|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| TRP name | Gland | Agent | Drug | Pathway | Related disease | Refs. |
| TRPA1 | Pancreas | 2-hydroxyestradiol ,  4-hydroxylated catechol estrogen,  Cinnamaldehyde,  allyl isothiocyanate (AITC),  hydrogen peroxide (H2O2),  4-hydroxynonenal (4-HNE),  Cyclopentenone prostaglandins (PGJ2),  methylglyoxal (MG),  HC030031,  AP-18 | Glibenclamide,  Methylglyoxal | collaborate with KATP channel blocking;  interfere with the transcription of PDX-1 | Affects cell cycle and cell migration in PDAC.  Promotes normal secretion of islets in diabetes.  Conduct pain in pancreatitis | (1-8) |
| Adrenal gland | Cinnamaldehyde,  allyl isothiocyanate,  β-eudesmol,  oleuropein aglycone |  |  |  | (9-11) |
| TRPC1 | Pancreas | Protein kinase C,  pressure | 2-aminoethoxydiphenyl borate (2-APB) | Mediate SOCE;  TRPC1 and Orai1 form cation channels that mediate calcium entry and are regulated by STIM1 via intermolecular electrostatic interaction. | In Type 2 Diabetes, SOCE is impaired and TRPC1 action is abnormal.  In PDAC, it promotes mechanical conduction, cell migration, and chemotactic neutrophils. | (12-17) |
| Salivary gland |  | Thapsigargin (Tg)，  SKF96365，  Febuxostat， |  | (18-20) |
| Adrenal gland | Muscarinic receptors |  | TRPC1 – TRPC4 heteromeric channels function as store-operated Ca2+ entry channels | Metabolic syndrome | (21, 22) |
| Mammary gland | Stromal interaction molecule 1 |  | TGF-β -induced EMT relies on Ca2+ entry through the TRPC1-STIM1 complex | Breast cancer | (23) |
| TRPC3 | Pancreas | GRP40,  phospholipase C,  PKC,  pyrazole-3 (Pyr3),  microRNA-26a (miR-26a) | Fasiglifam | Mediate SOCE | Upregulated in PDAC and cooperated with KCa3.1 channels to promote PSCs migration.  A target for prevention of pancreatic damage in acute pancreatitis. | (24-28) |
| Salivary Gland |  | Pyr3 | Mediate SOCE;  TRPC3-TRPC1 and Orai1 share a common ion channel and are regulated by STIM1. | A target for prevention of Sjögren syndrome | (29, 30) |
| Adrenal gland | GPCRs,  RTKs,  diacylglycerol |  | Mediate ROCC |  | (31) |
| Mammary gland | Arachidonic acid,  linolenic acid,  polyunsaturated fatty acids,  diacylglycerol |  | Mediate SOCE;  LPA-LPAR3-TRPC3 pathway |  | (32, 33) |
| TRPC4 | Pancreas | Ca2+ store depletion,  protein histidine phosphatase 1 (PHPT-1),  Leptin | Dexamethasone | Mediate SOCE | Mutations may occur in the congenital hyperinsulinism (CHI) | (34-36) |
| Adrenal gland | Histamine 1R,  leptin |  | Leptin-JAK-IP3K pathway |  | (37, 38) |
| Mammary gland | Englerin A | Digoxin | TRPC4-mediated Ca2+ influx induces proliferation and metastasis of cancer cells | Triple-negative breast cancers | (39) |
| TRPC5 | Adrenal gland | GPCRs,  RTKs |  | Gq/11-PLCβ pathway or Ca2+ store depleting pathway | metabolic syndrome | (22) |
| Mammary gland | Englerin A,  T5E3,  lenti-TRPC5-DN,  2-APB | Adriamycin | CaMKKβ/AMPKα/mTOR pathway;  TRPC5–NFATc3–P-gp pathway | Triple-negative breast cancers | (40-42) |
| TRPC6 | Pancreas | Anthranilic acid (ACA)  hypoxic condition,  microRNA-26a (miR-26a) | N-phenylcinnamides | Mediate SOCE | In Pancreatic cancer, TRPC6 is activated by hypoxia, which promotes migration of PSCs.  Therapeutic targets for acute pancreatitis | (28, 43, 44) |
| Adrenal gland | GPCRs,  RTKs,  diacylglycerol,  IP3R/RyanodineR coupling |  | Gq/11-PLCβ pathway;  Ca2+ store depleting pathway | metabolic syndrome | (22, 23) |
| Mammary gland | diacylglycerol |  | G protein-coupled receptor signaling pathway | Breast cancer | (45-47) |
| TRPM2 | Pancreas | Adenine dinucleotides (ADP ribose, NAD+, 2′-deoxy-ADPR)  H2O2, ROS,  Ca2+,  anthranilic acid (ACA),  temperature variation,  arachidonic acid,  PKA,  Alloxan,  GLP-1,  Ghrelin, | Epinephrine,  N-phenylcinnamides,  flufenamic acid,  clotrimazole, econazole,  Imeglimin | Activated by existing Ca2+, mediates the influx of cations such as Na+, activates VGCC. | In PDAC, ROS is sensed to promote the survival of tumor cells.  Diet-induced obesity and insulin resistance are promoted.  In diabetes, it mediates cell death.  Pancreatic cancer is promoted by PKC/MAPK pathway.  A potential treatment option for biliary pancreatitis. | (44, 48-57) |
| Salivary Gland | ROS，  ADP ribose,  NAD+,  Osmotic pressure | Tempol,  3-aminobenzamide,  TPL (4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl) | Mediate SOCE | Involved in post-radiation inflammatory damage and pSS | (18, 58) |
| TRPM3 | Pancreas | Pregnenolone sulfate,  Progesterone,  3,4-dihydro-N-(5-methyl-3-isoxazolyl)-a-phenyl-1(2H)-quinolineacetamide (CIM0216),  phosphatidylinositol 4,5-biphosphate (PIP2),  heat | Mefenamic acid,  nifedipine (Nif),  clotrimazole | Mediate cation influx such as Na+ and Zn2+, and activate VGCC | In insulinoma cells, it is indirectly involved in inducing signaling cascade. | (59-65) |
| TRPM4 | Pancreas | Ca2+,  adenine nucleotides,  glibenclamide,  PKA and PKC,  PIP2,  GLP-1 | 9-phenanthrol | Activated by extracellular Ca2+, mediates the influx of cations such as Na+, blocks KATP channel, activates VGCC. |  | (48, 52, 66) |
| Adrenal gland | PACAP |  | PACAP activate TRPM4 in PKC-dependent manner | Hypertension | (67) |
| Mammary gland | 9-phenanthrol,  aryloxyacyl-anthranilic 5 |  | TRPM4 may induce EMT through the β -catenin signaling pathway | Breast cancer | (68-70) |
| TRPM5 | Pancreas | Ca2+,  arachidonic acid,  PIP2,  PKC  G-protein coupled heterodimeric sweet taste receptor T1R2/T1R3,  GLP-1,  L-arginine | Stevioside | Activated by extracellular Ca2+, mediates the influx of cations such as Na+, blocks KATP channel, activates VGCC. | Dysfunction contributes to type 2 diabetes,  A therapeutic target of stevioside in type 2 diabetes mellitus,  Down-regulated as a biomarker in type 1 diabetes. | (48, 52, 66, 71-73) |
| TRPM7 | Pancreas |  |  |  | In pancreatic stellate cells of PDAC, it promotes mechanical conduction and neutrophil chemotaxis.  Biomarker and target in pancreatic adenocarcinoma, | (52, 74, 75) |
| Adrenal gland |  |  | activated pSTAT3 epigenetically regulates the transcription of TRPM7 | Obesity,  hypertension | (76) |
| Mammary gland | Carvacrol,  ginsenoside Rd | Waixenicin A | [Ca2+]i regulated by TRPM7 induce EMT and the cell cycle | Breast cancer | (77, 78) |
| TRPM8 | Pancreas | anthranilic acid (ACA),  menthol and icilin,  N-(3-aminopropyl)-2-{[(3-methylphenyl) methyl]oxy}-N-(2-thienylmethyl)benzamide hydrochloride salt | N-phenylcinnamides |  | Biomarker and target in pancreatic adenocarcinoma, | (44, 75) |
| Mammary gland | Menthol,  Frescolat ML,  Frescolat MAG,  Coolact P |  | Mediate VGCC | Breast cancer | (78) |
| TRPV1 | Pancreas | capsaicin |  |  | In type 1 diabetes, mediate insulin resistance and neurogenic inflammation,  Conduct pain in pancreatitis | (5, 8, 79, 80) |
| Adrenal gland | Capsaicin,  n-tert-butylcyclohexanol | Modafinil |  | chronic fatigue syndrome,  Neuropathic pain,  severe sepsis | (81-83) |
| Mammary gland | Capsaicin,  reactive oxygen species | Docetaxel,  tramadol |  | Breast cancer | (84, 85) |
| TRPV2 | Pancreas | heat,  mechanical stretch,  osmotic swelling,  phosphatidylinositol 3 kinase (PI3K),  anti-aging gene *Klotho* | Tranilast,  Nifedipine,  Diazoxide,  somatostatin | Translocation from the cytoplasm to the membrane | In cystic fibrosis, dysregulation of the TRPV2 signaling pathway leads to defective macrophage function, leading to chronic infection. | (26, 48, 86-88) |
| Mammary gland | LL-37 |  | PI3K/AKT-TRPV2 pathway | Breast cancer | (89) |
| TRPV3 | Mammary gland |  | Lapatinib |  | Breast cancer | (98) |
| TRPV4 | Pancreas | heat,  mechanical stretch,  osmotic swelling,  extracellular signal-regulated kinase 1/2（ERK1/2） | 4α-phorbol 12,13-didecanoate (4-αPDD),  GSK1016790A |  | In pancreatic stellate cells of PDAC, it promotes mechanical conduction and neutrophil chemotaxis.  Mediate pressure-induced pancreatitis.  Therapeutic targets for type 2 diabetes | (48, 52, 74, 90-93) |
| Salivary Gland | Heat,  Osmotic pressure,  4α-phorbol-12,13 didecanoate, | GSK1016790A |  |  | (18) |
| Mammary gland | 4a-PDD,  GSK1016790A,  body osmolarity,  mechanosensation,  temperature sensing |  | Activation of TRPV4 induces BK channel opening and claudin protein downregulation;  TRPV4 can deform cells through actin depolymerization and V-ASP phosphorylation | Lactation deficiency,  Breast cancer | (94, 95) |
| Sweat gland |  |  |  |  | (96) |
| TRPV5 | Pancreas | Estradiol |  |  |  | (97) |
| Mammary gland |  | Lapatinib |  | Breast cancer | (98) |
| TRPV6 | Pancreas | Estradiol |  |  | In pancreatic cancer, TRPV6 mediates cell proliferation, invasion and migration, and is a biomarker. | (99, 100) |
| Mammary gland | Diacylglycerol | Lapatinib,  tamoxifen | Ca2+ influx mediated by TRPV6 activation induces keratinocyte differentiation | Breast cancer | (101) |
| TRPP2 | Gallbladder | IP3R |  | PLC-IP3 pathway |  | (102) |

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