CANCER IMMUNOTHERAPY
OVERVIEW OF CURRENT LANDSCAPE

2018 AMWA Annual Meeting
1 November 2018
Petra Volna, Senior Regulatory Documentation Scientist
Genentech Inc.
When Was Cancer Immunotherapy First Used?

Hint: The answer may surprise you
William B. Coley, MD: The Father of Immunotherapy

November 09, 1893

MAJOR DISCOVERY

FIRST USE OF COLEY’S MIXED BACTERIAL TOXINS

William B. Coley creates a filtered mixture of bacteria and bacterial lysates, composed of Streptococcus pyogenes and Bacillus prodigiosus, called “Coley’s Toxins,” to treat tumors. His first patient is a 21-year old man named John Ficken with a large inoperable tumor (likely a malignant sarcoma). After treatment with the toxins, Ficken had a complete remission, lasting until his death 26 years later of a heart attack.

The Nobel Prize in Physiology or Medicine 1908
Awarded jointly to Ilya Mechnikov and Paul Ehrlich "in recognition of their work on immunity."

AWARDS & HONORS

EHRlich, METchnIKoFF SHARE NOBEL PRIZE

Paul Ehrlich, who made several seminal discoveries about the immune system and later proposed the theory of cancer immune surveillance, and Elie Metchnikoff, the first to provide evidence that cells provided protection against disease, share the Nobel Prize in Physiology or Medicine.

November 09, 1909

MAJOR DISCOVERY

CANCER "IMMUNE SURVEILLANCE" HYPOTHESIS INTRODUCED

Paul Ehrlich proposes that the immune system usually suppresses tumor formation, a concept that becomes known as the "immune surveillance" hypothesis. This theory would undergo several periods of acceptance and skepticism until 2001, when Robert Schreiber, Lloyd Old, and others provided firm experimental evidence of the phenomenon.

The Nobel Prize in Physiology or Medicine 2011

One half awarded jointly to Bruce A. Beutler and Jules A. Hoffmann "for their discoveries concerning the activation of innate immunity" and the other half to Ralph M. Steinman "for his discovery of the dendritic cell and its role in adaptive immunity."

November 09, 1973

MAJOR DISCOVERY

DENDRITIC CELL DISCOVERED

Zanvil Cohn and Ralph Steinman discover the dendritic cell, a new immune cell that plays a crucial role in bridging innate and adaptive immunity, and further characterize it over the next several years. For this seminal work, Dr. Steinman is later awarded the 2011 Nobel Prize in Physiology or Medicine.

Dendritic cells (DCs) have the unique capacity to initiate primary and secondary immune responses.

November 10, 1997
MAJOR DISCOVERY
THE KEY MISSING LINK BETWEEN THE INNATE AND ADAPTIVE IMMUNE RESPONSES PROVIDED

Ira Mellman, with Ralph Steinman and others, including Shannon Turley, and Antonio Lanzavecchia provide the first clear demonstration that dendritic cells “mature” in response to microbial products or pro-inflammatory mediators, activating their antigen processing and presentation capacities. By showing that ligands associated with innate immunity enable dendritic cells to initiate T cell responses, this work provided the key missing link between the innate and adaptive immune responses.


Discovery of T-cell Growth Factor (Interleukin-2)

November 09, 1977
MAJOR DISCOVERY

T CELL GROWTH FACTOR DISCOVERED

Francis W. Ruscetti, Doris Morgan, and Robert C. Gallo report the discovery of T cell growth factor (TCGF), later renamed interleukin-2 (IL-2), in mice, making it possible to grow and expand normal lymphocytes long term. The availability of TCGF made it possible to study cloned T cells with a single antigen specificity, leading to an understanding of how T cells recognize the TCGF/IL-2, to the identification of receptors for TCGF and antigens, and to the unanticipated identification of Th1- and Th2-polarized T-cell types.


November 09, 1983
MAJOR DISCOVERY

CLONING OF IL-2

Tadatsugu Taniguchi and collaborators report the cloning of IL-2.

T-cell-mediated Cytotoxicity against Autologous Malignant Melanoma

November 09, 1984

MAJOR DISCOVERY

CLINICAL EXPERIMENTS SHOW PROMISE OF T CELLS TO ATTACK TUMORS

Lloyd J. Old, Herbert F. Oettgen, and Alexander Knuth conduct the first clinical experiments demonstrating that T cells could be trained to recognize and attack an established tumor.


Out of 13 patients recurrent or metastatic malignant melanoma, only 1 patient, a 31-year-old male, who underwent resections of extensive metastatic melanoma of axillary, supraclavicular, and cervical lymph nodes in 1976 and 1978 and remained free of detectable melanoma.

This patient's lymphocytes were found to be strongly cytotoxic for autologous cultured melanoma cells
Binding of immunogenic peptides to Ia histocompatibility molecules

November 09, 1985

MAJOR DISCOVERY

THE ROLE OF THE MHC MOLECULE IN ANTIGEN PROCESSING AND PRESENTATION ESTABLISHED

Emil Unanue and colleagues demonstrate that a processed peptide can bind to an MHC molecule directly, establishing the role of the MHC molecule in antigen processing and presentation.


<table>
<thead>
<tr>
<th>Cytosolic pathogens</th>
<th>Intravesicular pathogens</th>
<th>Extracellular pathogens and toxins</th>
</tr>
</thead>
<tbody>
<tr>
<td>any cell</td>
<td>macrophage</td>
<td>B cell</td>
</tr>
</tbody>
</table>

- Degraded in: Cytosol
- Peptides bind to: MHC class I
- Presented to: Effector CD8 T cells
- Effect on presenting cell: Cell death
- Activation to kill intravesicular bacteria and parasites
- Activation of B cells to secrete Ig to eliminate extracellular bacteria/toxins

FOR EDUCATIONAL PURPOSES ONLY
Immunological Synapse Created

November 10, 1998

MAJOR DISCOVERY

IMMUNOLOGICAL SYNAPSE CREATED

Abraham Kupfer describes the three-dimensional structure of supramolecular activation clusters (SMACs), the interface between an antigen-presenting cell and a lymphocyte (including key molecules the T cell receptor and the major histocompatibility complex), later coined the immunological synapse and further elucidated by Anish Grokou, Michael Dustin, Paul Allen, and Andray Shaw.


Key steps for effective immune response

- Effective antigen presentation
- T-cell infiltration
- Tumor or pathogen killing
- Immunologic memory
  - High-affinity antibodies and memory T and B cells
CANCER-IMMUNE EQUILIBRIUM
Elimination, Equilibrium and Escape

Immunoediting:
Nonsilent point mutations (which lead to antigenic neoepitopes) are more frequently lost in cancers compared with silent point mutations (not recognized by T cells)

Adaptive Immune Resistance:
Tumor antigen-specific T cells attempt to attack the cancer, but the cancer changes in a reactive fashion to protect itself from this immune attack

Ribas A. Cancer Discov. 2015 5(9):915-9
Cancer Immunity Cycle and Immune Phenotypes

Antigen release

Antigen presentation (dendritic cells/APCs)

Priming and activation (APCs and T cells)

T-cell trafficking

T-cell infiltration (T cells and endothelial cells)

 IMMUNE EXCLUDED

 T-cell recognition

 IMMUNE DESERT

T-cell–mediated killing of tumor cells

Types of Cancer Immunotherapy (CIT)

Key to all forms of CIT:
Effective antigen presentation  
T-cell infiltration  
Tumor killing via CTLs

- Immune checkpoint blockade
- Dendritic cells and Therapeutic cancer vaccines
- Chimeric antigen receptor (CAR) T cells
- T-cell recruiting bispecific antibodies
- Preventative vaccines
IMMUNE CHECKPOINT BLOCKADE

Allison Bruce
The Nobel Prize in Physiology or Medicine 2018
Awarded jointly to James P. Allison and Tasuku Honjo "for their discovery of cancer therapy by inhibition of negative immune regulation."

One of several scientists who had made the observation that CTLA-4 functions as a brake on T cells

Investigated CTLA-4 blockade to disengage the T-cell brake and unleash the immune system to attack cancer cells

Discovery of PD-1 and its importance for cancer therapy

PD-1 is a protein expressed on the surface of T cells that functions as a T-cell brake
Immune Checkpoint Inhibitors

1994
CTLA-4 identified as negative regulator of T-cell activation

1996
CTLA-4 blockade could cause tumor rejection in mice

1999
PD-1 identified as immune checkpoint

2000
B7-H1 (PD-L1) and B7-DC (PD-L2) identified as ligands for PD-1

2001
CTLA-4-specific antibody induces clinical regressions in patients with advanced melanoma

2003
CTLA-4-specific antibody induces frequent tumor regressions in patients with advanced melanoma, renal, lung and colon cancer

2009
Improved survival with ipilimumab, CTLA-4-specific antibody, in patients with metastatic melanoma

2010
FDA approves Yervoy, ipilimumab, for advanced melanoma

2011
PD-1-specific antibody, induces frequent tumor regressions in patients with advanced melanoma, renal, lung and colon cancer

2012
Anti-PD-1 antibody shows dramatic efficacy results in Ph 1 trial

2014
Opdivo, nivolumab, a PD-1-specific antibody approved in Japan for advanced melanoma

2015
FDA approves Keytruda, pembrolizumab, for advanced melanoma

2015
FDA approves Tecentriq, atezolizumab, for bladder cancer
How Do Immune Checkpoint Inhibitors Work?

Activation of T cells requires that the T-cell receptor binds to structures on other immune cells recognized as "non-self". A protein functioning as a T-cell accelerator is also required for T cell activation. CTLA-4 functions as a brake on T cells that inhibits the function of the accelerator.

Antibodies (green) against CTLA-4 block the function of the brake leading to activation of T cells and attack on cancer cells.

PD-1 is another T-cell brake that inhibits T-cell activation.

Antibodies against PD-1 inhibit the function of the brake leading to activation of T cells and highly efficient attack on cancer cells.

Graphic courtesy of The Nobel Foundation
Blockade of CTLA-4 and of PD-1 and PD-L1 to induce antitumor responses

Antoni Ribas, and Jedd D. Wolchok Science 2018;359:1350-1355
Published by AAAS
Timing of clinical development of anti–CTLA-4, anti–PD-1, and anti–PD-L1 antibodies from first administration to humans to FDA approval

Antoni Ribas, and Jedd D. Wolchok Science 2018;359:1350-1355
Published by AAAS
Too Much of a Good Thing?

Trial explosion
More than 1000 clinical trials are combining other cancer treatments with immunotherapy drugs, called checkpoint inhibitors, that target the proteins PD-1 or PD-L1 (bottom bars). The number of subjects needed for those trials has skyrocketed, and some trials may not find enough patients.*

Jocelyn Kaiser Science 2018;359:1346-1347
DENDRITIC CELLS AND THERAPEUTIC CANCER VACCINES

Magnification 16,000x. (Rita Serda/FEI Image)
A landmark study showed that accumulation of CD8+ T cells within the tumor (TILs) predicted improved patient survival.

NKT cells enhance CD4+ and CD8+ T cell responses to soluble antigen in vivo through direct interaction with dendritic cells.

First data indicating that presence of tumor-infiltrating lymphocytes in the primary tumor strongly correlated with patient survival.

The first tumor antigenic peptides produced by peptide splicing reported.

First characterization of peptides from MHC class I.

Rapid and strong human CD8+ T cell responses to vaccination with peptide, IFA, and CpG oligodeoxynucleotide.

Type, density, and location of immune cells within tumor samples found to be a better predictor of patient survival than previous pathological criteria for tumor staging.

Mycobacterial cell wall-DNA complex showed antineoplastic activity in patients with bladder cancer.

Artificial antigen presenting cells (aAPC) could successfully enhance adoptive therapy of tumor antigen-specific CD8+ T cells.

Peptide vaccine + IL-2 improves melanoma responses.

FDA approves the use of sipuleucel-T (Provenge®) for the treatment of prostate cancer.

Peptide vaccine + IL-2 improves melanoma responses.
Personalized Vaccines for Cancer Immunotherapy
Customizing a patient-specific cancer vaccine

Ugur Sahin, and Özlem Türeci Science 2018;359:1355-1360
Published by AAAS
Neoepitope Vaccines Promote a Functional Cancer Immunity Cycle

Ugur Sahin, and Özlem Türeci Science 2018;359:1355-1360
Personalized Cancer Medicine

Stratified targeted medicine

In vitro diagnostic

Neg

Pos

Neg

Invariant drug off the shelf

Personalized mutanome vaccine

Mutanome vaccine design

Just-in-time production

Individually tailored drug on demand

Ugur Sahin, and Özlem Türeci Science 2018;359:1355-1360

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The Interconnected Dimensions of Cancer Heterogeneity

**Tumor heterogeneity**
Mutation and neoantigen profile, epigenetics, biology and evolution

**Immune system**
HLA restriction and immune SNPs

**Tumor environment**
Immunosuppression
Recognition and editing

**Host and environment**
Factors include HLA haplotype, microbiome, epigenome, age, antigen exposure, drugs, and comorbidities.

Ugur Sahin, and Özlem Türeci Science 2018;359:1355-1360
VISUALIZING A NEOANTIGEN VACCINE AT WORK

Computer visualization of metastatic melanoma cells, before (left) and after (right) the patient was treated with a neoantigen vaccine. After vaccination, about three-quarters of the cells were seen to be dying (red).

CHIMERIC ANTIGEN RECEPTOR (CAR) T CELLS
Chimeric antigen receptor (CAR) T cells

1992
Primary T-cell engineering

1993
First generation of CARs (CD3ζ-based)

2002
In vitro-expanded T cells can cause tumor regressions in advanced melanoma

2003
Demonstration of CD19 as a valid target for CARs

2002
Second generation of CARs (CD28-based)

2004
Third generation of CARs (4-1BB-based)

2006
Bulk T cells transduced with T cell receptor genes are used to treat patients with melanoma

2007
First IND for CD19 CAR therapy (BB-IND#11411)

2008
CAR T cells induce clinical responses in patients with B cell lymphomas

2011
Adoptive immunotherapy with CD8+ T cells genetically engineering to recognize the NY-ESO-1 induce remissions in sarcoma and melanoma

2011
New CAR T cell treatment cures patients with CLL

2013
CAR T cell therapy attains complete responses in ALL

2017
FDA approves CD19 CAR T therapy for pediatric ALL and NHL

FOR EDUCATIONAL PURPOSES ONLY
CAR T cell immunotherapy for human cancer
Engineered T cells: design of TCR versus CAR T cells

Carl H. June et al. Science 2018;359:1361-1365
Published by AAAS

FOR EDUCATIONAL PURPOSES ONLY
CAR-T Cell Therapy Is Associated with Cytokine Release Syndrome and Neurotoxicity

Carl H. June et al. Science 2018;359:1361-1365
Published by AAAS

FOR EDUCATIONAL PURPOSES ONLY
Conditionally Expressed CAR using Notch as a Signal Induction and Response Pathway System

Carl H. June et al. Science 2018;359:1361-1365
Published by AAAS
Regional disparities in studies of CAR T cell therapies

Carl H. June et al. Science 2018;359:1361-1365
Published by AAAS
T-CELL ENGAGING BISPECIFIC ANTIBODIES (T-BSAB)
T-cell engaging bispecific antibodies (T-BsAb) targeting CD20, a receptor on mature B lymphocytes
Cytotoxic (CD8+) T cell releases cytotoxic granules leading to apoptosis of the targeted tumor cell.
Apoptosis of malignant B cell
T-cell engaging bispecific antibodies (T-BsAb)

November 10, 2008
TOOLS & TECHNOLOGIES

NEW BISPECIFIC ANTIBODY TECHNOLOGY DEVELOPED

Micromet develops a recombinant antibody fragment that is bispecific, designed to target the CD19 antigen on B cell lymphoma and the CD3 antigen on T cells, effectively using the T cells to kill the lymphoma cells. The technology is named BITE, for Bispecific T cell Engager.


CD20 staining: Baseline After Treatment

Only one T-cell-engaging antibody approved by FDA

November 13, 2014

TREATMENT APPROVED

BLINATUMOMAB IS FDA APPROVED, MAKING IT THE FIRST APPROVED BITE IN THE U.S.

The FDA approves Blincyto (blinatumomab) for use in the treatment of B cell acute lymphoblastic leukemia (ALL). The drug, manufactured by Amgen, is the first of a novel class of agents known as bispecific T cell engagers (BiTE), which consist of two monoclonal antibodies joined together. One end of the BiTE binds to a molecule on T cells, and the other end binds to a molecule on cancer cells; by bringing the two together, the BiTE facilitates cancer cell killing. Blincyto (blinatumomab) is designed to treat cancers expressing a molecule called CD19—found on the surface of B cell ALL and also non-Hodgkin’s lymphoma. The FDA approval was based on a phase II clinical trial showing that, of the 185 patients evaluated, 41.6% achieved complete remission with Blincyto.
T-cell recruiting bispecific antibodies

Wu Z, Cheung NV. Pharmacol Ther. 2018;182:161-175
## Development overview of T-BsAb

<table>
<thead>
<tr>
<th>Tumor antigen</th>
<th>Name</th>
<th>Clinical phase(^a)</th>
<th>scCD3 clone used(^b)</th>
<th>Formats</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>BCMA</td>
<td>AMG 420 (a.k.a. davortuzumab, BI 836909)</td>
<td>I (2015/NCT02514239)</td>
<td>n.a.</td>
<td>BTE</td>
<td>(Hipp et al., 2017)</td>
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<tr>
<td>CD123</td>
<td>JNJ-63709178</td>
<td>I (2016/NCT02715011)</td>
<td>n.a.</td>
<td>mG</td>
<td>(Gaudet et al., 2016)</td>
</tr>
<tr>
<td>CD123</td>
<td>MGD0096</td>
<td>I (2014/NCT02152965)</td>
<td>proprietary</td>
<td>DART</td>
<td>(Chichili et al., 2015; Huang &amp; Johason, 2014)</td>
</tr>
<tr>
<td>CD123</td>
<td>Xm3Hi4045</td>
<td>I (2016/NCT02730032)</td>
<td>n.a.</td>
<td>Fab-scFv-Fc</td>
<td>(Chu, Pong, et al. 2014)</td>
</tr>
<tr>
<td>CD19</td>
<td>AFM11</td>
<td>I (2014/NCT02160091)</td>
<td>UCHT1 (h)</td>
<td>TandAb</td>
<td>(Reus et al., 2015)</td>
</tr>
<tr>
<td>CD19</td>
<td>MG0011 (a.k.a. JNJ-64052781)</td>
<td>I (2016/NCT02743546)</td>
<td>XR32 (h)</td>
<td>DART-Fc</td>
<td>(Liu et al., 2016)</td>
</tr>
<tr>
<td>CD19</td>
<td>MTI03 (blinatumomab)</td>
<td>Approved</td>
<td>L2K</td>
<td>BITE</td>
<td>(Deierli et al., 2002; 2003; Löffler et al., 2000; Melhu et al., 2007)</td>
</tr>
<tr>
<td>CD20</td>
<td>Bi20 (IBTA05)</td>
<td>I/II (2016/NCT01138579)</td>
<td>2B16 (i)</td>
<td>m/rhG</td>
<td>(Stangmair et al., 2008)</td>
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<tr>
<td>CD20</td>
<td>CD20-TDI (a.k.a. BTCT4465A, RG7828)</td>
<td>I (2015/NCT02500407)</td>
<td>UCHT1 (h)</td>
<td>MgG</td>
<td>(Sun et al., 2013)</td>
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<tr>
<td>CD33</td>
<td>AMG-330</td>
<td>I (2015/NCT02520427)</td>
<td>n.a.</td>
<td>BITE</td>
<td>(Smith, Olson, et al. 2015)</td>
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<tr>
<td>CEA</td>
<td>CEA TCR (RG7802, RO69586688)</td>
<td>I (NCT02324257 and NCT012650713)</td>
<td>Proprietary</td>
<td>L2K (de)</td>
<td>TriFab-Fc</td>
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<tr>
<td>CEA</td>
<td>MEDI-565 (a.k.a. AMG-211)</td>
<td>I (2017/NCT01284231)</td>
<td>Proprietary</td>
<td>L2K (de)</td>
<td>BITE</td>
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<tr>
<td>EpCAM</td>
<td>AMG110 (a.k.a. MT110, sol titomab)</td>
<td>I (2008/NCT0653596)</td>
<td>L2K (de)</td>
<td>BITE</td>
<td>(Brischwein et al., 2006; Herrmann et al., 2010)</td>
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<td>EpCAM</td>
<td>Gatuxomab</td>
<td>Approved</td>
<td>266L (i)</td>
<td>m/rhG</td>
<td>(Chelius et al., 2010; Ruff et al., 2004; Zeidler et al., 1999)</td>
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<tr>
<td>GPA33</td>
<td>MGD007</td>
<td>I (2014/NCT02248805)</td>
<td>n.a.</td>
<td>DART-Fc</td>
<td>(Moore et al., 2014)</td>
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<tr>
<td>GPC3</td>
<td>ERY 974</td>
<td>I (2016/NCT02748837)</td>
<td>n.a.</td>
<td>MgG</td>
<td>(Hisiguro et al., 2016)</td>
</tr>
<tr>
<td>Her2</td>
<td>Erbumomab</td>
<td>I (2007/NCT00522457)</td>
<td>266L (i)</td>
<td>m/rhG</td>
<td>(Hansen et al., 2016)</td>
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<tr>
<td>Her2</td>
<td>GRU100</td>
<td>I (2016/NCT02829372)</td>
<td>n.a.</td>
<td>BEAT</td>
<td>(Croset et al., 2014)</td>
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<td>HLA-A2/gp100</td>
<td>IMCgp100</td>
<td>Ib/II (2015/NCT02530578)</td>
<td>n.a.</td>
<td>TCR-scCD3</td>
<td>(Liddy et al., 2012)</td>
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<tr>
<td>p-cd28herin</td>
<td>PF-06671008</td>
<td>I (2016/NCT02596331)</td>
<td>XR32 (h)</td>
<td>DART-Fc</td>
<td>(Root et al., 2016)</td>
</tr>
<tr>
<td>PSMA</td>
<td>BAY20310112 (AMG212, pasituximab)</td>
<td>I (2012/NCT01723475)</td>
<td>Proprietary</td>
<td>BITE</td>
<td>(Friedrich et al., 2012; WHO, 2014)</td>
</tr>
<tr>
<td>PSMA</td>
<td>MOR299/ES414</td>
<td>I (2014/NCT02262910)</td>
<td>n.a.</td>
<td>scFv-Fc-scFv</td>
<td>(Hernandez-Toroyo et al., 2016)</td>
</tr>
</tbody>
</table>

\(^a\) This table excludes trials using pre-arm ATC.

\(^b\) Clinical trial stage shows the most advanced clinical phase for the molecule to date. The year of the trial is based on the date published on clinicaltrials.gov.

\(^c\) n.a. denotes clones whose information is not disclosed in the references given; proprietary denotes clones whose information is available in the patent issued or patent pending, as cited in the references; (h):humanized; (i):rat; (de):deimmunized.
PREVENTATIVE CANCER VACCINES

A 3D model of the human papillomaviruses virus.
Credit: Dr Microbe/iStock
The Nobel Prize in Physiology or Medicine 2008

One half awarded to Harald zur Hausen "for his discovery of human papilloma viruses causing cervical cancer", the other half jointly to Françoise Barré-Sinoussi and Luc Montagnier "for their discovery of human immunodeficiency virus."

November 09, 1983

MAJOR DISCOVERY

ZUR HAUSEN LINKS CERVICAL CANCER TO HPV

Harald Zur Hausen identifies the human papillomavirus as the causative agent of cervical cancer, leading to the development of preventive vaccines for cervical cancer.

Download PDF

© The Nobel Foundation. Photo: U. Montan

Harald zur Hausen
Human papilloma virus (HPV) lifecycle

HPV has a circular, double stranded DNA, protected by capsid proteins.

More than 100 HPV-types are known. HPV16 and 18 cause 70% of all cervix cancers.

Infection by HPV
HPV infects epithelial cells in the cervical mucosa. HPV DNA integrates into the cellular genome when causing cancer.

Infection by HPV
Viruses are replicated within two years.
~90% heal within two years.

HPV DNA integrated into tumour cell DNA
0.8% develop cancer.

Discovery of HPV DNA in cancer cells

Harald zur Hausen found HPV DNA in patient DNA (+).

Graphic courtesy of The Nobel Foundation
Preventative cancer vaccine(s)
Two HPV vaccines approved by FDA (and throughout the world)

November 10, 2006
TREATMENT APPROVED
PREVENTIVE VACCINE FOR CERVICAL CANCER APPROVED

FDA approves the "cervical cancer vaccine" Gardasil, which protects against two types of HPV that cause approximately 70 percent of all cases of cervical cancer worldwide. Gardasil was made possible by technology developed by CRI-funded scientist Ian H. Frazer.

“This new vaccine that prevents cervical cancer grew out of research funded by CRI” – Ian Frazer, 2003 CRI Annual Report

November 10, 2009
TREATMENT APPROVED
SECOND CERVICAL CANCER VACCINE APPROVED

The FDA approves Cervarix, a second vaccine that protects against persistent infection with the two types of HPV that cause approximately 70 percent of all cases of cervical cancer worldwide.
HPV Vaccines Experience from Australia
Both HPV and genital warts rapidly declined, largely thanks to herd immunity

Short-term impact of human papillomavirus (HPV) vaccination in Australia on anogenital warts cases (routine vaccination with or without catch-up): model predictions compared with empirical data.

(A) Girls aged <21 years old
(B) Boys aged <21 years old
(C) Women aged 21–30 years old
(D) Men aged 21–30 years old

Types of Cancer Immunotherapy (CIT)

Key to all forms of CIT:
- Effective antigen presentation
- T-cell infiltration
- Tumor killing via CTLs

- Immune checkpoint blockade
- Dendritic cells and Therapeutic cancer vaccines
- Chimeric antigen receptor (CAR) T cells
- T-cell recruiting bispecific antibodies
- Preventative vaccines
Science Magazine’s ‘Breakthrough or the Year’ in 2013

This year marks a turning point in cancer, as long-sought efforts to unleash the immune system against tumors are paying off—even if the future remains a question mark.

Science's Top 10 Breakthroughs of 2013

By Robert Coontz | Dec. 19, 2013, 2:00 PM

Every year, the editors of Science huddle together and pick an outstanding scientific achievement as the Breakthrough of the Year. This year’s winner is CANCER IMMUNOTHERAPY: harnessing the immune system to battle tumors. Scientists have thought for decades that such an approach to cancer therapy should be possible, but it has been incredibly difficult to make it work. Now, many oncologists say we have turned a corner, because two different techniques are helping a subset of patients. One involves antibodies that release a brake on T cells, giving them the power to tackle tumors. Another involves genetically modifying an individual’s T cells outside the body so that they are better able to target cancer, and then reinfecting them so they can do just that.
Thank you!

Questions? petra.volna@gene.com
SOURCES AND PUBLICATIONS
Source for overview and timeline multiple slides

Cancer Research Institute: Immunotherapy and timeline of progress:
https://www.cancerresearch.org/immunotherapy/timeline-of-progress
Publications: Immune Checkpoint Inhibitors


Publications: Dendritic cells and Therapeutic cancer vaccines


FOR EDUCATIONAL PURPOSES ONLY
Publications: Chimeric antigen receptor (CAR) T cells


Publications:

T-cell engaging bispecific antibodies (T-BsAb)


Publications: Preventative Cancer Vaccines
