC1 | 4EBP1 | Inhibition | mTORC1 | 4EBP1 | Inhibition |
| AKT | FOXG1 (phosphorylation) | Activation | AKT | FOXG1 (phosphorylation) | Activation |
| FOXG1 (phosphorylation) | Reelin | Activation | FOXG1 (phosphorylation) | Reelin | Activation |
| PTEN | PI3K | Inhibition | PTEN | PI3K | Activation |
| Rapamycin | mTORC1 | Inhibition | Rapamycin | mTORC1 |  |
| FOXG1 | Reelin | Inhibition | FOXG1 | Reelin |  |
| PIP3 | AKT | Activation | PIP3 | AKT |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 14 | 2 | 2 | 18 | 0.8750 | 0.777778 | 0.823529 |
| Claude-3 | 13 | 3 | 2 | 18 | 0.8125 | 0.722222 | 0.764706 |
| GEMINI | 12 | 3 | 3 | 18 | 0.8000 | 0.666667 | 0.727273 |
| pathway | 13 | 3 | 2 | 18 | 0.8125 | 0.722222 | 0.764706 |

*42*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Starter (gene1) | Receptor (gene2) | Relationship | Starter (gene1) | Receptor (gene2) | pathway |
| Rab7 | Lysosome | Activation | Rab7 | Lysosome | Activation |
| Lysosome | Endolysosome/Autolysosome | Activation | Lysosome | Endolysosome/Autolysosome | Activation |
| Endolysosome/Autolysosome | Lysosomal digestion | Activation | Endolysosome/Autolysosome | Lysosomal digestion |  |
| Lysosome | Lysosome reformation | Activation | Lysosome | Lysosome reformation | Activation |
| VapA | Lysosomal digestion | Inhibition | VapA | Lysosomal digestion |  |
| VapA | Membrane retrieval | Inhibition | VapA | Membrane retrieval | Activation |
| VapA | Lysosome reformation | Inhibition | VapA | Lysosome reformation | Activation |
| VapA | TFEB Signalling | Inhibition | VapA | TFEB Signalling |  |

Results

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 1 | 1 | 8 | 0.857143 | 0.750 | 0.800000 |
| Claude-3 | 5 | 2 | 1 | 8 | 0.714286 | 0.625 | 0.666667 |
| GEMINI | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |
| pathway | 5 | 1 | 2 | 8 | 0.833333 | 0.625 | 0.714286 |

*43*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| SDHDv | ROS | Activation | SDHDv | ROS |  |
| ROS | Oxi PTEN | Activation | ROS | Oxi PTEN | Activation |
| Oxi PTEN | Mono-Ub PTEN | Activation | Oxi PTEN | Mono-Ub PTEN | Activation |
| Mono-Ub PTEN | PTEN nuclear Localization | Activation | Mono-Ub PTEN | PTEN nuclear Localization | Activation |
| PTEN nuclear Localization | Mono-Ub PTEN p-Akt | Activation | PTEN nuclear Localization | Mono-Ub PTEN p-Akt | Activation |
| PTEN nuclear Localization | Acetylation-FOXO3a | Activation | PTEN nuclear Localization | Acetylation-FOXO3a |  |
| Acetylation-FOXO3a | p-FOXO3a | Activation | Acetylation-FOXO3a | p-FOXO3a | Inhibition |
| p-FOXO3a | ATG12, Beclin 1 transcription | Activation | p-FOXO3a | ATG12, Beclin 1 transcription | Inhibition |
| FOXO3a-14-3-3 | Degradation | Activation | FOXO3a-14-3-3 | Degradation | Inhibition |
| ATG12, Beclin 1 transcription | Autophagy | Activation | ATG12, Beclin 1 transcription | Autophagy |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 6 | 1 | 1 | 8 | 0.857143 | 0.750 | 0.800000 |
| Claude-3 | 5 | 1 | 2 | 8 | 0.833333 | 0.625 | 0.714286 |
| GEMINI | 4 | 2 | 2 | 8 | 0.666667 | 0.500 | 0.571429 |
| pathway | 5 | 1 | 2 | 8 | 0.833333 | 0.625 | 0.714286 |

*44*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Lm | c-di-AMP | Activation | Lm | c-di-AMP | Activation |
| c-di-AMP | STING | Activation | c-di-AMP | STING | Activation |
| STING | DDX41 | Activation | STING | DDX41 |  |
| DDX41 | p38 | Activation | DDX41 | p38 | Activation |
| DDX41 | TBK1 | Activation | DDX41 | TBK1 | Inhibition |
| p38 | IRF3 | Activation | p38 | IRF3 | Activation |
| TBK1 | IRF3 | Activation | TBK1 | IRF3 | Activation |
| IRF3 | Ifnb1 | Activation | IRF3 | Ifnb1 |  |
| BTK | DDX41 | Inhibition | BTK | DDX41 | Activation |
| BTK | STING | Inhibition | BTK | STING | Activation |
| C3a | BTK | Inhibition | C3a | BTK | Inhibition |
| C5a | BTK | Inhibition | C5a | BTK |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| Model | Correct Predictions | False Predictions | Missing Relation | Total Predictions | Precision | Recall | F1 |
| GPT-4 | 9 | 2 | 1 | 12 | 0.818182 | 0.750000 | 0.782609 |
| Claude-3 | 8 | 2 | 2 | 12 | 0.800000 | 0.666667 | 0.727273 |
| GEMINI | 6 | 3 | 3 | 12 | 0.666667 | 0.500000 | 0.571429 |
| pathway | 7 | 2 | 3 | 12 | 0.777778 | 0.583333 | 0.666667 |

*45*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| EtOH | FoxO1 | Activation | EtOH | FoxO1 | Activation |
| FoxO1 | AMPK | Activation | FoxO1 | AMPK | Activation |
| AMPK | ULK1 (S555) | Activation | AMPK | ULK1 (S555) | Activation |
| AMPK | PIK3C3 (S164) | Activation | AMPK | PIK3C3 (S164) | Activation |
| AMPK | BECN1 (S93) | Activation | AMPK | BECN1 (S93) |  |
| AMPK | BECN1 (S14) | Activation | AMPK | BECN1 (S14) | Activation |
| ULK1 (S555) | BECN1 (S93) | Activation | ULK1 (S555) | BECN1 (S93) | Activation |
| ULK1 (S555) | PIK3C3 (S164) | Activation | ULK1 (S555) | PIK3C3 (S164) | Activation |
| PIK3C3 | 14-3-3Θ | Activation | PIK3C3 | 14-3-3Θ | Activation |
| PIK3C3 | ATG14 | Activation | PIK3C3 | ATG14 | Activation |
| PIK3C3 | AMBRA1 | Activation | PIK3C3 | AMBRA1 | Activation |
| PIK3C3 | BECN1 | Activation | PIK3C3 | BECN1 |  |
| BECN1 | SQSTM1 | Activation | BECN1 | SQSTM1 | Activation |
| BECN1 | LC3B | Activation | BECN1 | LC3B |  |
| BECN1 | ATG7 | Activation | BECN1 | ATG7 | Inhibition |
| mTORC1 | ULK1 (S757) | Activation | mTORC1 | ULK1 (S757) |  |
| mTORC1 | AMPK | Inhibition | mTORC1 | AMPK |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 13 | 2 | 2 | 17 | 0.866667 | 0.764706 | 0.812500 |
| Claude-3 | 12 | 3 | 2 | 17 | 0.800000 | 0.705882 | 0.750000 |
| GEMINI | 10 | 4 | 3 | 17 | 0.714286 | 0.588235 | 0.645161 |
| pathway | 10 | 3 | 4 | 17 | 0.769231 | 0.588235 | 0.666667 |

*46*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| Wnt | Frizzled | Activation | Wnt | Frizzled | Activation |
| PDGF | PDGFR | Activation | PDGF | PDGFR | Activation |
| GLP-1 | GLP-1R | Activation | GLP-1 | GLP-1R | Activation |
| BTC | ErbB1 | Activation | BTC | ErbB1 | Activation |
| BTC | ErbB2 | Activation | BTC | ErbB2 | Activation |
| IGF-1 | IGF-1R | Activation | IGF-1 | IGF-1R |  |
| Frizzled | Dsh | Activation | Frizzled | Dsh | Activation |
| Dsh | cAMP | Activation | Dsh | cAMP | Activation |
| cAMP | MEK | Activation | cAMP | MEK |  |
| cAMP | PKA | Activation | cAMP | PKA | Activation |
| MEK | ERK1/2 | Activation | MEK | ERK1/2 |  |
| PKA | ERK1/2 | Activation | PKA | ERK1/2 | Activation |
| ERK1/2 | EZH2 | Activation | ERK1/2 | EZH2 | Activation |
| EZH2 | ErbBR | Activation | EZH2 | ErbBR |  |
| ErbBR | P16LINK4 | Activation | ErbBR | P16LINK4 | Activation |
| P16LINK4 | Tcf7L2 | Activation | P16LINK4 | Tcf7L2 | Activation |
| Dsh | GS3Kβ | Activation | Dsh | GS3Kβ | Activation |
| GS3Kβ | β-catenin | Activation | GS3Kβ | β-catenin |  |
| β-catenin | APC | Activation | β-catenin | APC | Activation |
| APC | Axin | Activation | APC | Axin | Activation |
| Axin | Tcf7L2 | Activation | Axin | Tcf7L2 | Activation |
| Tcf7L2 | CyclinD1-2, cMyc, cdk4 | Activation | Tcf7L2 | CyclinD1-2, cMyc, cdk4 |  |
| CyclinD1-2, cMyc, cdk4 | Proliferation | Activation | CyclinD1-2, cMyc, cdk4 | Proliferation | Activation |
| PDGFR | IRS | Activation | PDGFR | IRS | Inhibition |
| IRS | PI3K | Activation | IRS | PI3K | Inhibition |
| PI3K | PDK1 | Activation | PI3K | PDK1 | Activation |
| PDK1 | AKT/PKB | Activation | PDK1 | AKT/PKB | Activation |
| AKT/PKB | TSC1/2 | Activation | AKT/PKB | TSC1/2 |  |
| TSC1/2 | GTP | Activation | TSC1/2 | GTP | Inhibition |
| GTP | Rheb | Activation | GTP | Rheb | Inhibition |
| Rheb | mTORC1 | Activation | Rheb | mTORC1 | Activation |
| mTORC1 | 4E-BPs | Activation | mTORC1 | 4E-BPs |  |
| 4E-BPs | S6K1 | Activation | 4E-BPs | S6K1 | Activation |
| S6K1 | Proliferation | Activation | S6K1 | Proliferation | Activation |
| AKT/PKB | MDM2/P53 | Activation | AKT/PKB | MDM2/P53 | Activation |
| MDM2/P53 | P21cip1 | Activation | MDM2/P53 | P21cip1 | Activation |
| P21cip1 | Proliferation | Activation | P21cip1 | Proliferation |  |
| AKT/PKB | FOXO1 | Activation | AKT/PKB | FOXO1 |  |
| FOXO1 | P27kip1 | Activation | FOXO1 | P27kip1 |  |
| P27kip1 | Pdx1, GSK3 | Activation | P27kip1 | Pdx1, GSK3 |  |
| Pdx1, GSK3 | mTORC1 | Activation | Pdx1, GSK3 | mTORC1 |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 30 | 10 | 5 | 45 | 0.750000 | 0.666667 | 0.705882 |
| Claude-3 | 25 | 10 | 10 | 45 | 0.714286 | 0.555556 | 0.625000 |
| GEMINI | 20 | 10 | 15 | 45 | 0.666667 | 0.444444 | 0.533333 |
| pathway | 22 | 10 | 13 | 45 | 0.687500 | 0.488889 | 0.571429 |

*47*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| IGF-I | IGF-I-R | Activation | IGF-I | IGF-I-R | Activation |
| IGF-I-R | PI3-kinase | Activation | IGF-I-R | PI3-kinase | Activation |
| PI3-kinase | PKB (Akt) | Activation | PI3-kinase | PKB (Akt) | Activation |
| PKB (Akt) | Transcription or Splicing factors | Activation | PKB (Akt) | Transcription or Splicing factors | Activation |
| PDGFs | PDGF-R | Activation | PDGFs | PDGF-R |  |
| PDGF-R | MEK1 | Activation | PDGF-R | MEK1 | Inhibition |
| MEK1 | ERK | Activation | MEK1 | ERK | Inhibition |
| ERK | Transcription or Splicing factors | Activation | ERK | Transcription or Splicing factors | Activation |
| bFGF or EGF | bFGF-R or EGF-R | Activation | bFGF or EGF | bFGF-R or EGF-R | Inhibition |
| bFGF-R or EGF-R | MKK6 | Activation | bFGF-R or EGF-R | MKK6 | Inhibition |
| MKK6 | p38MAPK | Activation | MKK6 | p38MAPK | Activation |
| p38MAPK | Transcription or Splicing factors | Activation | p38MAPK | Transcription or Splicing factors | Activation |
| LY294002 or Wortmannin | PI3-kinase | Inhibition | LY294002 or Wortmannin | PI3-kinase | Activation |
| PD98059 | MEK1 | Inhibition | PD98059 | MEK1 | Activation |
| SB203580 | p38MAPK | Inhibition | SB203580 | p38MAPK | Inhibition |
| IGF-I-R | PKB (Akt) | Activation | IGF-I-R | PKB (Akt) | Activation |
| PI3-kinase | Transcription or Splicing factors | Activation | PI3-kinase | Transcription or Splicing factors | Activation |
| ERK | Induction of dedifferentiation | Activation | ERK | Induction of dedifferentiation |  |
| p38MAPK | Induction of dedifferentiation | Activation | p38MAPK | Induction of dedifferentiation |  |
| PI3-kinase | Maintaining of a differentiated phenotype | Inhibition | PI3-kinase | Maintaining of a differentiated phenotype |  |

:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 15 | 3 | 2 | 20 | 0.833333 | 0.750 | 0.789474 |
| Claude-3 | 14 | 3 | 3 | 20 | 0.823529 | 0.700 | 0.756757 |
| GEMINI | 12 | 4 | 4 | 20 | 0.750000 | 0.600 | 0.666667 |
| pathway | 13 | 3 | 5 | 20 | 0.812500 | 0.650 | 0.722222 |

*48*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| EGFR | Ras | Activation | EGFR | Ras |  |
| Ras | Raf | Activation | Ras | Raf | Activation |
| Raf | MEK | Activation | Raf | MEK | Activation |
| MEK | ERK | Activation | MEK | ERK | Activation |
| EGFR | PI3K | Activation | EGFR | PI3K | Activation |
| PI3K | Akt | Activation | PI3K | Akt |  |
| Akt | mTOR | Activation | Akt | mTOR | Activation |
| mTOR | Proliferation / Survival / Angiogenesis | Activation | mTOR | Proliferation / Survival / Angiogenesis | Activation |
| Cetuximab | EGFR | Inhibition | Cetuximab | EGFR | Activation |
| Erlotinib / Gefitinib | EGFR | Inhibition | Erlotinib / Gefitinib | EGFR | Activation |
| Salirasib | Ras | Inhibition | Salirasib | Ras |  |
| LY294002 | PI3K | Inhibition | LY294002 | PI3K | Activation |
| BEZ235 | PI3K | Inhibition | BEZ235 | PI3K | Inhibition |
| Rapamycin / RAD001 / CCI-779 | mTOR | Inhibition | Rapamycin / RAD001 / CCI-779 | mTOR | Inhibition |
| PF-00299804 / BIBW2992 | HER | Inhibition | PF-00299804 / BIBW2992 | HER | Inhibition |
| Antiangiogenic agents | VEGFR / PDGFR / FGFR | Inhibition | Antiangiogenic agents | VEGFR / PDGFR / FGFR |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 12 | 2 | 2 | 16 | 0.857143 | 0.7500 | 0.800000 |
| Claude-3 | 11 | 2 | 3 | 16 | 0.846154 | 0.6875 | 0.758621 |
| GEMINI | 9 | 3 | 5 | 16 | 0.750000 | 0.5625 | 0.642857 |
| pathway | 10 | 2 | 4 | 16 | 0.833333 | 0.6250 | 0.714286 |

*49*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| RTK | Ras | Activation | RTK | Ras | Inhibition |
| Ras | Raf | Activation | Ras | Raf | Inhibition |
| Raf | MEK | Activation | Raf | MEK |  |
| MEK | ERK1/2 | Activation | MEK | ERK1/2 | Activation |
| TRAF | MEKK1/ASK1/TAK1 | Activation | TRAF | MEKK1/ASK1/TAK1 |  |
| MEKK1/ASK1/TAK1 | MKK3/6 | Activation | MEKK1/ASK1/TAK1 | MKK3/6 | Activation |
| MKK3/6 | p38 α/β/γ/δ | Activation | MKK3/6 | p38 α/β/γ/δ | Activation |
| RAC1 | MEKK/MUK | Activation | RAC1 | MEKK/MUK | Activation |
| MEKK/MUK | MKK4/7 | Activation | MEKK/MUK | MKK4/7 | Activation |
| MKK4/7 | JNK1/2/3 | Activation | MKK4/7 | JNK1/2/3 | Activation |
| Shp2 | RTK | Inhibition | Shp2 | RTK |  |

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 8 | 2 | 1 | 11 | 0.800000 | 0.727273 | 0.761905 |
| Claude-3 | 7 | 2 | 2 | 11 | 0.777778 | 0.636364 | 0.700000 |
| GEMINI | 5 | 2 | 4 | 11 | 0.714286 | 0.454545 | 0.555556 |
| pathway | 6 | 2 | 3 | 11 | 0.750000 | 0.545455 | 0.631579 |

*50*

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Starter (gene1)** | **Receptor (gene2)** | **Relationship** | **Starter (gene1)** | **Receptor (gene2)** | pathway |
| c-MET | Ras | Activation | c-MET | Ras | Activation |
| c-MET | PI3K | Activation | c-MET | PI3K | Activation |
| EGFR | Ras | Activation | EGFR | Ras |  |
| EGFR | PI3K | Activation | EGFR | PI3K | Activation |
| IGFR1 | Ras | Activation | IGFR1 | Ras | Activation |
| IGFR1 | PI3K | Activation | IGFR1 | PI3K | Activation |
| AXL | Ras | Activation | AXL | Ras | Activation |
| AXL | PI3K | Activation | AXL | PI3K |  |
| Fyn | Ras | Activation | Fyn | Ras | Activation |
| Fyn | PI3K | Activation | Fyn | PI3K | Activation |
| Ras | Raf | Activation | Ras | Raf | Activation |
| Raf | MEK | Activation | Raf | MEK |  |
| MEK | ERK | Activation | MEK | ERK | Activation |
| Rho | PAK | Activation | Rho | PAK | Activation |
| PAK | Cell motility and invasion | Activation | PAK | Cell motility and invasion | Activation |
| ERK | Cell cycle progression and proliferation | Activation | ERK | Cell cycle progression and proliferation | Activation |
| PI3K | AKT | Activation | PI3K | AKT | Activation |
| AKT | mTOR | Activation | AKT | mTOR | Activation |
| mTOR | Protein synthesis and cell growth | Activation | mTOR | Protein synthesis and cell growth | Activation |
| AKT | Survival | Activation | AKT | Survival |  |
| PTEN | AKT | Inhibition | PTEN | AKT |  |
| miR-125a-3p | Fyn | Inhibition | miR-125a-3p | Fyn |  |
| miR-7 | FAK | Inhibition | miR-7 | FAK | Inhibition |
| miR-7, miR-23b, miR-145 | PAK | Inhibition | miR-7, miR-23b, miR-145 | PAK | Inhibition |
| miR-302-367, miR-612 | PI3K | Inhibition | miR-302-367, miR-612 | PI3K | Inhibition |
| miR-99, miR-145 | mTOR | Inhibition | miR-99, miR-145 | mTOR | Inhibition |
| Fyn | Rho | Activation | Fyn | Rho |  |
| Fyn | PAK | Activation | Fyn | PAK |  |

:

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Model** | **Correct Predictions** | **False Predictions** | **Missing Relation** | **Total Predictions** | **Precision** | **Recall** | **F1** |
| GPT-4 | 20 | 5 | 3 | 28 | 0.800000 | 0.714286 | 0.754717 |
| Claude-3 | 18 | 5 | 5 | 28 | 0.782609 | 0.642857 | 0.705882 |
| GEMINI | 16 | 4 | 8 | 28 | 0.800000 | 0.571429 | 0.666667 |
| pathway | 18 | 4 | 6 | 28 | 0.818182 | 0.642857 | 0.720000 |