| Cancer Type (alphabetical) | GSK-3 Isoform | Function | Type of Study | Reference |
|---------------------------|---------------|----------|--------------|-----------|
| Bladder cancer            | GSK-3β        | Prognostic marker and therapeutic target. Inhibition of GSK-3 resulted in apoptosis. GSK-3 was serving as a tumor promoter. Aberrant nuclear accumulation of GSK-3β in 62% and 91% of noninvasive and invasive human urothelial carcinomas. GSK-3β nuclear staining was associated with poor prognosis. | Human tumor samples and in vitro | [1] |
| Brain cancer              | GSK-3β        | Brain-derived neutrophilic factor/TrkB induced phosphorylation of GSK-3β which resulted in its inactivation and contributed to chemotherapeutic drug resistance. GSK-3β was acting as a tumor suppressor. | In vitro | [2] |
| Brain cancer              | GSK-3β        | Inhibition of AKT mediated phosphorylation of GSK-3β by an AKT inhibitor reduced cell growth. GSK-3β was acting as a tumor suppressor. | In vitro | [3] |
| Brain cancer              | GSK-3β        | GSK3β was linked with increased expression of TP53 and p21<sup>cip1</sup> in glioblastoma cells with wild-type p53 and with decreased Rb phosphorylation and expression of cyclin-dependent kinase 6. Treatment with GSK-3 inhibitor AR-A014418 sensitized GMB cells to temozolomide. GSK-3β was functioning as a tumor promoter. | Human tumor samples, in vitro studies. | [4] |
| Brain cancer              | GSK-3β        | Expression of high levels of GSK-3β was associated with poor prognosis. Treatment with a combination of temozolomide other drugs used to treat brain cancer improved prognosis. GSK-3β was acting as a tumor promoter. | In vitro, in vivo, clinical trial, 7 patients in clinical study | [5] |
| Brain cancer              | Suppression of GSK-3β by miR-101 restored sensitivity to temozolomide in brain cancer. | In vitro, in vivo | [6] |
| Tumor Type       | Gene      | Effect                                                                 | Sample Details                                                                 | References |
|------------------|-----------|------------------------------------------------------------------------|--------------------------------------------------------------------------------|------------|
| Breast cancer    | GSK-3β    | GSK-3β was acting as a tumor promoter.                                 |                                                                                 | [7]        |
|                  |           | GSK-3β expression was associated with MCL1 expression and inactivation. |                                                                                 | [7]        |
|                  |           | GSK-3β was acting as a tumor suppressor.                                |                                                                                 | [7]        |
| Breast cancer    | GSK-3β    | High GSK-3β expression was associated with reduced distant relapse-free survival (DRFS). Tissue microarrays of 1,686 patients, low expression in 36%, high expression in 38%. GSK-3β was acting as a tumor promoter. | Human tumor samples.                                                              | [8]        |
| Breast cancer    | GSK-3β    | Inhibition of GSK-3β inhibited tumor growth. GSK-3β was acting as a tumor promoter. | In vitro, in vivo                                                                | [9]        |
|                  |           | miR-34a binding to the PRKD1 suppressed cancer stemness through the GSK3β-catenin signaling pathway. GSK-3 was acting as a stemness suppressor. | In vitro, in vivo                                                                | [10]       |
| Breast cancer    | GSK-3β    | GSK-3 inhibition by the human THUMP domain-containing protein 1 (THUMPD1)/AKT resulted in SNAIL activation. GSK-3 was acting as a tumor suppressor. | In vitro, in vivo                                                                | [11]       |
| Cervical cancer  | GSK-3β    | High expression of forkhead box M1 (FOXM1) transcription factor was associated with poor prognosis and it activated AKT and inactivated GSK-3β which resulted in higher SNAIL activity and poor prognosis. GSK-3β was acting as a tumor suppressor. | In vitro, human tumor samples                                                    | [12]       |
| Colorectal cancer| GSK-3β    | Nuclear accumulation of GSK-3β was observed in 39% (33/85) and associated with short overall survival, larger tumor size, distant metastasis and loss of membranous β-catenin. This loss was present in 37% and associated with poor survival. Nuclear expression of GSK-3β and loss of membrane β-catenin were present in CRC with worse | Human tissue microarrays                                                           | [13]       |
| Tumor Type                  | GSK-3β Activity                                                                 | Additional Details                                                                 | Ref.   |
|-----------------------------|---------------------------------------------------------------------------------|-----------------------------------------------------------------------------------|--------|
| Colorectal cancer           | GSK-3β increased NF-κB expression, inhibition of GSK-3β inhibited growth. GSK-3β was serving as a tumor promoter. | Human tumors and in vitro studies                                                  | [14]   |
| Colorectal cancer           | CXCL5 induced ERK/ELK1/SNAIL and AKT/β-catenin, inhibited GSK-3β and promoted cancer metastasis. GSK-3β was serving as a tumor promoter. | In vitro, in vivo. chemokine ELISA arrays from CRC patients                     | [15]   |
| Gastric cancer              | P-GSK-3β (T216, active) was expressed in 46% of cases and associated with a good prognosis. GSK-3β was serving as a tumor suppressor. | Human tissue arrays containing 281 gastric cancer specimens and in vitro studies   | [16]   |
| Gastric cancer              | Higher GSK-3β levels were associated with a better prognosis. GSK-3β was serving as a tumor suppressor. | Gene expression profiling in 63 tumors                                             | [17]   |
| Hepatocellular carcinoma    | 59-P-GSK-3β was over-expressed in 50% of tumor tissues and was associated with a poor prognosis. GSK-3β was serving as a tumor suppressor. | 178 patients with HCC after curative partial hepatectomy                          | [18]   |
| Hepatocellular carcinoma    | Protein arginine methyltransferase 9 (PRMT9) activation of PI3K/AKT resulted in decreased GSK-3β activity and increased SNAIL signaling. GSK-3β was serving as a tumor suppressor | In vitro, in vivo, human tumor samples                                            | [19]   |
| Laryngeal Cancer            | Suppression of miR-27a interaction with GSK-3β altered laryngeal differentiation in response to retinoic acid treatment. GSK-3β. GSK-3β was serving as a tumor suppressor. | In vitro, human tumor samples                                                    | [20]   |
| Laryngeal Cancer            | Alterations in the Tat-interacting protein 30 (TIP30) tumor suppressor expression resulted in activation of AKT, inactivation of GSK-3β, deregulation of β-catenin and poor prognosis. Low TIP30 staining was observed in 43.8% of patient samples while minimal TIP30 staining in non-tumor cells was observed | In vitro, human tumor samples, 105 laryngeal carcinomas                          | [21]   |
| Tumor Type | GSK-3β and GSK-3α | Description | Additional Details |
|------------|-------------------|-------------|--------------------|
| Leukemia   | GSK-3β and GSK-3α | Genetic deletion of GSK-3β in mice led to myelodysplastic disease syndrome (MDS), subsequent deletion of GSK-3α led to AML. Different roles of GSK-3α and GSK-3β in MDS progression into AML. GSK-3α and GSK-3β were acting as tumor suppressors. | Gene knock out studies in mice, gene profiling. |
| Leukemia   | GSK-3α and GSK-3β | GSK-3 stimulated acute lymphoblastic leukemia with mixed-lineage leukemia gene (MLL) growth by destabilization of the cyclin-dependent kinase inhibitor p27(Kip1). GSK-3 promoted growth, GSK-3 was acting as a tumor suppressor. | In vitro, in vivo, in human AML patients |
| Leukemia   | GSK-3α             | GSK-3α was a target in AML. GSK-3α was serving as a tumor promoter. | Chemical small molecule screening, in vitro, in vivo |
| Leukemia   | GSK-3α and GSK-3β | GSK-3α and GSK-3β phosphorylation leading to their inhibition correlated with poor prognosis. S21-P-GSK3α and S9-P-GSK-3β positively correlated with phosphorylation of AKT, BAD, and P70S6K, and negatively correlated with β-catenin and FOXO3A. GSK-3α and GSK-3β were serving as tumor suppressors. | In vitro, human patient samples, reverse phase protein analysis (RPPA) in a cohort of 511 AML patients |
| Leukemia   | GSK-3β and GSK-3α | (GSK-3β) expression was elevated in AML-NK cells and decreased their activity as NK cells. Inhibition of GSK-3 restored NK cytotoxicity by increasing TNF-α production. GSK-3 was serving as a tumor suppressor. | In vitro, in vivo |
| Lung cancer| GSK-3β             | High levels of TGFβ induced integrin β3/AKT, inhibited GSK-3β activity, and induced SNAIL activity and promoted metastatic potential. GSK-3β was acting as a tumor suppressor. | In vitro, in vivo, clinical data base |
| Tumor Type     | Protein(s) Involved | Description                                                                 | Setting                           | Reference |
|---------------|--------------------|-----------------------------------------------------------------------------|-----------------------------------|-----------|
| Lung cancer   | GSK-3α             | CREB induced GSK-3α which promoted lung cancer cell growth. GSK-3α was acting as a tumor promoter. | In vitro, in vivo, human tumors   | [28]      |
| Lung cancer   | GSK-3α and GSK-3β | Tivantinib was initially thought to be a c-MET inhibitor. Subsequently, GSK-3α and GSK-3β were determined to be targets of tivantinib in lung cancer cells. GSK-3α and GSK-3β were acting as tumor promoters. | In vitro                          | [29]      |
| Lung cancer (non-small cell) | GSK-3α and GSK-3β | GSK-3β levels were elevated in 41% of human NSCLC samples and led to increased proliferation in comparison to normal tissues. GSK-3β was acting as a tumor promoter. | In vitro, in vivo, 29 human tumor specimens | [30]      |
| Melanoma      | GSK-3α             | Elevated expression of GSK-3α in 72% of samples, but not GSK-3β. 80% of tumors expressed elevated levels of catalytically active phosphorylated GSK-3α (Y279-P-GSK-3α), but not phosphorylated GSK3β (Y216-P-GSK-3β). Inhibition of GSK-3α induced apoptotic death to retard tumorigenesis. GSK-3α was acting as a tumor promoter. | In vitro, in vivo, 39 human tumor samples. | [31]      |
| Melanoma      | GSK-3β             | Neuron navigator 2 (NAV2) inhibited GSK-3β which increased β-catenin and SNAIL activity. GSK-3β was acting as a tumor suppressor. | In vitro, in vivo, human tumor samples | [32]      |
| Myeloma       | GSK-3α and GSK-3β | Treatment with Thiadiazolidinone (TDZD; a GSK-3 non-competitive inhibitor) resulted in Forkhead transcription factors (FOXO3a) activation. TDZD induced apoptosis in primary myeloma cells but not in normal CD34 cells. GSK-3 was acting as a tumor promoter. | In vitro, human myeloma cells, primary hematopoietic cells | [33]      |
| Neuroblastoma | GSK-3β             | Inhibition of GSK-3β with 9-ING-41 suppressed growth via inhibition of XIAP. GSK-3β was acting as a tumor promoter. | In vitro, in vivo                 | [34]      |
| Oral Cancer   | GSK-3β             | AKT and GSK-3β expression was associated with a poor prognosis. Phosphorylated Human tumor specimens (118 patient samples) | In vitro                           | [35]      |
| Cancer Type                     | Gene Expression | Description                                                                 | Reference |
|--------------------------------|-----------------|-----------------------------------------------------------------------------|-----------|
| Oral squamous cell cancer      | GSK-3α and GSK-3β | Inactive GSK-3β was associated with cervical lymph node (CLN) metastasis. GSK-3β was acting as a tumor suppressor. | In vitro, 179 human patient samples [36] |
| Osteosarcoma                   | GSK-3β          | The P2X7 receptor promoted P3K/AKT and β-catenin activity and inhibited GSK-3β. GSK-3β was acting as a tumor suppressor. | In vitro, in vivo, human tumor samples [37] |
| Ovarian cancer                 | GSK-3β          | GSK-3 expression was associated with increased tumor growth, poor prognosis and chemoresistance. GSK-3 was functioning as a tumor promoter. | In vitro, in vivo, 71 human tumor samples [38] |
| Ovarian cancer                 | GSK-3β          | Constitutively active GSK-3β induced entry into the S phase, increased cyclin D1 expression and facilitated the proliferation of ovarian cancer cells. GSK-3 inhibition prevented the tumor formation of the tumor in nude mice. GSK-3 was acting as a tumor promoter. | In vitro, in vivo [39] |
| Pancreatic cancer              | GSK-3α and GSK-3β | GSK-3 promoted NF-κB activity. GSK-3β may have been the more important isozyme in regulating in NF-κB. GSK-3β was acting as a tumor promoter. | Human tumors and in vitro studies [40] |
| Pancreatic cancer              | GSK-3β          | Inhibition of GSK-3 activity caused stabilization of β-catenin activity. GSK-3β expression was a strong prognosticator in PDAC. High expression of GSK-3β was associated with better survival. PDAC Patients with GSK-3β expression > than the third quartile (Q3) had a 46% reduced risk of dying of | Immuno-fluorescence on human tumor microarray from 163 patients [41] |
| Tumor Type                  | Isoforms       | Description                                                                 | Ref.            |
|-----------------------------|----------------|-----------------------------------------------------------------------------|-----------------|
| Prostate Cancer             | Both           | GSK-3α and GSK-3β were detected at higher levels in 25/79 and 24/79 tumor samples respectively, in comparison to normal prostatic tissue. GSK-3α was elevated in low Gleason sum score tumors while GSK-3β was expressed in high Gleason tumors, and both isoforms correlated with high expression of the androgen receptor (AR). Treatment with a GSK-3 inhibitor suppressed proliferation. GSK-3 was functioning as a tumor suppressor. | In vitro, in vivo and in 79 human tumor samples [42] |
| Renal Cell Carcinoma        | GSK-3β         | miR-199a downregulated GSK-3β and suppressed growth of RCC. GSK-3β was acting as a tumor promoter. | Human tumor samples and in vitro. [43] |
| Renal Cell Carcinoma        | GSK-3β         | miR-203a targeting GSK-3β was detected at high levels in RCC and associated with a poor prognosis. miR-203a was overexpressed in 27 of 40 (68%) RCC patient samples. GSK-3β was acting as a tumor suppressor. | In vitro, 40 RCC tumor samples. [44] |
| Thyroid carcinomas          | GSK-3α and GSK-3β | Junctional adhesion molecule A (JAM-A) was downregulated in anaplastic thyroid carcinomas and resulted in increased GSK-3α, GSK-3β, and TP53 phosphorylation. | Human tissue arrays [45] |
| Tongue (oral) cancer        | GSK-3β         | GSK-3β was detected at lower levels in 39% of patient samples in comparison to normal epithelial cells and was associated with reduced survival. In contrast, cyclinD, a target of GSK-3β was detected at higher levels in 65.9% of samples and was associated with a poor prognosis. GSK-3β was acting as a tumor suppressor. | 41 Human tissue samples, immunohistochemistry. [46] |

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| Molecule | Result | Reference |
|----------|--------|-----------|
| Lithium chloride | Lithium chloride inhibited GSK-3 which suppressed proliferation in Eca-109 human esophageal cancer cells. GSK-3 was functioning as a tumor promoter. | [1] |
| AR-A014418 | Treatment with GSK-3β inhibitor AR-A014418 sensitized GMB cells to temozolomide. GSK-3β was functioning as a tumor promoter. | [2] |
| BIO | BIO induced apoptosis, cell cycle arrest in glioblastoma cells. | [3] |
| Tideglusib, AZD1080, and BIO | These GSK-3 inhibitors suppressed GSK-3 mediated phosphorylation of substrates involved in proliferation such as c-MYC in KRAS-dependent tumors. | [4] |
| ABC1183 | ABC1183 inhibited GSK-3α and GSK-3β. ABC1183 inhibited the growth of a numerous cancer cell lines by decreasing cell survival by inducing G2/M arrest by altering GSK-3 and WNT/β-catenin signaling. | [5] |
| SB21673 | SB21673 inhibits GSK-3α and GSK-3β. c-JUN degradation was enhanced by SB21673 and breast cancer tumorigenesis was inhibited. | [6] |
| SB216763, GSK inhibitor XIII, and AR-A014418 | SB216763 and the GSK inhibitor III suppressed AR-transcriptional activity as well as AR expression in prostate cancer cells. In contrast, AR-A014418 stimulated proliferation. | [7] |
| Lithium chloride, SB216763, and GSK-3 IX (BIO) | Treatment of MLL LSC with GSK-3 inhibitors resulted in reversion of MLL LSCs to a pre-LSC stage and reduced their growth. | [8] |
| GSK-3 IX (BIO) and SB216763 | Inhibition of GSK-3 suppressed maintenance of MLL leukemia. | [9] |
| GSK3-IX | The GSK-3α and GSK-3β inhibitor GSK3-IX inhibited MLL leukemia maintenance and growth. | [9] |
| GS87 | GS87 is a novel GSK-3 inhibitor that was isolated upon screening for more optimal effective inhibitors that induce AML differentiation. GS87 inhibits both GSK-3α and GSK-3β. | [10] |
| Thiazolidinone (TDZD) | TDZD is a non-competitive inhibitor of GSK-3. Treatment of primary myeloma cells with TDZD resulted in apoptosis in primary myeloma cells but not in normal CD34 cells. | [11] |
| Combination of GSK-3 inhibitors with immunotherapy | | |
| SB415286 and CD8+ CTLs | GSK-3 inhibitor treatment of CD8+ T cells inhibited TBX21 (T-bet) expression and decreased PD-1 expression and increased cytolytic T cell responses. | [12] |
| LY2090314, tideglusib, SB415286 GSK-3 inhibitors and NK cells | Treatment of NK cells with GSK-3 inhibitors LY2090314, tideglusib or SB415286, increased TNF-α levels and cytotoxicity towards AML cells. | [13] |
| SB216763 and GMB-specific CAR-T cells | Treatment with GSK-3 inhibitor of antigen specific CAR-T cells lowered PD-1 expression and promoted long term survival, memory and tumor elimination. | [14] |
| Enzastaurin | Enzastaurin was initially developed as a PKC-β inhibitor. One of its targets is GSK-3. It has been examined in clinical | [15] |
studies with various cancer types, often in combination with bevacizumab.

| SB415286 or LiCl and TRAIL | Inhibition of GSK-3 enhanced the induction of apoptosis mediated by TRAIL in gastric cancer cells. |
|-----------------------------|--------------------------------------------------------------------------------------------------|

**Combination of GSK-3 inhibitors with chemotherapy**

| CHIR9021 and paclitaxel | Effects of combination of the GSK-3 inhibitor CHIR9021 and paclitaxel on lung cancer. |
|--------------------------|--------------------------------------------------------------------------------------|

| SB415286, RO 318220, lithium chloride and paclitaxel | SB415286 inhibits both GSK-3α and GSK-3β. RO 318220 inhibits PKC and GSK-3. More mitotic arrest was observed when GSK-3 inhibitors were combined with paclitaxel than in the absence of the GSK-3 inhibitors. |
|------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|

| LY2090314 and nab-paclitaxel | LY2090314 suppressed TAK1 levels. LY2090314 plus nab-paclitaxel combined treatment increased the survival of mice in orthotopic pancreatic tumor models. |
|-------------------------------|------------------------------------------------------------------------------------------------------------------|

| AR-A014418, TDZD-8, 9-ING-41 and Camptosar | AR-A014418, TDZD-8, and 9-ING-41 suppressed neuroblastoma growth, 9-ING-41 was most effective. The combination of 9-ING-41 and Camptosar was effective in suppressing tumor growth of xenografts. |
|------------------------------------------|------------------------------------------------------------------------------------------------------------------|

| 9-ING-41, 9-ING-87 and irinotecan | Treatment with GSK-3 inhibitors and the chemotherapeutic drug irinotecan reduced drug resistance in a breast cancer PDX model. |
|-----------------------------------|------------------------------------------------------------------------------------------------------------------|

| AR-A014418 and gemcitabine | GSK-3 inhibitor suppressed some of the genes induced by gemcitabine that are involved in drug resistance of PDAC cells. |
|---------------------------|------------------------------------------------------------------------------------------------------------------|

**Combination of GSK-3 inhibitors with other inhibitors or agonists**

| 9-ING-41 and either chloroquine and bafilomycin | 9-ING-41 have been examined either by itself or in combination with autophagy inhibitors chloroquine and bafilomycin on RCC lines |
|----------------------------------------|------------------------------------------------------------------------------------------------------------------|

| lithium chloride, SB216763, inhibitor IX (BIO) and NF-κB inhibitors PDTC parthenolide, or BAY 11-7082 and chemotherapeutic drugs. | Combining GSK-3, NF-κB inhibitors and certain chemotherapeutic drugs resulted in increased osteosarcoma death both in vitro and in animal xenograft studies. |
|-------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|

| AR-A014418 and Troglitazone | Treatment of prostate cancer cells with GSK-3 inhibitor and PPAR agonist suppressed NF-κB activity increased cell death. |
|-------------------------------|------------------------------------------------------------------------------------------------------------------|

| 6BIO and AR-ASO | 6BIO improved the targeting of antisense oligonucleotide (ASO) inhibitor and resulted in increased inhibition of AR signaling. |
|-----------------|------------------------------------------------------------------------------------------------------------------|

| AR-A014418, 5-chloro-2,4-dihydroxypyridine (CDHP) and 5FU | GSK-3β inhibitor AR-A014418 induced head and neck cancer stem cells [CD44 (high)/ESA (low)] to undergo mesenchymal-to-epithelial transition (MET) back to CD44 (high)/ESA (high) cells. Furthermore, this combined treatment induced the cells to differentiate. |
|----------------------------------------------------------|------------------------------------------------------------------------------------------------------------------|

**Inhibitors originally developed to target other signaling molecules which also target/inhibit GSK-3 activity**

| Tivantinib | Tivantinib was initially developed as a c-MET inhibitor but it was subsequently determined to target GSK-3α and GSK-3β in lung cancer cells. |
|------------|------------------------------------------------------------------------------------------------------------------|

| GDC-0941 | GDC-0941 is a PI3K inhibitor. It increased the sensitivity of GBM cells to radiotherapy and reduced chemoresistance to temzolomide. |
|----------|------------------------------------------------------------------------------------------------------------------|

| AktX, Lithium chloride | AktX is an AKT inhibitor. The effects AktX and lithium chloride on brain cancer cells were determined. AktX |
|-----------------------|------------------------------------------------------------------------------------------------------------------|
| **Zidovudine** | Zidovudine is an anti-viral drug. Treatment of drug resistant pancreatic cells with zidovudine re-sensitized the cells to gemcitabine. Zidovudine suppressed the AKT/GSK-3/SNAIL pathway. [31] |
| **Doxazosin** | Doxazosin is an antihypertensive drug. It was observed to inhibit PI3K/AKT signaling in GBM by upregulation of active GSK-3β and TP53. Treatment with doxazosin was associated with low neurotoxicity. [32] |
| **Erlotinib, SU11274, XAV939, everolimus** | EGFR, c-MET, WNT, mTORC1 blocker treatments in various combinations overcame drug resistance of NSCLC cells. [33] |
| **miR-101, temozomide** | Suppression of GSK-3β by miR-101 inhibits GSK-3β expression and restored sensitivity to temozomide in brain cancer cells. [34] |

**Nutraceuticals/Natural Products which may alter GSK-3 activity**

| **Curcumin** | Curcumin suppressed Syk activity which inhibited AKT and induced GSK-3 activity and inhibited B lymphoma growth. [35] |
| **Curcumin and Tetrahydrocurcumin** | Curcumin induced GSK-3 activity and inhibited WNT/β-catenin signaling and suppressed azoxymethane-induced colon carcinogenesis. [36] |
| **Berberine** | Berberine inhibited AKT which resulted in GSK-3 activity in melanoma cells treated with alpha melanocyte stimulating hormone (α-MSH). Berberine suppressed induction of microphthalmia-associated transcription factor (MITF) and tyrosinase activity. [37] |
| **Berberine and lapatinib** | Combining berberine with the dual EGFR and HER receptor inhibitor lapatinib decreased lapatinib-resistance of breast cancer cells. Treatment with berberine and lapatinib induced higher levels of ROS and increased GSK-3 activity and decreased c-MYC levels. [38] |
| **Resveratrol** | Resveratrol increased GSK-3 activity which suppressed WNT/β-catenin signaling and decreased invasion and migration in breast cancer cells. [39] |
| **Apocynin** | The effects of apocynin and resveratrol on pancreatic cancer cells were mediated by decreased levels of phosphorylated GSK-3β and ERK1/2 present in the nucleus. [40] |
| **Microsclerodermin A** | Microsclerodermin A inhibited NF-κB activity in PDAC. Potential involvement of GSK-3. [41] |
| **Caffeine** | Caffeine inhibited JB6 mouse epidermal cells proliferation by suppression of AKT and activation of GSK-3. [42] |
| **Indirubin** | Indirubin inhibited GSK-3 and cyclin dependent kinase activity in leukemia cells. Indirubin may have competed for the ATP binding sites in the kinase domains of the proteins. [43] |
| **Tetrandrine** | Tetrandrine inhibited AKT which resulted in GSK-3 activation in colon cancer cells. [44] |
| **Differentiation-inducing factor-1** | Differentiation-inducing factor-1 inhibited AKT and induced GSK-3 activity in colon cancer cells which resulted in apoptosis. [45] |
The effects of dioscin on proliferation were examined with osteosarcoma cells. Dioscin inhibited AKT activity which resulted in GSK-3 activation. [46]

Nimbolide inhibited PI3K activity in oral cancer cells which resulted in increased GSK-3 activity and inhibition of cytoprotective autophagy. [47]

Oridonin increased GSK-3 expression which resulted in c-MYC degradation and growth inhibition and apoptosis in leukemia cells. [48]

Apicidin resistance in HCC may result from decreased GSK-3 activity and increased WNT/β-catenin activity. [49]

Wogonin inhibits cell growth and induces apoptosis by inhibiting the expression of GSK-3β in lung cancer cells. [50]

Sulforaphane treatment resulted in induction of miR-19 and suppression of GSK-3β and increased WNT/β-catenin expression. [51]

Butyrate induced ROS and miR-22/SIRT1 pathway in hepatic cancer cells which resulted in suppression of AKT, increased PTEN and GSK-3 and apoptosis. [52]

Ursolic acid treatment of ovarian carcinoma cells with ursolic acid resulted in inhibition of GSK-3 and induction of apoptosis. [53]

Gambogenic acid stimulated GSK-3 activity and inhibited growth in GBM cells. [54]

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