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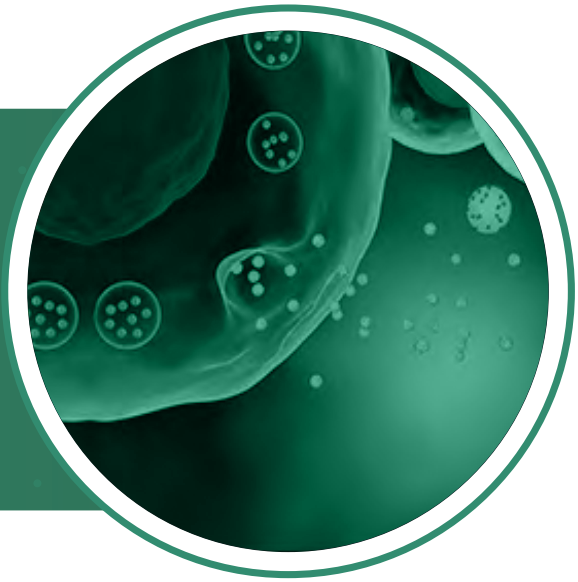
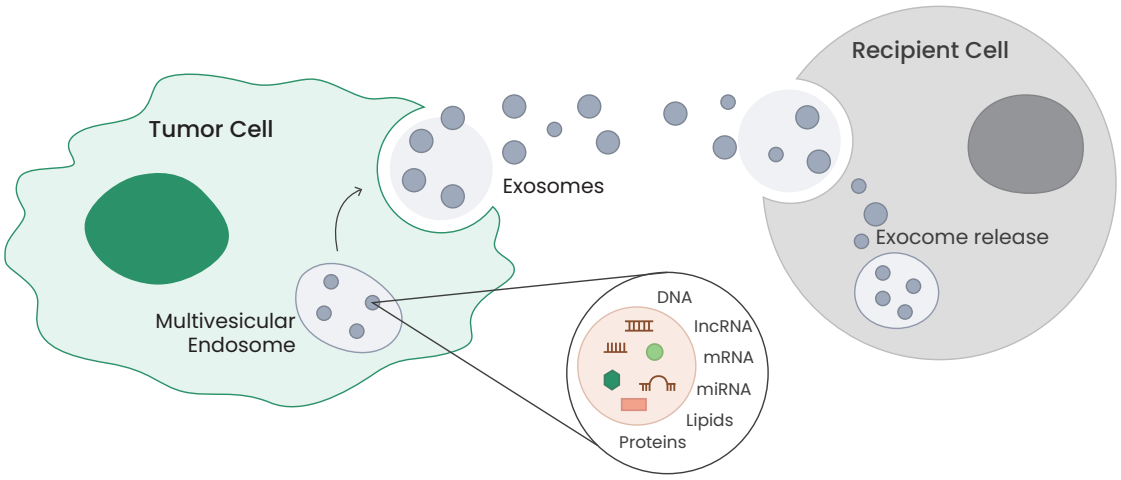
Tumor Exosomes: A Messenger for Cancer Progression



Exosomes are extracellular vesicles ranging from 30 to 150 nm in diameter that are released from various types of cells, including tumor cells. They can induce apoptosis, modulate the immune system, and function as biomarkers for diagnosis. In addition, as an important component of cell-to-cell communication, exosomes can regulate the tumor microenvironment and are involved in the development, progression, and metastasis processes of numerous cancers[1,2].

Tumor-derived exosomes contain proteins, nucleic acids, lipids, and metabolites that can act as effective messengers in the communication between tumor cells and various types of cells, including immune cells, vascular endothelial cells, and mesenchymal cells. Communication among these cells has important effects on tumor biological activities, such as immune regulation, angiogenesis, and epithelial-mesenchymal transition (EMT), which further influence tumor cell growth, proliferation, and metastasis[3].



Exosomes and Tumor Immune Response

Tumor exosomes may play a dual role in immune regulation. On the one hand, exosomes exert an important effect in promoting antitumor immune responses through their immune activity. Some exosomes released by tumor cells carry tumor-specific antigens, such as CEACAM5, HER2, mesothelin, CD24, and EpCAM, which can activate cytotoxic T cell responses, and induce protective antitumor immune responses. Tumor-derived exosomes can also directly activate NK cells by expressing the stress protein HSP70, which helps elicit antitumor immune responses and promote tumor regression.

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On the other hand, some evidence suggests that tumor-derived exosomes can promote cancer progression by suppressing the host immune response. The mechanisms include inhibition of immune cell effectors and activation of suppressor immune cells. Some tumor-derived exosomes carry PD-L1, with IFN-γ increasing the amount of PD-L1 on these exosomes. PD-L1 binds to PD-1 through its extracellular structural domain, which inactivates CD8 T cells, thereby inhibiting CD8 T cell function and promoting tumor growth. Exosomes may also suppress T cell receptor activity or regulate effector T cell transcriptome. In addition, TGF-β from tumor-derived exosomes exerts an inductive effect on Treg cells and blocks IL-2-mediated NK cell activation and decreases NK cell activation receptor expression[3-5]. Overall, the role of tumor-derived exosomes in the immune response is complex and related to the local microenvironment generated by the tumor itself.

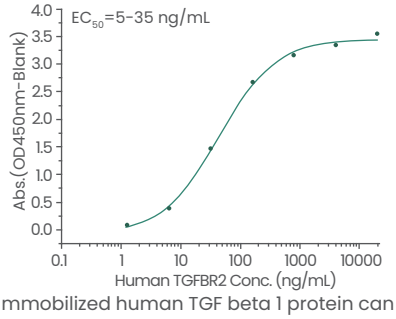
As a leading global supplier of bioreagents and CRO services for the biopharmaceutical field, Sino Biological offers a comprehensive collection of high-quality recombinant proteins and corresponding antibodies to support research on exosomes and tumor immune response.

(1)CEA, HER2, mesothelin, CD24, and EpCAM: Tumor-specific antigens

Cat#	Proteins	Purity	Expression Host
11077-H02H	CEACAM5 (Human)	≥95% (SEC-HPLC)	HEK293 Cells
10004-H08H	HER2 (Human)	>90% (SEC-HPLC)	HEK293 Cells
13128-HNCH	Mesothelin (Human)	≥95% (SEC-HPLC)	HEK293 Cells
11030-H02H	CD24 (Human)	>92%	HEK293 Cells
10694-H08H	EpCAM (Human)	≥90% (SEC-HPLC)	HEK293 Cells

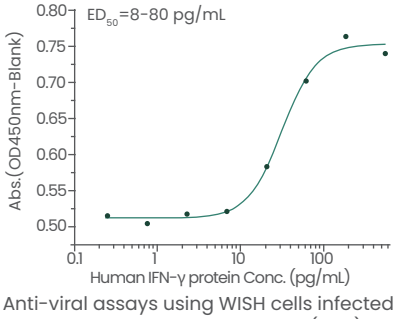
(2)TGF-β, IFN-γ, PD-L1: Associated with immunosuppression

Human TGF-β1 Protein
Cat#: 10804-H08H 16 Citations



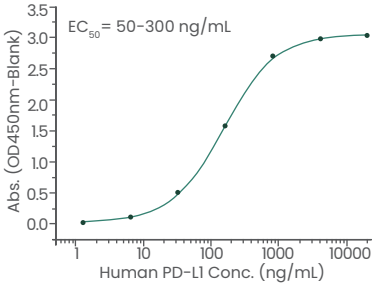
Immobilized human TGF beta 1 protein can bind human TGFBR2 protein.

Human IFN-γ Protein
Cat#: 11725-HNAE HPLC Verified



Anti-viral assays using WISH cells infected with vesicular stomatitis virus (VSV).

Human PD-L1 Protein
Cat#: 10084-H08H-B 8 Citations



Immobilized human PD-1 (Cat#: 10377-H03H) can bind human PD-L1.

Exosomes and Angiogenesis

Cancer progression is closely associated with angiogenesis. Nascent capillaries provide nutrients, oxygen, and growth factors to the tumor and play an important role in tumor cell proliferation and metastasis. Exosomes released from tumor cells, which are involved in tumor angiogenesis, can be taken up by vascular endothelial cells, thereby stimulating angiogenesis. Under hypoxic conditions, exosome production is enhanced. This process is associated with the pro-angiogenic secretory group of endothelial cells[3].

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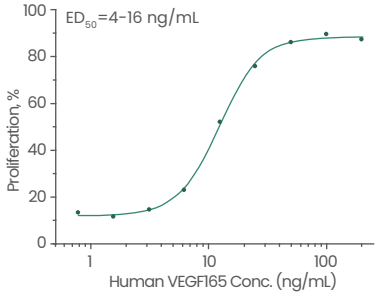
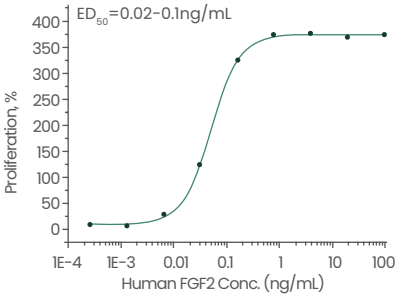
Evidence suggests that exosomes play an important role in angiogenesis. Myeloid leukemia-derived exosomes regulate angiogenesis through the enrichment of vascular cell adhesion molecule-1 (VCAM-1) and intercellular adhesion molecule-1 (ICAM-1). Skin cancer cells secrete exosomes that deliver EGFR to endothelial cells and promote angiogenesis. Moreover, certain tumor-derived exosomes can drive the secretion of pro-angiogenic cytokines, including FGF, G-CSF, TNF-α, VEGF, and more[6]. Among them, VEGF-A, a member of the VEGF family, plays a key role in tumor angiogenesis. Other members of this family, which include VEGF-B, VEGF-C, VEGF-D, VEGF-E, and PlGF, show affinity to VEGFR. Except for PlGF, other members play important roles in the process of angiogenesis, thereby promoting cancer progression[7,8]. Sino Biological has developed a comprehensive collection of cytokines and corresponding receptors associated with angiogenesis, which have been validated to be of high purity and activity.

Human VEGF165 Protein
Cat#: 11066-H27H-B 14 Citations



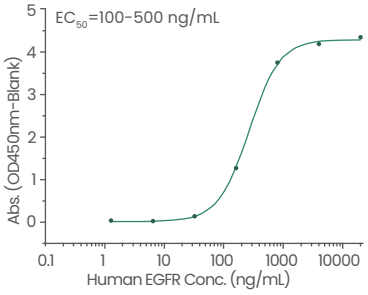
Cell proliferation assay using human umbilical vein endothelial cells (HUVEC).

Human FGF2 Protein
Cat#: 10014-HNAE 45 Citations



Cell proliferation assay using BALB/c 3T3 mouse embryonic fibroblasts.

Human EGFR Protein
Cat#: 10001-H08H 12 Citations



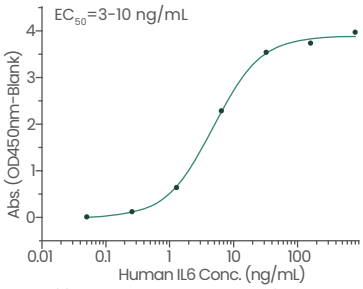
Immobilized human EGF protein (Cat#: 10605-H01H) can bind human EGFR protein.

Exosomes and Epithelial–mesenchymal Transition (EMT)

EMT is a cellular process in which epithelial cells lose cell polarity and intercellular adhesion and transform into loosely structured mesenchymal cells. During this process, the expression of epithelial cell markers, such as E-cadherin and β-catenin, is downregulated, whereas that of hypodermal cell markers, such as N-cadherin and vimentin, is upregulated. EMT is associated with cancer progression and induces tumor invasion and metastasis, which promote poor patient prognosis. From the initial activation of the invasive phenotype to metastasis, tumor-derived exosomes play an important role in the induction of tumor-associated EMT[9,10].

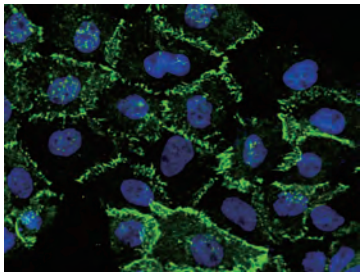
Tumor-derived exosomes contain EMT-associated inducers, such as TGF-β, TNF-α, IL-6, β-catenin, caveolin-1, and HIF-1α, which contribute to the induction of EMT, enhance cell invasion, and promote tumor cell development and metastasis. Under hypoxic conditions, the release of exosomes from different tumor cells, such as breast and prostate cancer, glioma, and leukemia cells, is increased and can further enhance the occurrence of metastasis through EMT. In addition, exosomes contain nucleic acids, such as DNA, RNA, non-coding RNA, and miRNA, which can be involved in EMT regulation in cancer. The common EMT-related regulatory pathways include the β-catenin, Hippo, and MAPK/ERK pathways. Sino Biological provides EMT-related recombinant proteins and corresponding antibodies products to support exosome and EMT research[10,11].

Human IL-6 Protein
Cat#: 10395-HNAE 19 Citations



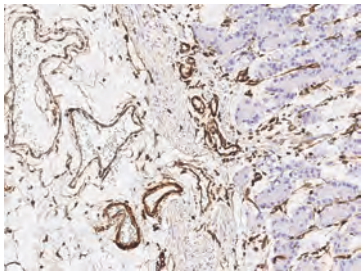
Immobilized human IL-6 can bind human IL-6R hFc(Cat#: 10398-H02H)

Anti-β-Catenin Antibody
Cat#: 11279-R021 Rabbit MAb



Immunofluorescence staining of Human CTNNB1 in A431 cells.

Anti-Vimentin Antibody
Cat#: 100254-R001 Rabbit MAb



Immunochemical staining of human Vimentin in human stomach.

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Exosomes in Cancer Therapies

Targeting tumor-derived exosomes may have a positive effect on cancer therapy. Exosomes secreted by malignant cells have a tumor-promoting effect. In general, tumor cells secrete more exosomes than normal cells. These secretomes carry miRNAs, lncRNAs, and proteins that may act as biomarkers for cancer diagnosis and prognostic monitoring[4]. In addition, exosomes play an important role in resistance to therapy. Exosomes carry a specific set of miRs that can transfer resistant phenotypes to sensitive cancer cells, conferring resistance to chemotherapy and radiation, which is achieved by altering the cell cycle and inducing anti-apoptotic processes. Exosomes may also inhibit the entry of chemotherapeutic agents into target cancer cells, thereby affecting the efficacy of chemotherapy[3]. Therefore, targeting exosomes may provide a new direction for cancer therapy, and relevant clinical trials are already underway.

Summary

Exosomes are biologically active extracellular vesicles containing proteins, nucleic acids, and lipids that mediate cell-to-cell communication. Communication among cells can shape the tumor microenvironment and is critical for tumor growth, invasion, and immune surveillance. Exosomes may function as new biomarkers for cancer diagnosis, therapeutic intervention, and prognostic prediction, which may represent a new opportunity for cancer therapy. In the future, research on exosomes may focus on the purification, characterization, and compositional assay of exosomes associated with cancer progression[5]. As a leading global supplier of bioreagents and CRO services for the biopharmaceutical field, Sino Biological is at the forefront of supporting exosome and tumor progression research by providing researchers with a comprehensive range of high-quality reagents and services.

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