Supplementary materials:

**Figure S1:** Visualisation of the M-P link map for liver cancer and its degree distribution. (A) The red circles and green rectangles correspond to the small molecules and metabolic pathways, respectively. Node size is proportional to the degree of the node. (B) The degree distribution of small molecules and pathways.

**Figure S2:** Visualisation of the M-P link map for lung cancer and its degree distribution. (A) The red circles and green rectangles correspond to the small molecules and metabolic pathways, respectively. Node size is proportional to the degree of the node. (B) The degree distribution of small molecules and pathways.
Figure S3. Hierarchical clustering in the M-P link map for liver cancer from GSE5364. (A) Hierarchical clustering between 263 small molecules and 18 pathways. The corresponding cells are coloured red where small molecules link to the pathways in the M-P link map. The labels for the corresponding pathways are shown on the right of the figure. (B) Zoomed-in plot of an sM-sP link between isoniazid and the glutathione metabolism pathway. The gene indicated by the arrow is the drug target of isoniazid. Differentially expressed genes in this pathway are coloured pink, while other genes in green are human disease-related genes. (C) Zoomed-in plot of mM-sP links between 15 small molecules and the focal
adhesion. These 15 small molecules target only the focal adhesion pathway. Their structures are given. The differentially expressed genes in this pathway are coloured pink, while other genes in green are human disease-related genes.
FIGURE S4: Hierarchical clustering in the M-P link map for lung cancer from GSE5364. (A) Hierarchical clustering between 276 small molecules and 16 pathways. The corresponding cells are coloured red where small molecules link to the pathways in the M-P link map. The labels for the corresponding pathways are shown on the right of the figure. (B) Zoomed-in plot of an sM-sP link between alsterpaullone and the
insulin signaling pathway. The gene indicated by the arrow is the drug target of alsterpaullone. Differentially expressed genes in this pathway are coloured pink, while other genes in green are human disease-related genes. (C) Zoomed-in plot of mM-sP links between 16 small molecules and the Cell Communication. Their structures are given. The differentially expressed genes in this pathway are coloured pink, while other genes in green are human disease-related genes.

**TABLE S1:** The characteristics of molecules with the sM-mP pattern in liver cancer

| Small molecule  | Degree in M-P link map | Description of the small molecule                        |
|-----------------|------------------------|----------------------------------------------------------|
| doxylamine      | 8                      | used as an antitussive, antiemetic, and hypnotic          |
| helveticoside   | 5                      | unknown                                                  |
| thioridazine    | 5                      | a phenothiazine antipsychotic agent                       |

**TABLE S2:** The characteristics of molecules with the sM-mP pattern in lung cancer

| Small molecule  | Degree in M-P link map | Description of the small molecule                        |
|-----------------|------------------------|----------------------------------------------------------|
| trichostatin A  | 8                      | serves as an antifungal antibiotic                       |
| vorinostat      | 6                      | as histone deacetylase inhibitors                       |
| thiamphenicol   | 5                      | an antibiotic                                            |
| tanespimycin    | 5                      | treatment of cancer                                      |
| mM_GrugEmM_name | mM_Description | target_GeneSym |
|-----------------|----------------|----------------|
| DB00227 Lovastatin | Lovastatin is a cholesterol-lowering agent. | ITGAL |
| DB00877 Sirolimus | Sirolimus is a potent immunosuppressant. | MTOR |
| DB01118 Amiodarone | It increases the duration of ventricular action. | ADRB1 |
| DB01235 L-DOPA | It is used for the treatment of parkinsonism. | DRD1 |
| DB00589 Lisuride | An ergot derivative that acts as an agonist. | HTR2B |
| DB04820 Nialamide | Withdrawn from the Canadian, US, and MAOA. | MAOA |
| DB01041 Thalidomide | It is used as an antineoplastic and antitumor agent. | TNF |

**Marker/mechanism:**

| marker/mechanism | DB01645 Genistein | It is used as an antineoplastic and antitumor agent. |
|------------------|-------------------|-----------------------------------------------------|
| DB00814 Trifusals | Trifusals appear to be equally effective. | NFKB1 |
| DB00877 Sirolimus | Sirolimus is a potent immunosuppressant. | MTOR |
| DB00811 Ribavirin | A nucleoside antimetabolite antiviral. | ADK |
| DB00811 Ribavirin | A nucleoside antimetabolite antiviral. | ENPP1 |
| DB00811 Ribavirin | A nucleoside antimetabolite antiviral. | IMPDH1 |
| DB00811 Ribavirin | A nucleoside antimetabolite antiviral. | NT5C2 |
| DB01037 Selegiline | It is used in newly diagnosed patients. | MAOA |
| DB01037 Selegiline | It is used in newly diagnosed patients. | MAOB |
| DB04841 Flunarizine | It is effective in the prophylaxis of migraines. | CACNA1G |
| DB02375 Myricetin | Not Available | PIK3CG |
| DB01055 Mimosine | An antineoplastic alanine-substituted. | TYR |
| DB03585 Oxyphenbutazone | Oxyphenbutazone was withdrawn from the market. | PLA2G2E |
Leukocyte transendothelial migration

Leukocyte migration from the blood into tissues is vital for immune surveillance and inflammation. During this process, the leukocytes bind to endothelial cell adhesion molecules (CAM) and then migrate across the vascular endothelium.

Adipocytokine signaling pathway

Increased adipocyte volume and number are positively correlated with leptin production, and negatively correlated with production of adiponectin.

Gap junction

Gap junctions contain intercellular channels that allow direct communication between the cytosolic compartments of adjacent cells. These channels permit the passage of small molecules including ions, amino acids, nucleotides, second messengers and other metabolites between adjacent cells.

Glycine, serine and threonine metabolism

Serine is derived from 3-phospho-D-glycerate, an intermediate of glycolysis, and glycine is derived from serine. Threonine is an essential amino acid, which animals cannot synthesize. In bacteria and plants, threonine is derived from aspartate.

Hematopoietic cell lineage

Blood-cell development progresses from a hematopoietic stem cell (HSC), which can undergo either self-renewal or differentiation into a multilineage committed progenitor cell: a common lymphoid progenitor (CLP) or a common myeloid progenitor (CMP).

MAPK signaling pathway

The mitogen-activated protein kinase (MAPK) cascade is a highly conserved module that is involved in various cellular functions, including cell proliferation, differentiation and migration.

mTOR signaling pathway

Purine metabolism

Purine metabolism

Purine metabolism

Tryptophan metabolism

Tryptophan metabolism

Type II diabetes mellitus

"Diabetogenic" factors including FFA, TNFalpha and cellular stress induce insulin resistance through inhibition of IRS1, modification of the cellular localization, and degradation represent the molecular mechanisms stimulated by them.

Tyrosine metabolism

VEGF signaling pathway

There is now much evidence that VEGFR-2 is a key mediator of VEGF-driven responses in endothelial cells and it is considered to be a crucial signal transducer in both physiologic and pathologic angiogenesis.
Leukocyte migration from the blood into tissues is vital for immune surveillance and inflammation. During this diapedesis of leukocytes, the leukocyte binds to endothelial cell adhesion molecules (CAM) and then migrates across the vascular endothelium.

Increased adipocyte volume and number are positively correlated with leptin production, and negatively correlated with production of adiponectin.

Gap junctions contain intercellular channels that allow direct communication between the cytosolic compartments of adjacent cells. Each gap junction contains a set of connexins that form a hexameric channel through which small molecules including ions, amino acids, nucleotides, second messengers and other metabolites can pass between adjacent cells.

Serine is derived from 3-phospho-D-glycerate, an intermediate of glycolysis, and glycine is derived from serine. Threonine is an essential amino acid, which animals cannot synthesize. In bacteria and plants, threonine is derived from aspartate.

Blood-cell development progresses from a hematopoietic stem cell (HSC), which can undergo either self-renewal or differentiation into a multilineage committed progenitor cell: a common lymphoid progenitor (CLP) or a common myeloid progenitor (CMP).

The mitogen-activated protein kinase (MAPK) cascade is a highly conserved module that is involved in various cellular functions, including cell proliferation, differentiation and migration. "Diabetogenic" factors including FFA, TNFalpha and cellular stress induce insulin resistance through inhibition of IRS1 function. Serine/threonine phosphorylation and cellular stress induce insulin resistance through inhibition of IRS1 function. Serine/threonine phosphorylation of IRS1 is a major mediator of VEGF-driven responses in endothelial cells and it is considered to be a crucial signal.
Leukocyte migration from the blood into tissues is vital for immune surveillance and inflammation. During this process, the leukocytes bind to endothelial cell adhesion molecules (CAM) and then migrate across the vascular endothelium.

Channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell. Each channel is formed by docking of two 'hemichannels', each containing six connexins, contributed by each cell.

Gap junctions contain intercellular channels that allow direct communication between the cytosolic compartments of adjacent cells. These channels facilitate the exchange of small molecules including ions, amino acids, nucleotides, second messengers and other metabolites between adjacent cells.

Serine is derived from 3-phospho-D-glycerate, an intermediate of glycolysis, and glycine is derived from serine. Threonine is an essential amino acid, which animals cannot synthesize. In bacteria and plants, threonine is derived from aspartate.

Blood-cell development progresses from a hematopoietic stem cell (HSC), which can undergo either self-renewal or differentiation into a multilineage committed progenitor cell: a common lymphoid progenitor (CLP) or a common myeloid progenitor (CMP).

The mitogen-activated protein kinase (MAPK) cascade is a highly conserved module that is involved in various cellular functions, including cell proliferation, differentiation and migration.

“Diabetogenic” factors including FFA, TNFalpha and cellular stress induce insulin resistance through inhibition of IRS1. Phosphorylation, interaction with SOCS, regulation of the expression, modification of the cellular localization, and degradation represent the molecular mechanisms stimulated by them.

There is now much evidence that VEGFR-2 is the major mediator of VEGF-driven responses in endothelial cells and it is considered to be a crucial signal transducer in both physiologic and pathologic angiogenesis.
Leukocyte migration from the blood into tissues is vital for immune surveillance and inflammation. During this process, the leukocytes bind to endothelial cell adhesion molecules (CAM) and then migrate across the vascular endothelium.

Gap junctions contain intercellular channels that allow direct communication between the cytosolic compartments of adjacent cells. These channels permit the direct transfer of small molecules including ions, amino acids, nucleotides, second messengers, and other metabolites between adjacent cells.

Blood-cell development progresses from a hematopoietic stem cell (HSC), which can undergo either self-renewal or differentiation into a multilineage committed progenitor cell: a common lymphoid progenitor (CLP) or a common myeloid progenitor (CMP).

"Diabetogenic" factors including FFA, TNFalpha, and cellular stress induce insulin resistance through inhibition of IRS1, modification of the cellular localization, and degradation. These represent the molecular mechanisms stimulated by them.
Gap junctions contain intercellular channels that allow direct communication between the cytosolic compartments of adjacent cells. This includes the exchange of small molecules such as ions, amino acids, nucleotides, second messengers, and other metabolites between adjacent cells.