ROCKLAND | ANTIBODIES ONLINE

Hallmarks of Cancer

Overview, Related Products, and Pathways

March 2025 (V2.2)

Cancer is one of the leading causes of death worldwide, affecting millions of people every year. It is a complex and multifaceted disease that arises from the uncontrolled growth of abnormal cells in the body. Despite significant advancements in cancer research and treatment, the fight against this disease is far from over. There is a need for continued research into the mechanisms of cancer development and progression, as well as the development of new and effective treatments.

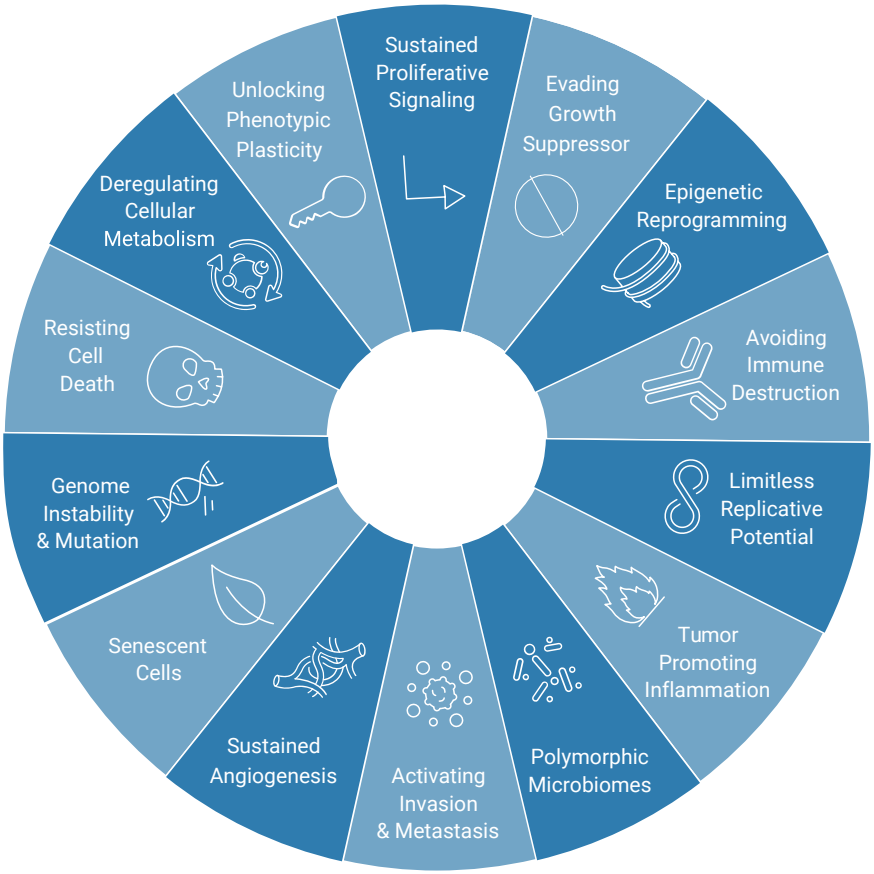
This book aims to give an introduction into cancer research, focusing on the publication “Hallmarks of Cancer” by Douglas Hanahan and Robert A. Weinberg, which identifies key features of cancer. The book provides an in-depth analysis of each of these hallmarks, highlighting the key molecular pathways and cellular processes involved.

As a platform for high-quality research antibodies, proteins, and kits, antibodies-online has a deep understanding of the importance of reliable and accurate research materials for cancer research. This book also provides a comprehensive guide to the various research materials available for cancer research, including antibodies, proteins, and assay kits. It offers insights into the selection and use of these materials, highlighting the critical role they play in cancer research.

Contents

1. Hallmarks of Cancer

Hallmarks of Cancer



In 2000, Douglas Hanahan and Robert Weinberg published the paper 'The hallmarks of cancer', conceptualizing six core rules which orchestrate the multistep transformation of normal cells into malignant cells. More than 20 years later, in the third update 'Hallmarks of cancer: new dimensions', these six original hallmarks have expanded to 14. These hallmarks outline a set of criteria that explain how normal cells can develop into malignant tumors by identifying specific characteristics and describing how they interact with one another. These characteristics include sustained proliferative signaling, evasion of growth suppressors, resistance to cell death, limitless replicative potential, angiogenesis, and genomic instability. Together, these hallmarks allow cancer cells to evade the normal controls that regulate cell growth and division, enabling them to continue to divide and proliferate, forming a tumor that can invade nearby tissues and spread to other parts of the body. Below you may find a brief summary of the respective hallmarks as well as related resources (e.g. pathway illustrations) and research tools (i.e. antibodies, ELISA kits, recombinant proteins).

Sustaining Proliferative Signaling

The most fundamental trait of cancer cells involves their ability to sustain chronic proliferation. This refers to the ability of cancer cells to activate signaling pathways that promote cell growth and division. Normally, these pathways are tightly regulated, but in cancer cells, they are constantly activated, allowing the cells to continue to divide and proliferate even in the absence of normal growth signals. This can be the result of mutations in genes that encode proteins involved in these signaling pathways, leading to the activation of downstream signaling molecules that promote cell growth.

Jump to:
RTK Signaling Pathway

Evading Growth Suppressors

A highly complementary hallmark capability for sustaining proliferative signaling in cancer cells is the ability to evade growth suppression. Growth suppressor genes normally function to inhibit cell growth and division. Several tumor suppressive protein-coding genes that operate in diverse ways to inhibit cellular growth and proliferation had been discovered. Prominent examples are the retinoblastoma protein (RB) or the human tumor suppressor p53. The transcription factor regulates the expression of genes involved in cell cycle control, induction of apoptosis or DNA repair after DNA damage. In cancer cells, these genes are often inactivated, either through mutations that disable their function or by mechanisms that prevent them from being expressed. This allows cancer cells to avoid the normal constraints on cell growth and division, enabling them to continue to proliferate unchecked.

Jump to:
Cell Division Cycle Pathway
DNA Damage Repair

Resisting Cell Death

In addition to evading growth suppressors, cancer cells also have a high degree of resistance to cell death. Normally, cells undergo programmed cell death, or apoptosis, when they become damaged or no longer needed. The cancer cells may alter the mechanisms that detect the damage or irregularities, preventing proper signaling and apoptosis activation. Cancer cells may also introduce defects in the downstream signaling itself, or the proteins involved, which would also prevent proper apoptosis. This can be the result of mutations in genes that regulate the apoptotic pathway, or it can be due to the activation of signaling pathways that promote cell survival.

Jump to:
Apoptosis Pathway

Limitless Replicative Potential

The potential to replicate without limitation is another key aspect in tumor development, which is also recognized as hallmark of cancer. In contrast to human body cells, cancer cells can overcome the 'Hayflick Limit' and divide indefinitely, without undergoing the normal process of cellular aging. Normally cells entering the state of senescence, or cell death stop replication. This is mainly due to the DNA at the end of chromosomes, known as telomeres. Telomeric DNA shortens with every cell division, until it becomes so short it activates senescence, so the cell stops dividing. Cancer cells bypass this barrier by manipulating the enzyme telomerase to increase the length of telomeres. Thus, they can divide indefinitely, without initiating senescence.

Jump to:
Cell Division Cycle Pathway
Hedgehog Signaling Pathway

The Hayflick Limit

In mammalian cells the Hayflick Limit defines the amount of maximal cell divisions. After 60–70 doublings the cells reach a stage of senescence and multiplication is stopped. This limit can be overcome by disabling their RB and P53 tumor suppressor proteins, which allows them to continue doubling until they reach a crisis, with apoptosis or rare occuring emergence of an immortalized cell that can double without limit. Most tumor cells are immortalized.

Telomere decreases in size during each cell cycle. About 85% of cancers upregulate telomerase to extend their telomeres and the remaining 15% use alternative lengthening of telomeres.

RB P53

Senescent Cells

Cellular senescence is a form of cell growth arrest that is typically irreversible, and it is thought to have evolved as a protective mechanism to maintain tissue homeostasis. It is considered as a complementary mechanism to programmed cell death, which serves to deactivate and eventually remove cells that are diseased, dysfunctional, or no longer needed. Senescence can be induced in cells by a variety of conditions, including microenvironmental stresses like nutrient deprivation and DNA damage, as well as damage to organelles and cellular infrastructure, and imbalances in cellular signaling networks.

Cellular senescence has long been considered a protective mechanism against tumors, whereby cancerous cells are induced to undergo senescence. Majority of triggers mentioned above are associated with malignancy—particularly DNA damage as a consequence of aberrant hyperproliferation, also know as oncogene-induced senescence due to hyperactivated signaling. However, new publications question this linear relationship. In certain contexts, senescent cells variously stimulate tumor development and malignant progression. The principal mechanism by which senescent cells promote tumor phenotypes is thought to be via senescence-associated secretory phenotypes (SASP).

Jump to:
Apoptosis Pathway
DNA Damage Repair Pathway

Senescence-Associated Secretory Phenotype (SASP)

Multiple types of stimuli can provoke cellular senescence and SASP. When irreversible cell-cycle arrest is triggered by severe DNA damage (i.e. dysfunctional telomeres or oncogenic stress), the SASP occurs in senescent cells. The acquisition of a SASP turns senescent fibroblasts into proinflammatory cells that have the ability to promote tumor progression. Senescent cells secrete interleukins, inflammatory cytokines, and growth factors that can affect surrounding cells. The most prominent cytokine of the SASP is interleukin-6 (IL-6), a pleiotropic proinflammatory cytokine. IL-6 has been shown to be associated with DNA damage– and oncogenic stress–induced senescence of mouse and human keratinocytes, melanocytes, monocytes, fibroblasts, and epithelial cells. Further, IL-6 secretion appears to be directly controlled by persistent DNA-damage signaling (ATM and CHK2), independent of the p53. Through IL-6 expression, senescent cells can directly affect neighboring cells.

IL-6 ATM CHK2

Deregulating Cellular Metabolism

For unhindered growth, tumors not only benefit from deregulated control of cell proliferation but also corresponding adjustments of energy metabolism to fuel cell growth and division. They have the capability to modify or reprogram cellular metabolism to efficiently support neoplastic proliferation. Under aerobic conditions, normal cells process glucose, first to pyruvate via glycolysis in the cytosol and secondly, to carbon dioxide in the mitochondria; under anaerobic conditions, glycolysis is favored, and relatively little pyruvate is dispatched to the oxygen-consuming mitochondria. Otto Warburg was the first to observe an anomalous characteristic of cancer cell energy metabolism.

Jump to:
Warburg Effect

Avoiding Immune Destruction

Some cancer cells adapt mechanisms to evade both immune surveillance and attack by the host's immune system. One way cells do this is by hijacking normal mechanisms of immune checkpoint control. Immune checkpoints refer to the built-in control mechanisms of the immune system that maintain self-tolerance and help to avoid collateral damage during a physiological immune response. Tumor-specific T cells must discriminate between destruction of the tumor cell and survival of the target cell. What is important for discrimination are proteins on both the T-cell and the target cell. Tumor cells express molecules to induce apoptosis or to inhibit T lymphocytes, for example, PD-L1 on the surface of tumor cells leads to suppression of T lymphocytes. FasL on the other hand may induce apoptosis of T lymphocytes. Some cancer cells also try to gain resistance against possible cytotoxic CD8+ T cell which are a fundamental element of anti-tumor immunity. They lower their MHC I expression and avoid being detected by the cytotoxic T cells. Disruption of the apoptotic signal pathway molecules also leads to successful immune evasion by the tumor. Caspase 8, Bcl-2 or IAP are key targets, among others.

Jump to:
Cancer Immune Checkpoints

Sustained Angiogenesis

An expanding tumor has an increased need for nutrients to sustain his growth and spread. The tumor requires new blood vessels to deliver adequate oxygen to the cancer cells. To do this, the cancer cells acquire the ability to undergo angiogenesis, the process of forming new blood vessels. Cancer cells orchestrates the production of new vasculature by releasing signaling molecules that activate the 'angiogenic switch'. By exploiting the switch, non-cancerous cells that are present in the tumor are stimulated to form blood vessels.

Tissue Inhibitors of Metalloproteinases (TIMPs)

The TIMP family consist of members (TIMP 1-4). They are able to are able to inhibit matrix metalloproteinases (MMPs) by forming tight-binding, noncovalent associations with the active site of the MMPs. MMPs play a big role in the proliferation of tumors, they facilitate tumor cell invasion and metastasis by at least three distinct mechanisms. First, proteinase action removes physical barriers to invasion through degradation of ECM macromolecules such as collagens, laminins, and proteoglycans. Second, MMPs have the ability to modulate cell adhesion, crucial for cell movement through the ECM. The ratio of MMP-2 to TIMP-2 significantly impacts variation in the adhesive phenotype of tumor cells. Finally, MMPs especially MMP-2, MMP-9 and MMP-14 are prone to metastasis, they support the degradation of basement membranes and the establishment of tumorigenic blood vessels. Laminin-alpha-5 induces MMP-9 expression and thus supports Epithelial-Mesenchymal Transition (EMT).

MMP-2 MMP-9 MMP-12 MMP-13 TIMP-2 Laminin-alpha-5

Activating Invasion & Metastasis

The ability to invade neighboring tissues is what dictates whether the tumor is benign or malignant, and it renders cancer a mortal threat. Metastasis enables their dissemination around the body complicates treatment by a large margin. The cancer cells must undergo a multitude of changes in order for them to acquire the ability to metastasize. The metastatic cascade represents a multi-step process which includes local tumor cell invasion, invasion of blood vessels followed by the exit of carcinoma cells from the circulation and colonization in the new tissue. At the earliest stage of successful cancer cell dissemination, the primary cancer adapts the secondary site of tumor colonization involving the tumor-stroma crosstalk.

Epithelial- Mesenchymal Transition

The ‘Epithelial-Mesenchymal Transition’ (EMT), a process involved in various steps of embryonic morphogenesis and wound healing, is being used by carcinoma cells to acquire multiple attributes that enable invasion and metastasis. This multifaceted EMT program can be activated transiently or stably, and to differing degrees, by carcinoma cells during the course of invasion and metastasis. The transition is an example for the hallmark enabling characteristic ‘phenotypic plasticity’. Transcriptional factors, including Snail, Slug, Twist, and Zeb1/2, orchestrate the EMT and related migratory processes during embryogenesis. They are also expressed in various combinations in a number of malignant tumor types and are involved in carcinoma formation and for programming invasion.

Snail | Slug | Twist | Zeb1/2 | SETD1B

Unlocking Phenotypic Plasticity

Relative to the huge amount of development and differentiation that occurs during organogenesis, mammalian cells are typically restricted in the extent to which they can differentiate. This restriction allows cells to remain organized and functional within their respective tissue. In cancer, however, cells undergo molecular and phenotypic changes that allow them to adopt different identities along a phenotypic spectrum referred to as cellular plasticity. This includes dedifferentiation from mature to progenitor states, blocked differentiation from progenitor cell states, and transdifferentiation into different cell lineages. The EMT and mesenchymal-to-epithelial (MET) transitions are well-characterized examples of developmental regulatory programs that resemble transdifferentiation. Changes in cellular phenotype are important to cancer progression because these changes can facilitate tumor initiation and metastasis, immune invasion, chemoresistance and many other aspects of tumor progression.

Click here to see an online version of this article and its associated references

2. Additional Resources

Cancer Immune Checkpoints

Immune checkpoints are receptors on the membrane of T-lymphocytes that can regulate their immune response. They are refinely tuned and alternate between stimulation and inhibition1. The immuno checkpoints pathway is crucial to promote self-tolerance and prevent autoimmunity and related diseases.

T-cell receptors are in focus of medical research, however, global immunosuppression greatly increases the risk of acquiring life-threatening infections and is associated with organ toxicity when used long-term. Thus, alternative approaches that inhibit only the unwanted immune responses and preserve general immunity are highly desirable. The tumor necrosis factor (TNF) receptor superfamily represents the largest part of receptors with CD27, CD40, OX40, GITR and CD137. Two additional stimulatory checkpoint molecules belong to the B7-CD28 superfamily: CD28 itself and ICOS.

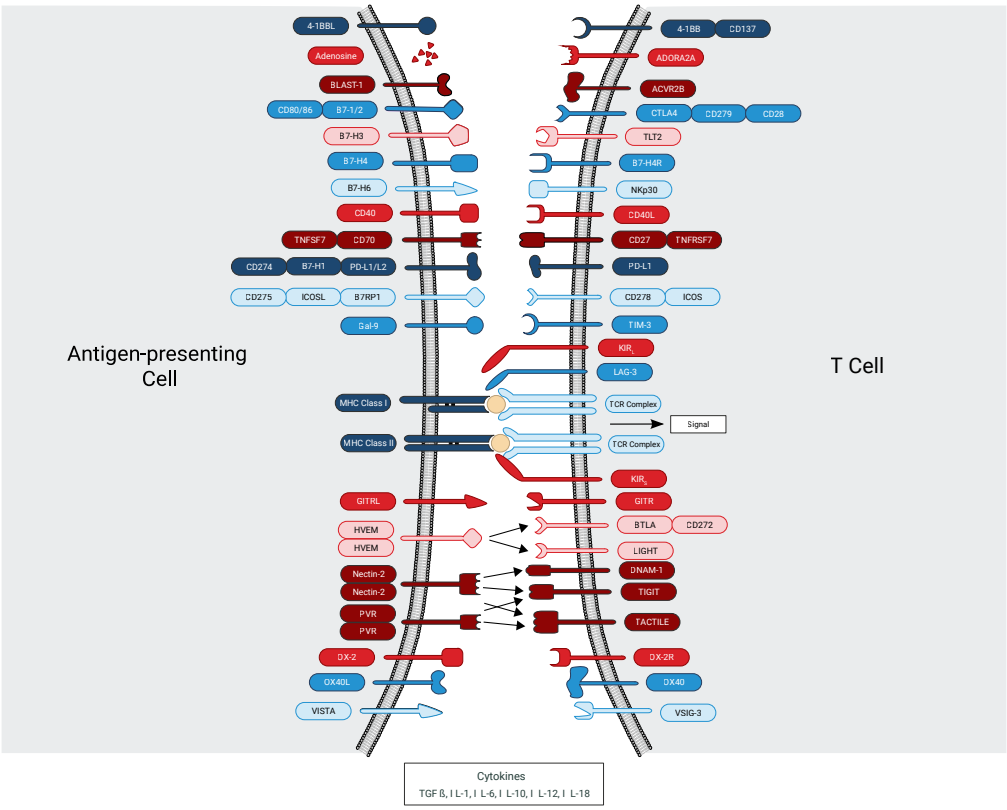
Co-Stimulation and Inhibition with BTLA and HVEM

The HVEM/ LIGHT/BTLA/CD160 costimulatory/ coinhibitory pathway has emerged as a potential target for the development of immune therapeutic interventions. The interaction between BTLA, short for B and T Lymphocyte Attenuator, an inhibitory receptor whose extracellular domain belongs to the immunoglobulin superfamily, and herpesvirus-entry mediator (HVEM), a co-stimulatory tumour-necrosis factor receptor, is unique in that it is the only receptor–ligand interaction that directly links these two families of receptors. Recent studies show that engagement of HVEM with its endogenous ligand (LIGHT) from the tumour-necrosis factor family induces a powerful immune response. LIGHT stimulates the proliferation of T cells, and triggers apoptosis of various tumor cells, whereas HVEM interactions with BTLA negatively regulate T-cell responses.

Importance of Checkpoint Inhibitors for Cancer Immunotherapy

Inhibitory checkpoint molecules are promising targets for cancer immunotherapy. The discovery and clinical application of immune-checkpoint inhibitors has dramatically improved the treatments, outcomes and therapeutic concepts in multiple tumor settings. Of the immune checkpoint proteins identified to date, CTLA-4 is a critical regulator of T-cell responses. CTLA-4 is structurally similar to the co-stimulating receptor CD28, with both receptors also binding to CD80 and CD86 (also known as B7-1 and B7-2). Binding to CD80 or CD86 leads to a competition between an inhibitory signal (by CTLA-4) and a co-stimulating signal (by CD28). In 2018 the research on monoclonal antibodies blocking the inhibitory molecule CTLA-4 and or the PD-1/PD-L1 axis by James P. Allison & Tasuku Honjo, was awarded with The Nobel Prize in Physiology or Medicine.

Click here to see an online version of this article and its associated references



Cancer Immunity Cycle

The cancer immunity cycle provides a framework for understanding the complex interactions between cancer cells and the immune system. For an anticancer immune response to lead to effective killing of cancer cells, all stages of the cycle must be passed through. By understanding the different stages of the cycle, researchers can develop new therapies that target specific stages and improve the ability of the immune system to recognize and eliminate cancer cells.

In the first stage neoantigens created by oncogenesis are released and captured by dendritic cells for processing. For a successful anticancer T cell response, they must be accompanied by signals that specify immunity to avoid peripheral tolerance to the tumor antigens. Important signals like proinflammatory cytokines and factors released by dying tumor cells or by the gut microbiota.

Next, dendritic cells present the captured antigens on MHCI and MHCII molecules to T cells (stage 2). This presentation of cancer cell antigens is essential for the activation of the immune response. The presentation results in the priming and activation of effector T cell responses against the cancer-specific antigens (stage 3). Priming prepares them to recognize and attack cancer cells. At this stage, the type of immune response is determined, with the ratio of T effector cells and T regulatory cells being decisive for the final outcome.

Finally, the activated effector T cells migrate to the tumor microenvironment (stage 4) in order to infiltrate (stage 5). They specifically recognize and bind to cancer cells through the interaction between its T cell receptor (TCR) and its cognate antigen bound to MHCI (stage 6). Once bound to cancer cells, T cells release toxic molecules that kill the cancer cells (stage 7), which leads to lysis and re-release of new neoantigens. The cycle repeats.

In cancer patients, the Cancer-Immunity Cycle does not perform optimally. Tumor antigens may not be detected, dendritic cells and T cells may treat antigens as self rather than foreign thereby creating T regulatory cell responses rather than effector responses, T cells may not properly home to tumors, may be inhibited from infiltrating the tumor, or (most importantly) factors in the tumor microenvironment might suppress those effector cells that are produced.

Virus-like particles in Immuno-Oncology

Virus-like particles (VLPs) are an emerging tool in immuno-oncology, capable of modulating the cancer immunity cycle to enhance anti-tumor responses. Engineered VLPs can function as immunotherapeutic agents by delivering tumor-specific antigens, adjuvants, or gene-editing components to reprogram immune responses. Their structural similarity to infectious viruses allows them to engage innate immune sensors through pathogen-associated molecular patterns (PAMPs) and danger-associated molecular patterns (DAMPs), triggering type I interferon (IFN) responses that promote tumor recognition and immune activation. Additionally, intratumoral immunotherapy using virus-based nanomaterials and gene-delivery vectors offers advantages such as lower dosing requirements, reduced systemic toxicity, and cost-effective therapeutic applications7. These properties position VLPs as a promising platform for enhancing the efficacy of immunotherapies within the cancer immunity cycle. Learn more about VLPs and discover our high-quality VLPs.

Learn more

Click here to see an online version of this article and its associated references

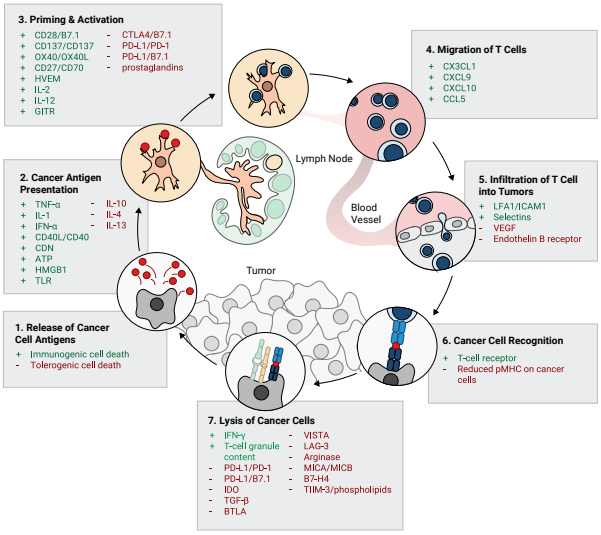


Fig. 1: Cancer immunity cycle

CAR-T Immunotherapy Research

As revolutionary immuno-oncology changes to cancer treatment, cell therapies have attracted widespread attention with their high clinical remission rate in hematological cancers. Since 2018, cell therapies have accounted for more remissions than cancer vaccines, with chimeric antigen receptor T (CAR-T) therapies leading the global cell therapy development race. With rapid development in the past ten years, CAR-T immunotherapy has become a hot area in which commercial organizations compete fiercely and universities ans industry collaborate intensively.

Chimeric antigen receptor (CAR) T-cell therapy represents a major advancement in personalized cancer treatment. In this strategy, a patient's own T cells are genetically engineered to express a synthetic receptor that binds a tumor antigen. CAR-T cells are then expanded for clinical use and infused back into the patient's body to attack and destroy chemotherapy-resistant cancer. CAR-T cell therapy leverages the power of the patient's own immune system by serving as a bridge to connect genetically modified T cells to the surface antigens of tumor cells based on targeted ligands. Clinical trials have demonstrated compelling overall response and survival rates in individuals with B-cell malignancies.

The most popular CAR-T Targets

According to data from the U.S. Patent and Trademark Office (USPTO), the number of CAR-T related patents filed showed a sharp increase during the last decade. In this context, the USA and China are leading the way with the largest increase in patent documents, followed by the European countries. A look at the most common targets in CAR-T patent documents reveals an interesting and clearly structured picture. CD19 is by far the most worked target, followed by BCMA, CD20, Mesothelin, PD-1/PD-L1.

Click here to see an online version of this article and its associated references

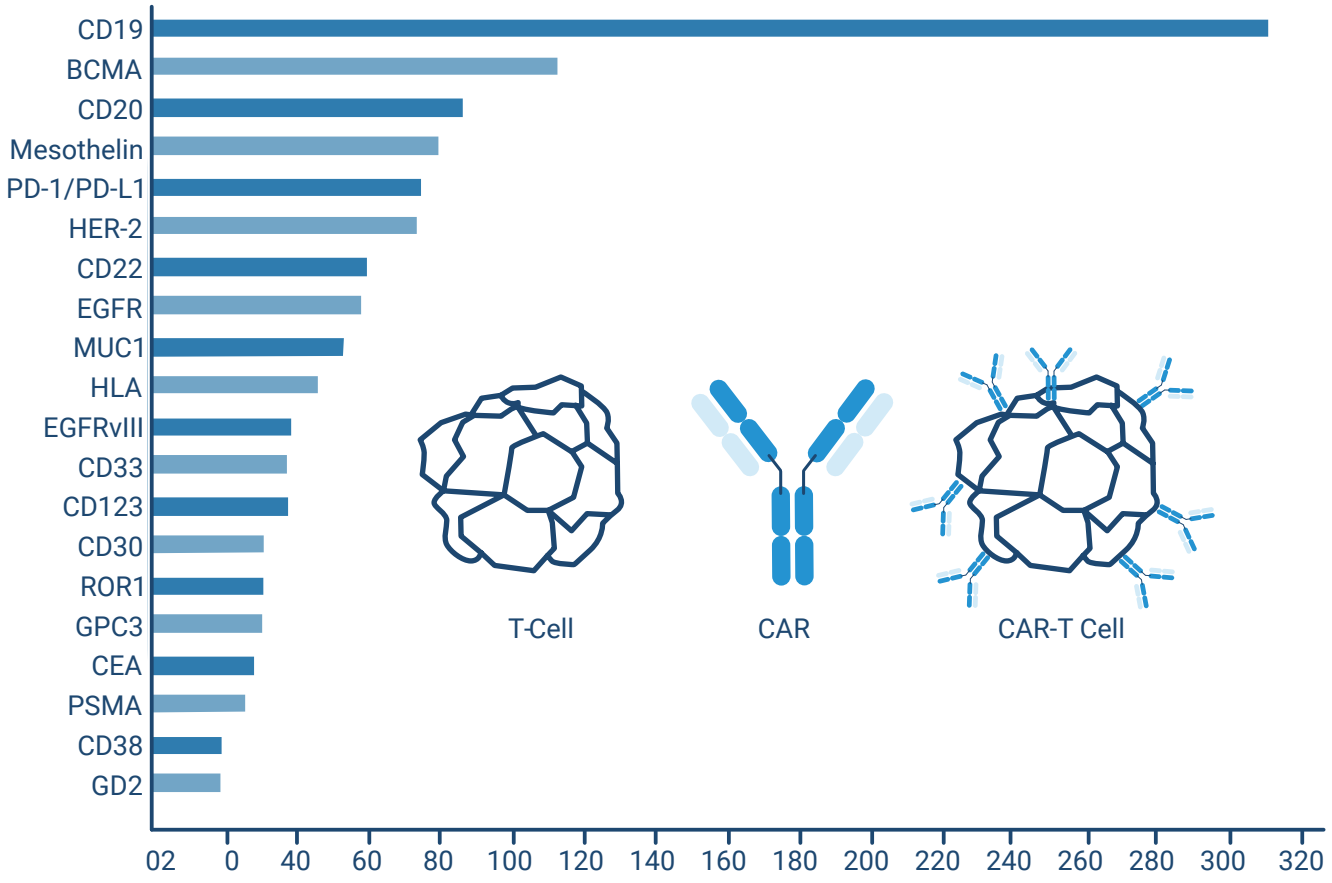


Fig. 1: Top-20 targets in CAR-T patents

Popular CAR-T Immunotherapy Targets

Product	Reactivity	Clonality	Clone	Application	Cat. No.	Validations
CD19 antibody	Human	Monoclonal	CD19-3116	Coat, ELISA, FACS, IHC, StM	ABIN6941101	(5)
BCMA antibody	Human	Monoclonal	BCMA-2366	Coat, ELISA, IHC, StM	ABIN6940533	(4)
CD20 antibody	Human	Monoclonal	MS4A1-3409	Coat, ELISA, FACS, IF, IHC, StM, WB	ABIN6941105	(6)
Mesothelin antibody	Human	Monoclonal	MB-G10	IHC, WB	ABIN233752	(2) (3)
PD-1 antibody	Human	Monoclonal	3E12A10	ELISA, FACS, ICC, IHC, Neut, WB	ABIN5611149	(4)
ErbB2/Her2 antibody	Human, Mouse, Rat	Polyclonal		ELISA, ICC, IF, IHC, WB	ABIN6256630	(12)
CD22 antibody	Human	Monoclonal	1A3A11	ICC, FACS, ELISA, WB	ABIN1724887	(2) (5)
EGFR antibody	Human	Polyclonal		IP, ELISA, WB	ABIN98862	(3) (2)
MUC1 antibody	Human, Mouse, Rat	Monoclonal		Coat, ELISA, FACS, IF, IHC, StM, WB	ABIN6940096	(6)
HLAG antibody	Human	Monoclonal	MEM-G-9	ELISA, FACS, ICC, IHC (fro), IP	ABIN94373	(11) (4)
EGFRviii antibody	Human	Polyclonal	IF (p), IHC (p), WB		ABIN742035	(9) (5)
CD33 antibody	Human	Polyclonal	IF, IHC, WB		ABIN3022816	(6)
IL3RA antibody	Human	Monoclonal	IL3RA-2947R	Coat, ELISA, IHC, ISt, StM	ABIN6939784	(3)
TNFRSF8 antibody	Human	Monoclonal	3B10	FACS, ELISA, WB	ABIN969019	(1) (4)
ROR1 antibody	Human	Monoclonal	2H6	ICC, ELISA, WB	ABIN969385	(1) (2)
Glypican 3	Human, Mouse	Monoclonal	9C2	ICC, FACS, IHC, ELISA, WB	ABIN969523	(2) (7)
CEA antibody	Human	Monoclonal	Arcitumomab	BI, FACS, IHC (p)	ABIN5668278	(2)
PSMA antibody	Human, Mouse, Pig, Rat	Monoclonal	GCP-04	ICC, IHC (p), WB	ABIN1302364	(9) (8)
CD38 antibody	Human	Monoclonal	5C5C3	ELISA, IHC, WB	ABIN5542494	(5)
GM2A antibody	Human	Polyclonal		ELISA, IHC, IP, WB	ABIN7153574	(4)

3. Related Pathways

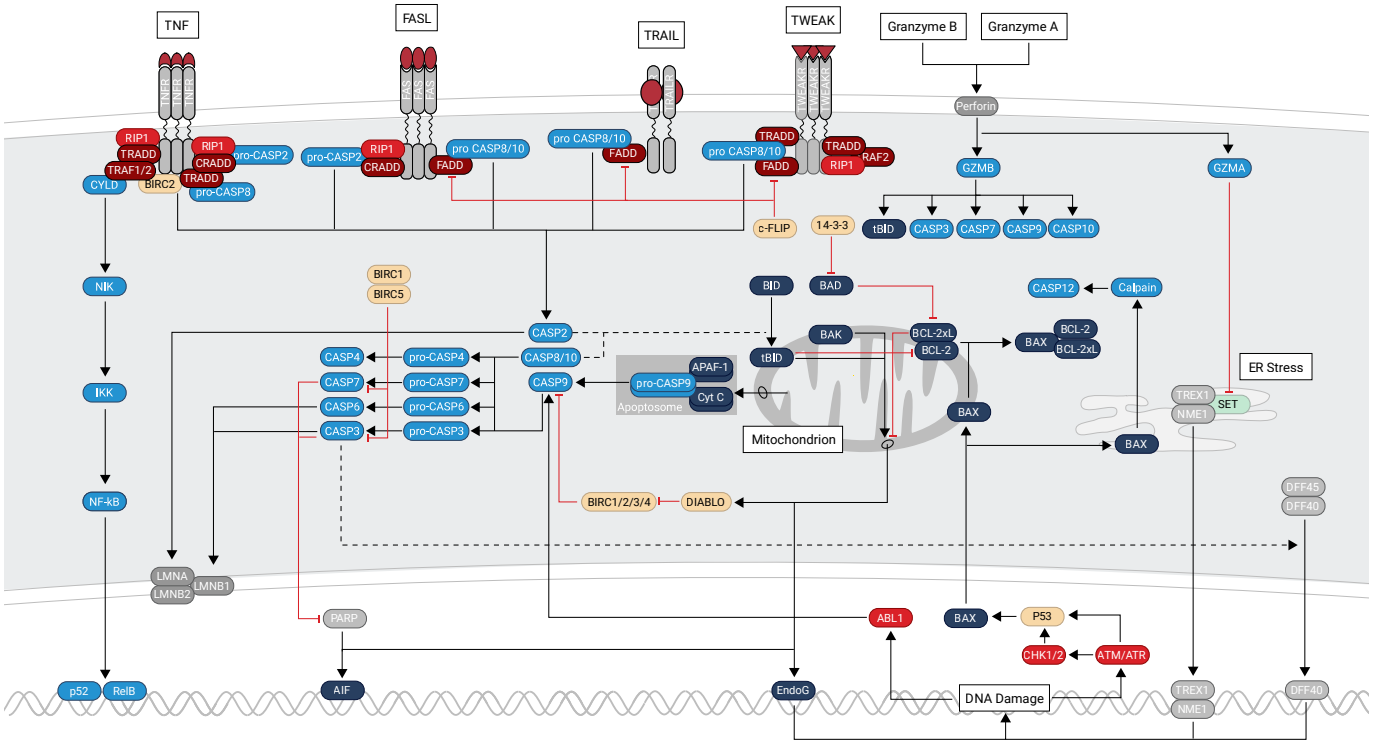
Apoptosis Pathway

Programmed cell death or apoptosis is an important physiological process in multicellular organisms. The equilibrium between cell growth and division and the rate at which cells undergo cell death allows for dynamic adjustment of the cell number depending on internal or external parameters. For example, during the development of the vertebrate nervous system about half of the cells undergo apoptosis shortly after they have been formed. In an adult organism, this equilibrium is essential to maintain for example the size and function of organs and tissues. Dysregulation of this equilibrium oftentimes leads to cancer. Unlike necrosis which causes a potentially damaging inflammatory response after affected cells burst, apoptosis unfolds in a very organized way: the cell shrinks and condenses while the internal structures are disassembled and the DNA is fragmented. The dying cell is then rapidly phagocytosed by neighboring cells or macrophages.

At the core of the apoptotic process are caspases, a family of cysteine proteases. They are produced as pro-caspases which are rendered active subsequently to cleavage by other caspases. This caspase cascade is triggered when initiator procaspases (e.g. procaspases 8, 9, 10) are aggregated with the help of adaptor proteins, thus facilitating mutual activation due to low protease activity or conformational changes of the procaspases. The activated caspases are then free to activate effector caspases (e.g. caspases 3, 6, and 7) and promote apoptosis. Their effect is further regulated by Bcl-2 family proteins (e.g. Bcl-2, Bcl-xL) and IAPs (inhibitors of apoptosis, e.g. BIRC1, XIAP).

Apoptotic processes follow several pathways. Extrinsic death receptor pathways are induced through ligands that bind to a family of death receptor proteins (e.g. the FAS and TRAIL receptors) containing a cytoplasmic death domain. The intrinsic pathway is engaged in response to DNA damage or mitochondrial stress and is particularly relevant in cancer. Besides these canonical apoptotic pathways there are also caspase independent pathways, triggered e.g. by granzyme B and A. These caspase independent pathways are thought to have evolved in response to viruses that inhibit caspases.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Cell Division Cycle Pathway

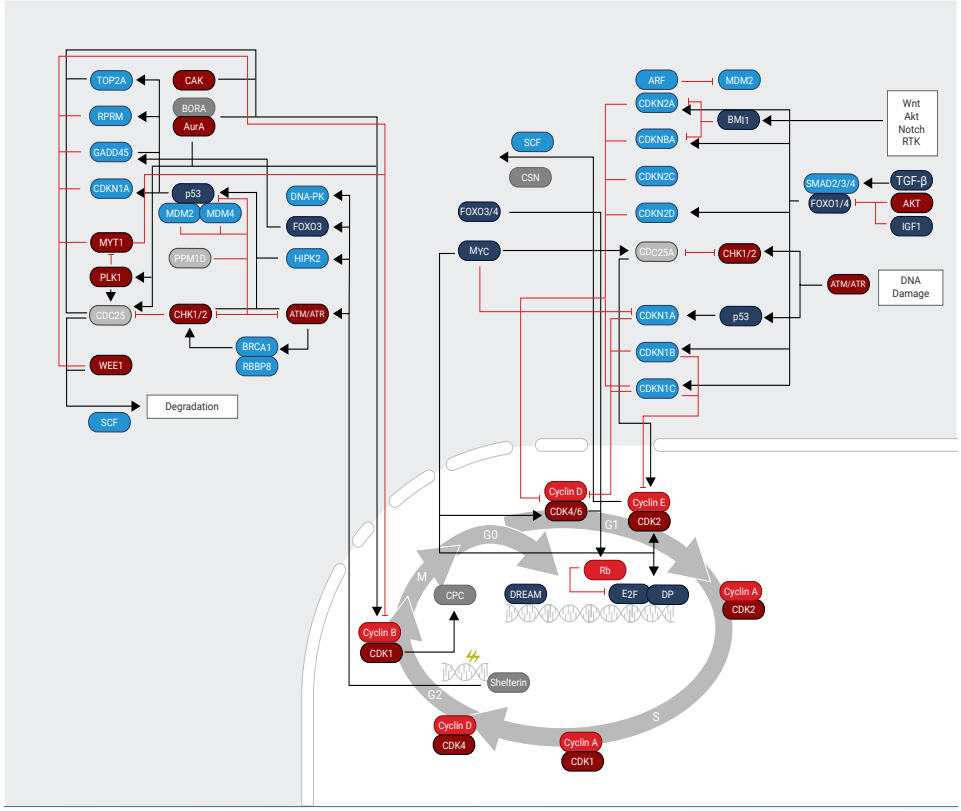
All organisms (single and multi-cellular) rely upon reiteration of growth and division of existing cells under favorable conditions. During each round of this process, the cell cycles through an ordered series of events in which its genetic information is duplicated and then divided among two daughter cells. These events are tightly regulated and certain checkpoints must be passed in order for the cell cycle to be completed. The loss of control of these processes is a hallmark of cancer.

The cell cycle is split up into four major phases based on the events unfolding in the cell. During the first gap phase (G1) the proteins are produced that are essential for DNA replication. The genetic information is then being replicated during the synthesis (S) phase. In the second gap phase (G2) all the components that are necessary for the separation of the duplicated DNA during the subsequent mitosis (M phase). Cells that are not actively dividing are considered to be in a quiescent state in the resting phase G0.

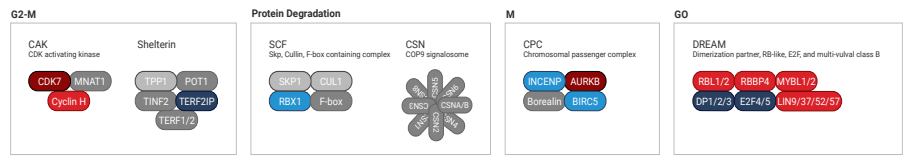
Cell division is necessary for life, but unregulated division is dangerous and counterproductive. Therefore, the cell has an impetus for maintaining tight regulatory control over how and when division takes place. There are two major checkpoints in the cell cycle. The first choke-point the cell must pass is between the G1 and S phase. A second opportunity for arrest is provided between G2 and M phases. Once DNA replication has been initiated, it must be finished. Therefore, the major checkpoint in the cell cycle is the restriction (R) point between G1 and S phases, prior to DNA duplication, at which the cycle progresses depending on mitogenic or inhibitory factors such as DNA damage and signals from various signaling pathways.

Progression from one phase to another is controlled by cyclin dependent kinases (CDK) and their activators, cyclins. Latter proteins are unstable and their cellular concentration cycles throughout the cell cycle. Accordingly, specific cyclin-CDK complexes persist in an active form for a very short period of time after translation, and are then degraded or inactivated by the time that particular phase of the cell cycle completes. Activation of specific cyclin-CDK complexes are characteristic for the different cell cycle phases, and drive production of specific molecules associated with, and necessary for that phase of division. Additional levels of dynamic control are also provided by CDK inhibitors, which block CDK function even in the presence of their requisite cyclin.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Protein Complexes



DNA Damage Repair Pathway

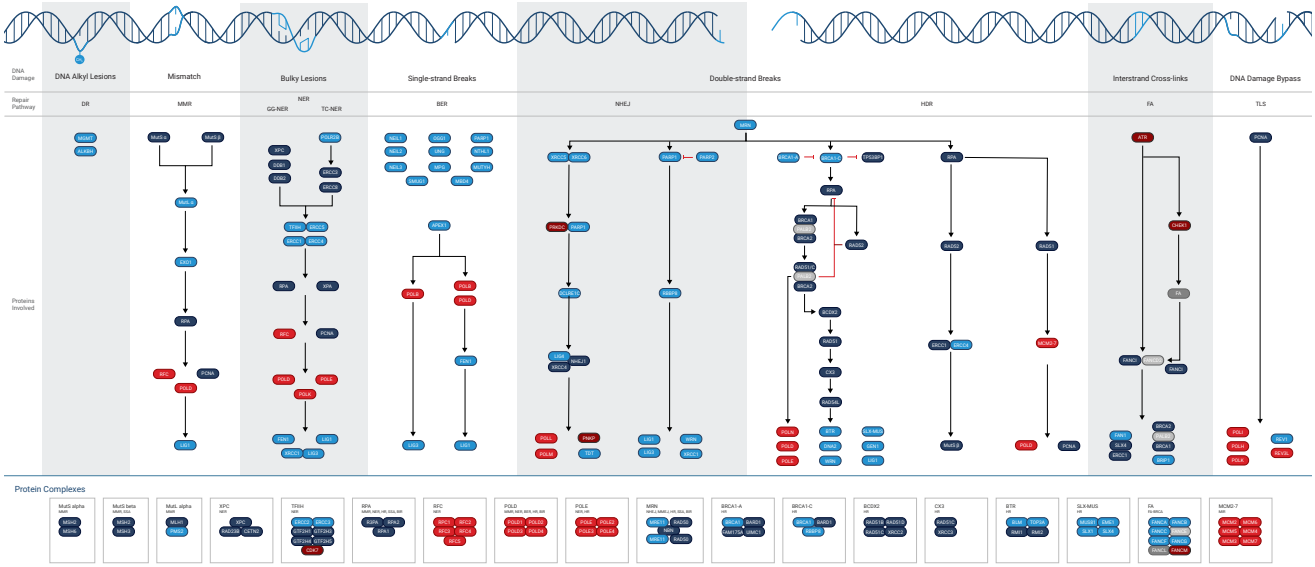
DNA is the carrier of the genetic information that defines any living being. The genetic code fixed in DNA is crucial for processes on a subcellular scale up to the appearance and function of the organism as s whole. Nonetheless, DNA is constantly exposed to insults from endogenous sources such as hydrolysis, oxidation, alkylation, or replication errors. In addition, ionizing radiation, UV radiation, and a plethora of chemical reagents are external factors that threaten the integrity of DNA.

Unlike RNA and proteins, DNA is not being degraded and re-synthesized upon damage. Instead, various repair pathways are in existence to assure that the DNA remains intact. Francis Crick noted in 1974 that “we totally missed the possible role of enzymes in [DNA] repair. I later came to realize that DNA is so precious that probably many distinct mechanisms could exist.”

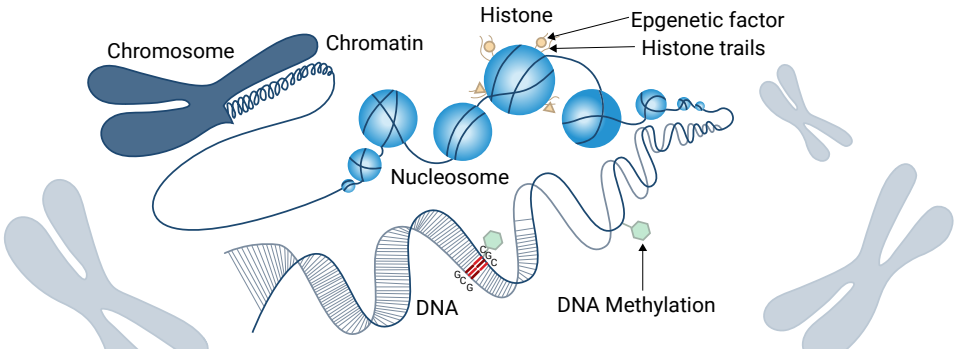
This presage holds true today: over a hundred genes have been characterized since that are involved in an intricate network of DNA repair pathways. DNA damage can be repaired via six different pathways depending on the nature of the lesion: chemical modifications, misincorporated nucleotides, and cross-links are reverted through direct reversal (DR), mismatch repair (MMR), and nucleotide excision repair mechanisms. DNA single strand breaks are being mended via base excision repair. Highly mutagenic DNA double strand breaks finally are repaired through a number of complex pathways that rely on homologous recombination (HR) with the sister chromatid (in the S or G2 phase of the cell cycle) or non-homologous end-joining (NHEJ) of both ends of the double strand break. The Fanconi Anemia pathway is or particular importance for the repair of DNA interstrand crosslinks. In case a DNA lesion cannot be repaired in time, specialized DNA polymerases enable trans-lesion synthesis (TLS) in order to prevent the DNA replication fork from stalling. Mutations that render components of these repair pathways non-functional lead to diseases such as xeroderma pigmentosum, ataxia telangiectasia, Fanconi anemia, and a predisposition for cancer.

Besides, these repair mechanisms are of high interest for current targeted genome editing approaches that typically take advantage of the cellular DNA repair machinery.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Epigenetics



Epigenetics is defined as heritable changes in gene expression that are, unlike mutations, not attributable to alterations in the sequence of DNA. The predominant epigenetic mechanisms are DNA methylation, modifications to chromatin, loss of imprinting and non-coding RNA. Epigenetic regulation of gene expression appears to have long-term effects and wide-ranging effects on health. There is a clear and prescient implication of benefits to both basic science and human health research that stems from a more complete understanding of the epigenome. These benefits have driven researchers to flock this field, and funding organizations have followed suit.

A large part of epigenetics is controlled by post-translational modifications on proteins. Methylations, acetylations, ubiquitination or phosphorylations lead to changes that for example influence transcription. Epigenetic modifications happen often during an organism's lifetime; however, these changes can be transferred to the next generation if they occur in germ cells. Paramutation, bookmarking, imprinting, gene silencing, X chromosome inactivation, position effect, changeable disorder or phenotypic severity, reprogramming, maternal attributes, carcinogenic processes, teratogenic effects, regulation of histone modifications, heterochromatin states and cloning are known to involve epigenetic processes.

DNA Modifications

Covalent attachment of a methyl group to the C5 position of cytosine comprises the principal epigenetic modification of DNA. The presence of a methylated cytosine can repress transcription by inhibiting the binding of transcription factors or may promote the binding of other transcriptional repressors, including histone-modifying proteins, such as histone deacetylases.

DNA demethylation plays an important role in development and tumorigenesis in mammals. DNA demethylation, occurring in primordial germ cells and in early embryos, is essential for cells to return to a pluripotent state.

Histone Modifications

Similarly to DNA methylation, posttranslational histone modifications do not affect DNA nucleotide sequence but can modify its availability to the transcriptional machinery. Several types of histone modifications are known, amongst which acetylation, methylation, phosphorylation, and ubiquitination are the best studied and most important in terms of the regulation of chromatin structure and (transcriptional) activity. 5 While DNA methylation is considered to be a very stable epigenetic modification, histone modifications are comparably more labile with their levels being maintained by a balance between histone modifying enzymes, which add or remove specific modifications. Aberrant histone modification levels result from an imbalance in these modifying enzymes in diseased tissue, thus correcting the increased or decreased level of a particular enzyme will restore the natural balance in the affected cells.

Chromatin Remodeling

The presence of histones acts as a barrier to protein access; thus chromatin remodeling must occur for essential processes such as transcription and replication. In conjunction with histone modifications, DNA methylation plays critical roles in gene silencing through chromatin remodeling. Chromatin remodeling is also interconnected with the DNA damage response, maintenance of stem cell properties, and cell differentiation programs. Chromatin modifications have increasingly been shown to produce long-lasting alterations in chromatin structure and transcription. Recent studies have shown environmental exposures in utero have the potential to alter normal developmental signaling networks, physiologic responses, and disease susceptibility later in life during a process known as developmental reprogramming.

Transcription Factors

Chemical modifications of histones and DNA, such as histone methylation, histone acetylation, and DNA methylation, play critical roles in epigenetic gene regulation. Many of the enzymes that add or remove such chemical modifications are known, or might be suspected, to be sensitive to changes in intracellular metabolism. They (often) utilize cosubstrates generated by cellular metabolism, thereby providing a potential link between nutrition, metabolism, and gene regulation.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits

Extracellular Matrix

The Extracellular Matrix (ECM) is a complex network of proteins, sugars, and other molecules that not only surround and support cells in our body but also play critical roles in communication between cells. The ECM functions as a scaffold, providing mechanical support, but it also influences a wide range of cellular behaviors such as growth, differentiation, and repair.

Biological Role of ECM

The extracellular matrix (ECM) plays diverse roles and is a crucial component of the cellular microenvironment. It is a highly dynamic structure that undergoes constant remodeling, involving the deposition, degradation, and modification of ECM components. ECM remodeling is vital for tissue architecture reorganization. It serves as a regulatory mechanism for cell differentiation. It influences essential processes such as stem cell niche formation, branching morphogenesis, angiogenesis, bone remodeling, and wound healing. On the other hand, abnormal ECM dynamics disrupt cell proliferation and invasion, impair cell death, and hinder cell differentiation, leading to congenital defects and diseases such as tissue fibrosis and cancer. To develop new therapeutic approaches for diseases and innovative strategies for tissue engineering and regenerative medicine, it is crucial to understand the mechanisms and regulation of ECM remodeling.Mechanisms of ECM function.

Importance of ECM in Research

The ECM plays a crucial role in understanding the functioning of cells and tissues. It provides the necessary environment for cellular communication, regulates cell behavior, and influences the response to disease and injury. By studying the ECM, researchers can gain insights into tissue architecture, cellular interactions, and disease mechanisms. Understanding the ECM is essential for advancing fields such as regenerative medicine, cancer research, and tissue engineering.

Research on ECM is supported by various tools, including high-quality antibodies targeting key components of the ECM environment. These tools are essential for advancing regenerative medicine, cancer research, and tissue engineering.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits

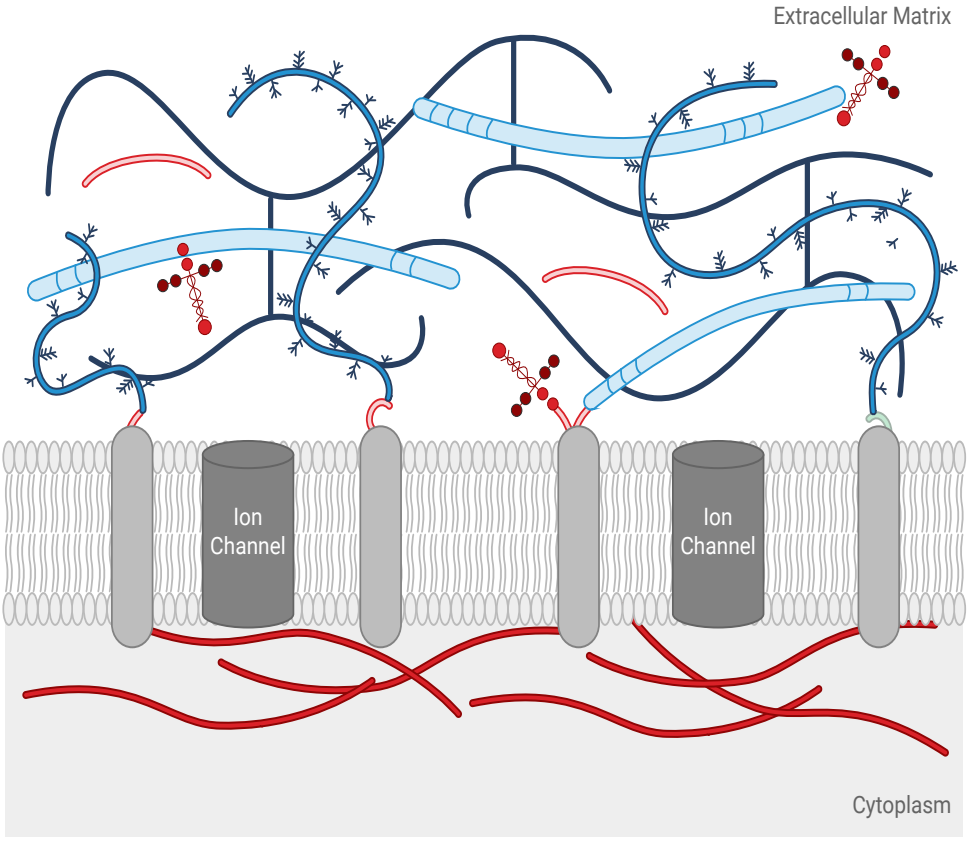


Fig. The ECM plays a multifaceted role in cellular functions, such as anchoring cells (stage 1), guiding migration (stages 2–3), and shaping signal gradients (stage 4). Additionally, specific ECM molecules, such as proteoglycans, act as co-receptors to modulate signaling (stages 5–6), while proteases can release functional fragments that impact cell behavior (stage 7). Finally, cells can detect and respond to the biomechanical properties of the ECM (stage 8).

Hedgehog Signaling Pathway

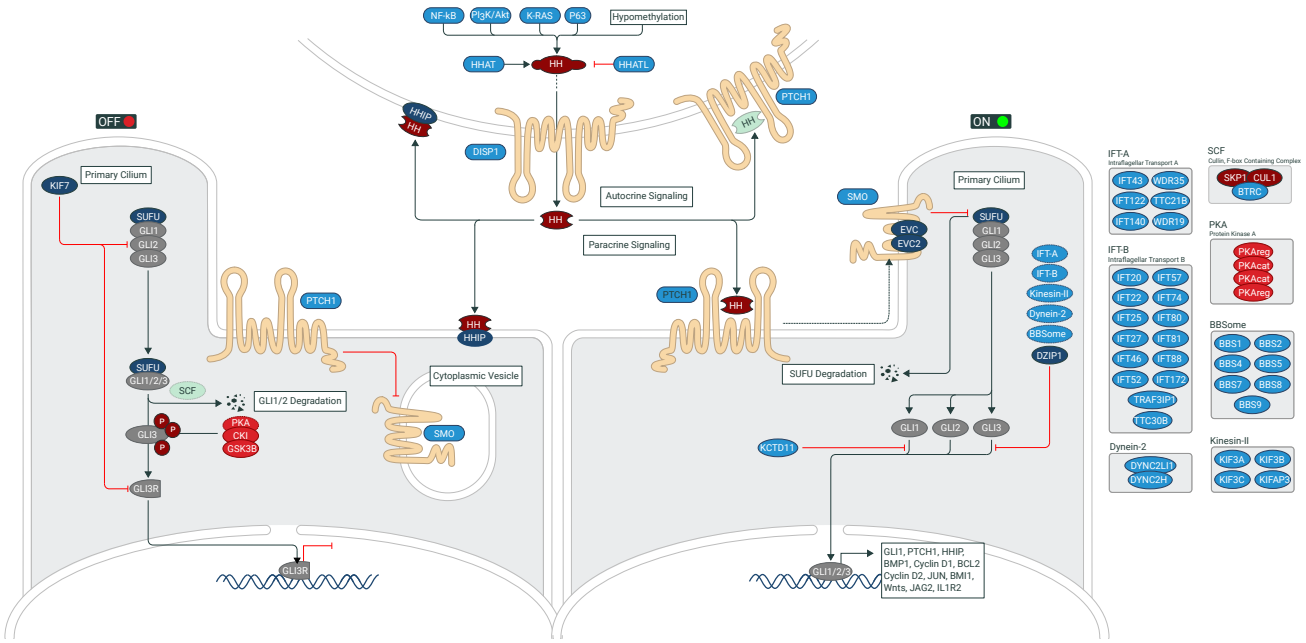
Hedgehog (Hh) signaling is highly conserved across chordates of different taxonomical classification. It is essential for development of the embryo. The Hedehog pathway was first described and characterized in the fruit fly, Drosophila melanogaster. In mammals, Hh signaling regulates cell-fate, tissue polarity, and patterning during early embryogenesis and the morphogenesis of specific organs and tissues. It is subsequently silenced in most adult tissues but can be reactivated following injury to promote repair and regeneration.

Different Hh ligands, including homologs sonic hedgehog (SHH), indian hedgehog (IHH), and desert hedgehog (DHH) are produced as precursors that undergo autocatalytic cleavage, C-terminal cholesterol attachment, and N-terminal palmitoylation prior to secretion. Release and extracellular accumulation of the mature ligands is regulated by the homologs of the Drosophila dispatched (Disp) protein. Binding of secreted Hh ligands to the receptor homolog (PTCH1, PTCH2) triggers the stimulation of the signaling network: the repressive effect of PTCH on the transmembrane receptor SMO is relieved which leads to the activation of glioma-associated oncogene (GLI) transcription factors.

A key specialized structure in this process is the microtubule-based primary cilium. In the absence of the Hh signal unprocessed, non-activating GLI proteins as well as their regulator SUFU are concentrated in the distal tip of the primary cilium. Upon binding of the Hh ligand, PTCH relocates to the cell surface, thus rendering translocation of SMO to the primary cilium and the down-regulation of SUFU possible. Several structurally essential primary cilium proteins have also regulatory effects on the Hh signaling cascade.

Aberrant Hh/GLI regulation leads to major tissular disorders and the development of a wide variety of aggressive cancers. The Hh/GLI cascade has also been linked to the regulation of stemness genes and the survival of cancer stem cells.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Inflammasome Pathway

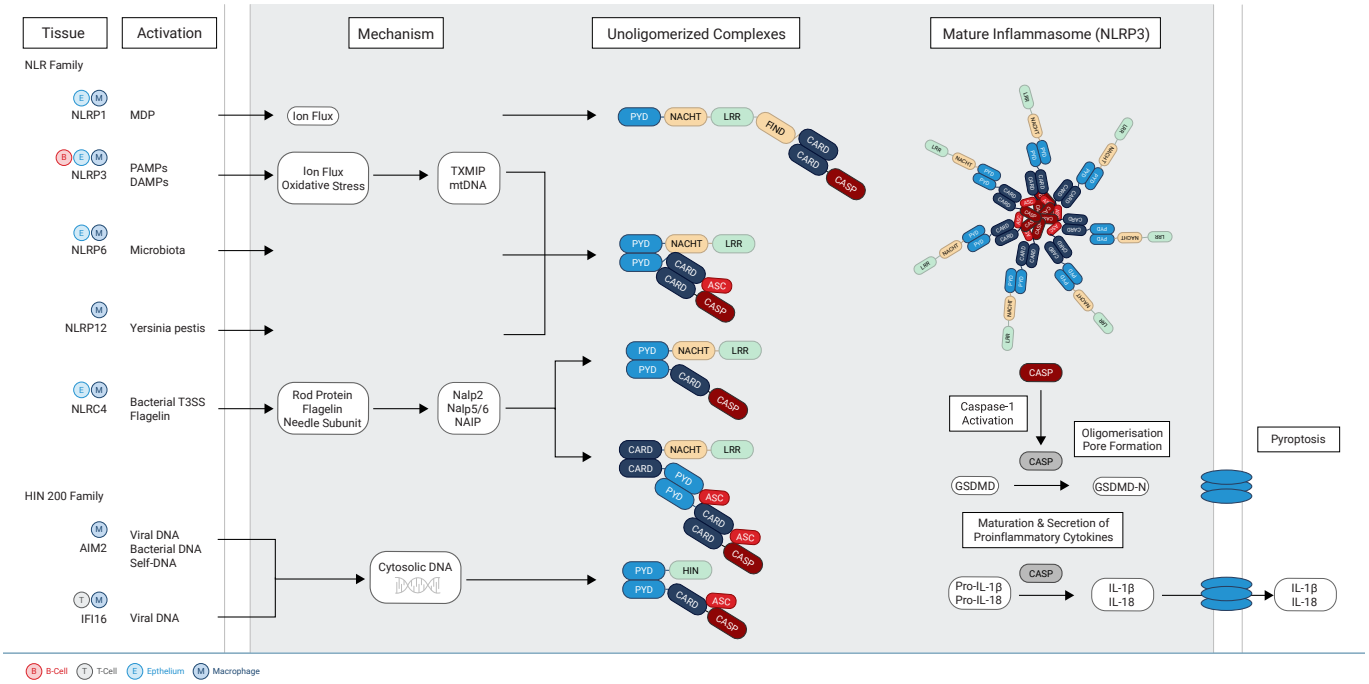
Inflammasomes are multiprotein complexes located in the cytosol. Typically, they consist of a sensor protein, an adaptor protein containing an caspase recruitment domain, and a pro-inflammatory caspase. In case of the NLRP3 inflammasome, presently the best characterized inflammasome, the respective proteins are NLRP3, ASC/PYCARD, and CASP1. The caspase promotes maturation of pro-inflammatory cytokines IL-1beta and IL-18 and Gasdermin D through proteolytic cleavage. Processing of IL-1beta and IL-18 and Gasdermin D drive pyroptosis, a highly inflammatory form of apoptosis. Subsequently to cleavage, the N-terminal part of Gasdermin D (GSDMD-N) localizes to the plasma membrane and forms pores through which IL-1beta and IL-18 are released. In addition, due to osmotic pressure the cell swells and ultimately bursts.

The formation of inflammasomes is triggered upon recognition of inflammatory stimuli by cytosolic pattern recognition receptors (PRRs). NOD-like receptors (NLRs) were the first class of these sensors to be discovered. More recently, AIM2-like receptors (ALRs) and RIG-I-like receptors (RLRs) have been added to this list. Assembly of different inflammasomes is in response to specific inflammatory ligands sensed by the respective receptors. These inflammatory ligands are molecular patterns that associated with pathogens (PAMPs) - such as bacteria, bacterial components (e.g. LPS , toxins, type III secretion systems components), and viruses - or with cellular damage (DAMPs), such as nucleic acids, heat shock proteins, or markers for oxidative stress.

As part of the innate immune system, the primary role the inflammasome is likely the protection against invading pathogens. It is also involved in the initiation of the adaptive immune response through stimulation of the macrophages and regulation of Th17 cell differentiation. The NLRP3 inflammasome in particular has been implicated in metabolic disorders, allergic responses to environmental stimuli, and more recently in driving the cytokine storm in COVID-19.

Furthermore cardiovascular diseases, depression, neurogenerative diseases, diabetes, and cancer are linked to inflammasome. Risk factors for said diseases, e.g. stress, smoking or diet activate the inflammasome which in turn leads to chronic inflammation that contributes to atherosclerosis, mood change and insulin resistance. The case is more difficult with cancer. Here cell type and context define whether inflammasomes support or combat cancer. Clinical trials targeting the NLRP3/CASP1 pathways show promising results in treatment of disease mentioned above. However, in order to explore the full therapeutic potential of inflammasomes greater understanding of involved signaling molecules is required.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Notch Signaling Pathway

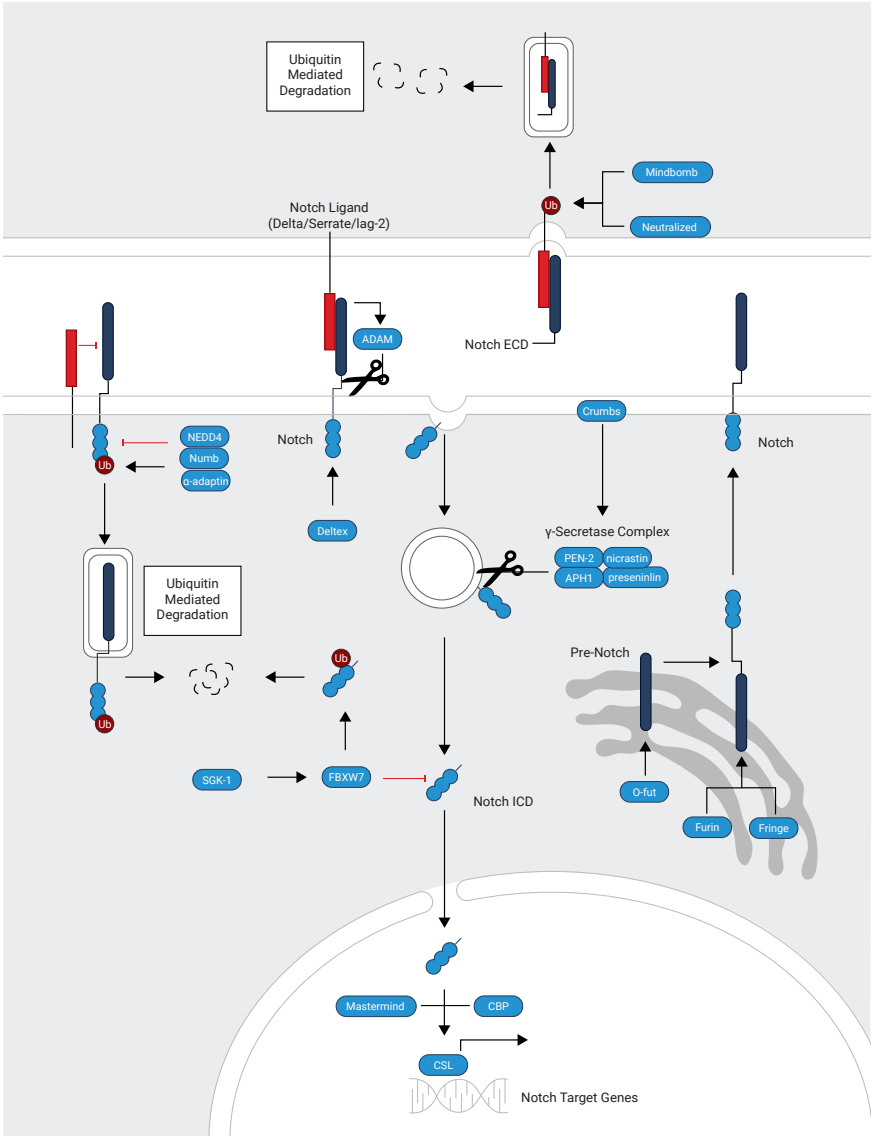
The highly-conserved Notch signaling pathway is unique, as both the Notch receptor and most of its respective ligands (canonically the DSL or Delta/Serrate/lag-2 family members) are transmembrane proteins attached to the cell surface. Therefore, Notch signaling is limited to interaction between adjacent cells.

Communication between adjacent cells is paramount, particularly during early development, when cell fate and function are yet to be determined. Notch signaling provides a method for cells to specify their own identity, and to simultaneously influence the role and identity of neighboring cells through lateral inhibition.

The core of the Notch signaling pathway involves two adjacent cells, one expressing a DSL family ligand, and the other expressing the Notch (the receptor). When receptor and ligand interact, two separate protease enzymes cleave Notch into extracellular and cytosolic components. ADAM proteases cleave the extracellular portion of Notch, which remains bound to its respective ligand and is endocytosed by the signaling cell. γ-secretase cleaves the cytosolic portion of notch. This cytosolic region migrates to the nucleus where it binds to the transcription factor CSL, transforming it from a transcriptional repressor to an activator, and upregulating expression of Notch target genes.

Recent research has unveiled significant insights into the Notch signaling pathway, highlighting its complex roles in various biological processes and diseases. Notch signaling exhibits both oncogenic and tumor-suppressive functions, varying by cancer type and cellular context. For example, in prostate cancer, Notch acts as an oncogene in early stages but shifts to a tumor suppressor role during progression to neuroendocrine prostate cancer. Additionally, the pathway plays a crucial role in regulating macrophage phenotypes within the tumor microenvironment, influencing tumor progression and metastasis. Targeting this pathway could enhance cancer treatment efficacy while advancing mathematical models of Notch-Delta signaling have provided new insights into tissue patterning and developmental biology.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



RTK Signaling Pathway

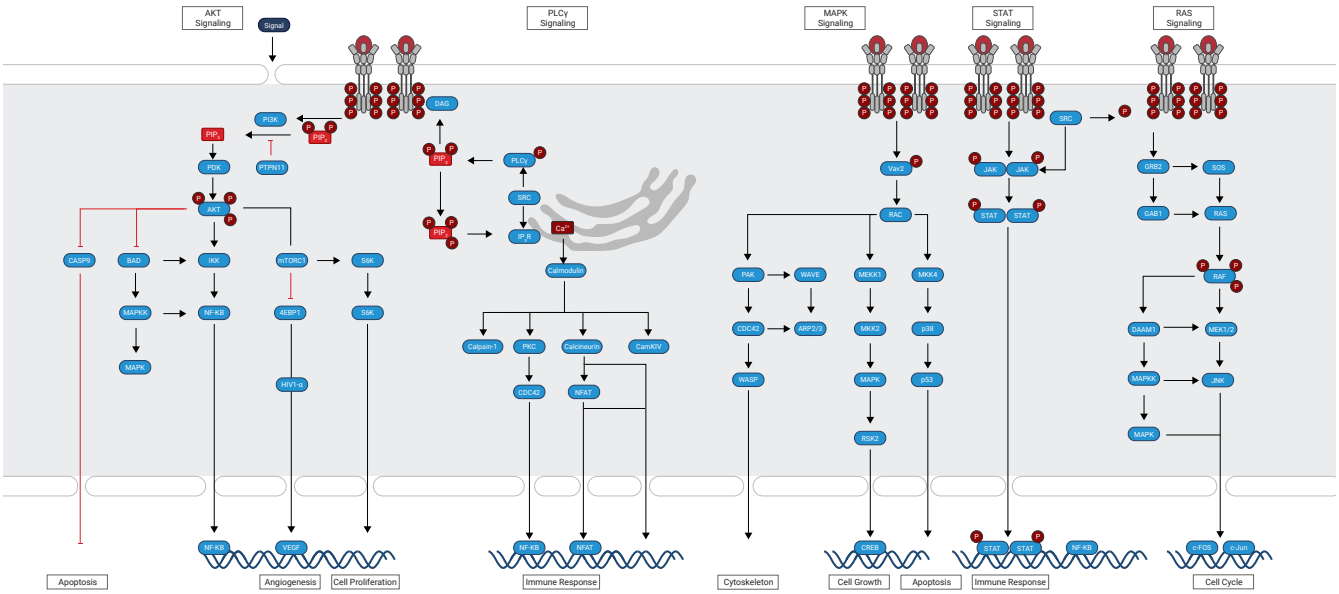
Receptor Tyrosine Kinases (RTKs) are membrane bound kinases that are activated upon binding of receptor specific ligands. They make up the largest class of membrane receptors that trigger signaling cascades through their inherent enzymatic activity. These structures, activation mechanisms and key components of the signaling pathways are highly conserved in metazoans. The RTK family includes, epidermal growth factor receptors (EGFR), platelet-derived growth factor receptors (PDGFR), fibroblast growth factor receptors (FGFR), vascular endothelial growth factor receptors (VEGFR), the insulin receptor, and many more. There are in total 58 known RTKs in humans, which are grouped into 20 classes depending on topology.

RRTKs are fairly promiscuous receptors, and activating stimuli comprise a plethora of growth factors, hormones, and cytokines. Most RTKs form dimers and become active upon ligand binding. The active RTK phosphorylates activators of downstream signaling cascades such as NF-kB, MAPK, Ca2+ dependent signaling, and the JAK-STAT pathway.

RTKs affect a wide spectrum of processes ranging from cytoskeleton dynamics, cell growth and differentiation to inflammation, apoptosis, and tumor progression. In spite of the exceptionally high variety of receptors and outcomes, RTKs engage only a limited set of core processes. Therefore, quantitative analysis of factors like an RTK's expression profile are crucial for the understanding of the signaling processes and predicting qualitative outcomes.

Dysregulated RTK signaling, often triggered by overexpression or mutation of RTKs like insulin receptor (IR) or fibroblast growth factor receptor (FGFR), contributes to metabolic imbalances, including impaired insulin sensitivity and adipogenesis. These disruptions promote excessive fat accumulation and chronic inflammation, hallmark features of obesity, while also influencing energy homeostasis by altering pathways like PI3K-AKT and MAPK signaling. Moreover, RTK-mediated cross-talk with other signaling networks, such as leptin and mTOR pathways, exacerbates the metabolic derangements observed in obesity, making RTKs a critical target for understanding and mitigating this condition.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



TCR Signaling

The T-Cell Receptor (TCR) is a protein complex on the surface of T-cells responsible for the recognition of antigens on the surface of antigen presenting cells (APC). Cell surface glycoproteins CD4 and CD8 serve as coreceptors with the TCR primarily for the interaction with the major histocompatibility complex class II (MHC II) loaded with peptides derived from cytosolic proteins and MHC I with extracellular protein peptides respectively. Activation of the TCR induces a number of signaling cascades, ultimately leading to the transcription of several gene products essential for T cells differentiation, proliferation and secretion of a number of cytokines.

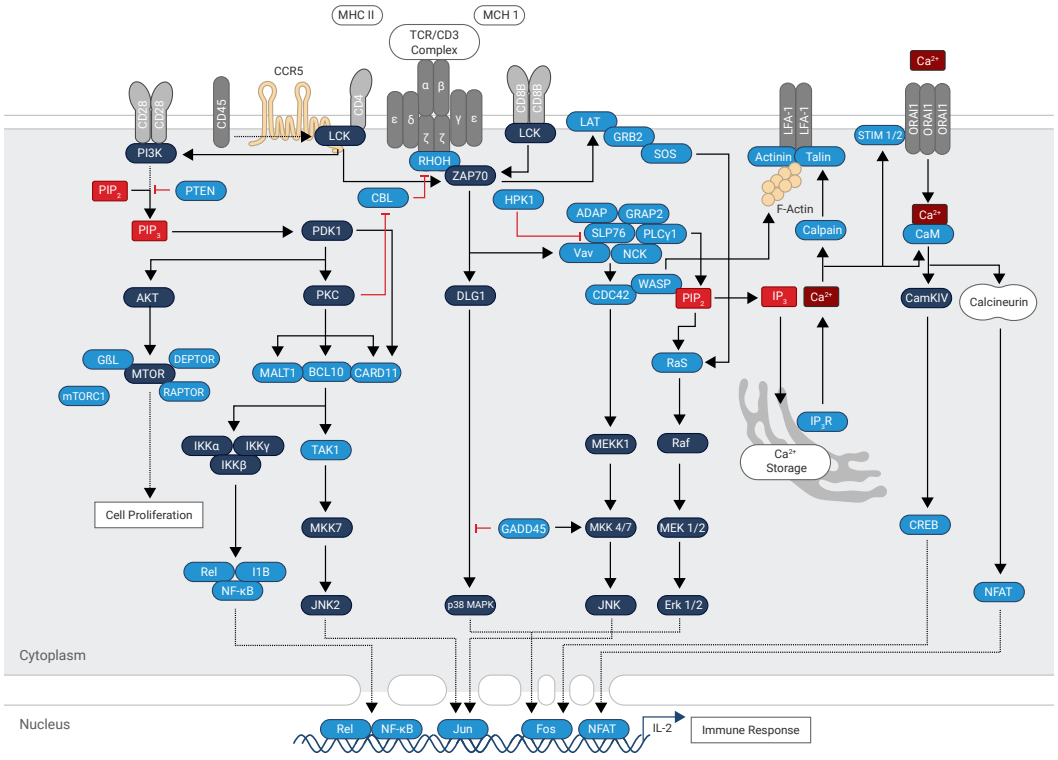
CD45 regulated activation of Src-family kinases LCK and FYN leads to phosphorylation of TCR immunoreceptor tyrosine-based activation motifs (ITAMs) in CD3, creating a docking site for ZAP-70. Phosphorylation and activation is modulated by CD45. ZAP-70 binds to the CD3 zeta chain, which positions the protein kinase to phosphorylate the transmembrane protein linker of activated T cells (LAT). Signaling proteins like SLP-76 can now dock to LAT and are also phosphorylated by ZAP-70. SLP-76 promotes recruitment of Vav, the adaptor proteins NCK and GRAP2, and an inducible T cell kinase (Itk).

Further recruitment of other protein upon LAT and SLP-76 phosphorylation leads to calcium mobilization, Ras Activation and cytoskeletal reorganization. Phosphorylation of phospholipase C γ1 (PLCγ1) by the Itk results in the hydrolysis of phosphatidylinositol 4,5-bisphosphate (PIP2) to produce the second messenger inositol trisphosphate (IP3) and diacylglycerol (DAG). DAG activates PKC4 and the MAPK/Erk pathways cascade which leads to activation of transcription factor NF-κB and ATF2 activation and relocation into nucleus. IP3 promotes release of Ca2+ from the ER, which triggers entry of extracellular Ca2+ into cells through calcium release-activated Ca2+ (CRAC) channels. Calcium-bound calmodulin (Ca2+/CaM) activates the phosphatase calcineurin. Transcription factor NFAT gets activated and promotes IL-2 gene transcription.

TCR signaling is regulated on several levels to diversify the cell response. Extracellular signals are recognized by additional cell surface receptors like CD28 or LFA-1 and modulate cellular response further. Besides, tight negative regulation is essential to prevent hyperactivation of the pathway and the associated immune response.

Aberrant TCR signaling can lead to immune dysregulation, contributing to conditions such as multiple sclerosis, rheumatoid arthritis, and type 1 diabetes. In oncology, modulating TCR signaling is central to adoptive T-cell therapies, including chimeric antigen receptor (CAR) T-cell therapy and engineered TCR-T cells, which enhance antigen recognition and tumor clearance. Furthermore, checkpoint inhibitors targeting molecules downstream of TCR activation, such as CTLA-4 and PD-1, have revolutionized cancer treatment by reinvigorating exhausted T cells. Current research continues to explore ways to fine-tune TCR signaling, aiming to develop more precise immunotherapies with reduced toxicity and novel strategies to restore immune homeostasis in autoimmune disorders. These advances underscore the clinical relevance of TCR signaling and its potential as a therapeutic target in diverse disease settings.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Warburg Effect

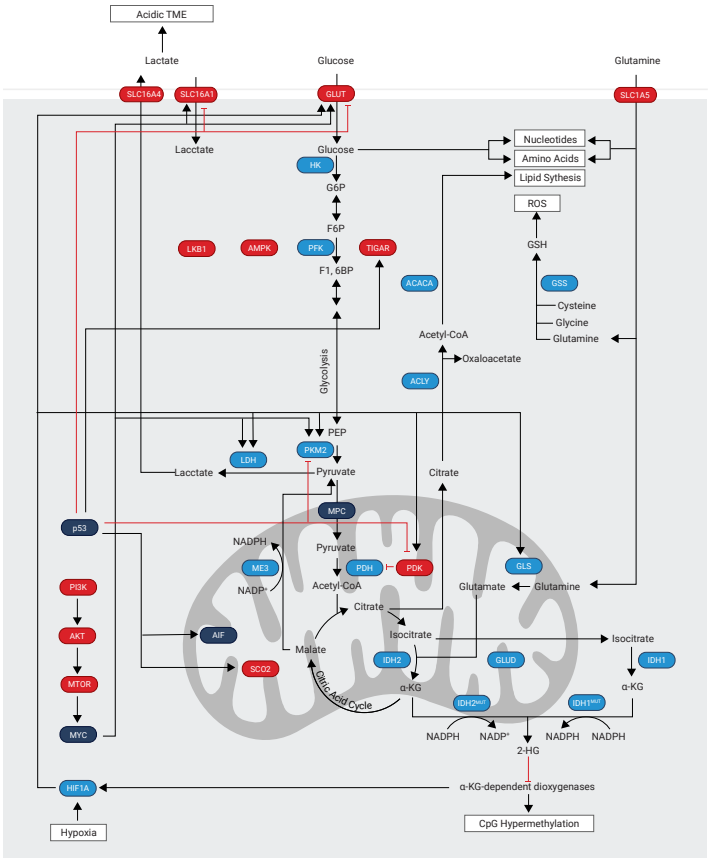
Oncogenic alterations of the cellular metabolism were long regarded as a secondary effect of cancer, precipitated by genetic changes. More recently, this perception has changed and the deregulation of cellular energetics is now included in the Hallmarks of Cancer since their second iteration in 2011. This understanding is corroborated by the fact that many cancer driver mutations are also implicated in cellular metabolism and an estimated two thirds of cancers have mutations in glycolytic genes.

The most well-known adaptation of cancer cell metabolism is the Warburg effect, or aerobic glycolysis. It is named after Otto Heinrich Warburg who observed in the 1920s the production of lactic acid in tumor cells under aerobic conditions. The Warburg effect describes the preference of tumors for fermentation of glucose to lactate even in the presence of sufficient amounts of oxygen. Pyruvate, the end product of glycolysis, is reduced to lactate instead of being transported into the mitochondria for oxidative phosphorylation through the citric acid cycle. Lactate is transported out of the cell and contributes to the acidification of the tumor microenvironment (TME).

The catabolic efficiency of aerobic glycolysis is considerably lower than for oxidative phosphorylation: aerobic glycolysis only produces 2 ATP molecules per glucose molecule whereas oxidative phosphorylation yields between 32 and 34 molecules of ATP per molecule of glucose. However, it provides a different selective advantage to cancer cells by providing building blocks – nucleotides, amino acids, and lipids - necessary for the proliferation of rapidly growing cancer cells. Because of the diversion of pyruvate towards lactate, glutamate becomes the main carbon source to replenish metabolic intermediates in the mitochondrial citric acid cycle to cover the cancer cells' energy needs.
Gain of function mutations in the isocitrate dehydrogenase in the cytosol (IDH1) and in mitochondria (IDH2) lead to reduction of the α-ketoglutarate (α-KG) - one of the citric acid cycle metabolites – to R-2-hydroxyglutarate (2-HG). This oncometabolite inhibits α-KG-dependent dioxygenases by decreasing the concentration of their obligate cofactor α-KG. The class of α-KG-dependent dioxygenases comprises various chromatin-modifying demethylases and methyl transferases. Their inhibition leads to CpG island hypermethylation and affects cell fate. α-KG-dependent dioxygenases also include prolyl hydroxylases, which influence activity of the hypoxia-inducible factor 1 (HIF1), a master regulator of transcription in the adaptive response to hypoxia.

Regulation of transcription factors like HIF1 and Myc and activation of signaling pathways like PI3K/AKT signaling have been shown to contribute to the Warburg phenotype in cancer. Inactivation of tumor suppressors like p53 is also an important mechanism. Under normal conditions, p53 negatively regulates glycolysis and promotes oxidative phosphorylation. However, these mechanisms fail under aerobic glycolysis conditions, thus supporting continuous growth and survival of cancer cells.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



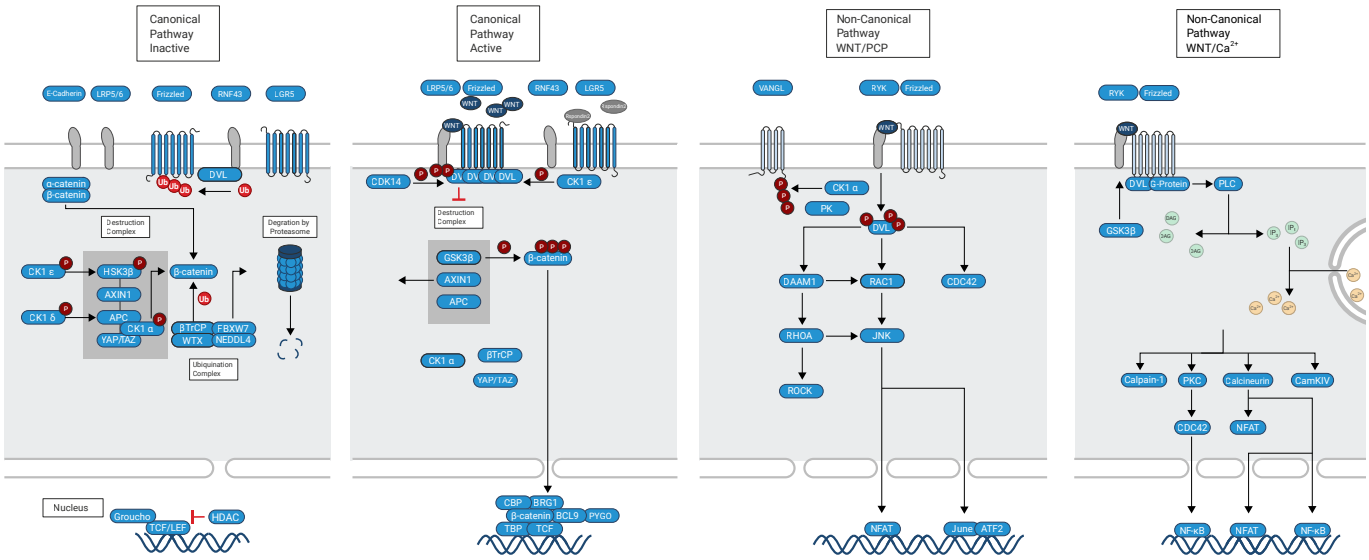
WNT Signaling Pathway

Wnts are a class of evolutionarily-conserved, lipid-modified glycoproteins that play a pivotal role in development and homeostasis through a number of different paracrine and autocrine signal-transduction pathways. During early development, Wnt signaling plays a major role in axon guidance, cell polarity, and body axis specification. Extracellular Wnts bind a variety of different receptors, and initiate signaling in several distinct pathways. Receptors include seven-pass transmembrane Frizzleds and receptor tyrosine kinases ROR and Ryk.

Wnt signaling pathways can result in changes to gene transcription. For example, in the canonical β-catenin signaling pathway Wnt signaling prevents destruction of the transcriptional regulator β-catenin. Upon ligation to their receptors, the cytoplasmic protein disheveled (DVL) is recruited, phosphorylated and activated. Activation of DVL induces the dissociation of GSK-3β from Axin and leads to the inhibition of GSK-3β. Next, the phosphorylation and degradation of β-catenin is inhibited as a result of the inactivation of the “destruction complex”. Subsequently, stabilized β-catenin translocates into the nucleus leading to changes in different target gene expressions. Wnt signaling can also prompt morphological changes to cellular structure e.g., the non-canonical planar cell polarity pathway induces a kinase cascade that results in reorganization of actin, a core component of the cytoskeleton. The non-canonical Wnt/Ca2+ pathways lead to release of intracellular Ca2+ via G-proteins. Elevated Ca2+ can activate the phosphatase calcineurin, which leads to dephosphorylation of the transcription factor NF-AT and its accumulation in the nucleus.

Genetic and epigenetic deregulation of Wnt/β-catenin signaling contributes to human cancer, which has led to the development of extensive approaches targeting Wnt/β-catenin signaling as cancer therapies. PORCN inhibitors, Wnt ligand antagonists, and FZD antagonists/monoclonal antibodies are beeing examined in clinical trials of various Wnt signaling-associated human cancers. Nonetheless, the blockade of Wnt signaling causes side effects such as impairment of tissue homeostasis and regeneration. Recent studies have identified several Wnt signaling regulators whose expression is specific to cancer cells. These cancer-specific regulatory processes of Wnt signaling may be druggable vulnerabilities of Wnt signaling-associated cancer.

Click here to see the online version of this article, its associated references, and related antibodies, proteins, and ELISA kits



Contact Us

Rockland
PO Box 5199
Limerick, PA 19468
USA

www.rockland.com
info@rockland.com
+1 484-791-3823

antibodies-online
PO Box 5201
Limerick, PA 19468
USA

www.antibodies-online.com
support@antibodies-online.com
+1 877 302 8632

antibodies-online GmbH
Schloss-Rahe-Str. 15
52072 Aachen
Deutschland

www.antikoerper-onliine.de
info@antikoerper-online.de
+49 (0)241 95 163 153