

BATTLE EQUIPPING THE BODY TO FIGHT CANCER FROM WITHIN LINES

Since the late 1800s, the field of immuno-oncology has been exploring the relationship between the immune system and the development, progression, and treatment of cancer. With over a century's worth of discoveries as the guide, the past decade has seen an explosion in the translation of this research into new treatment modalities, often with unprecedented success. Advancements in genomic technologies, like next-generation sequencing (NGS), are helping advance our understanding of interactions between the immune system and cancer, guiding therapeutic development.

IMMUNO-ONCOLOGY: ADVANCING BIOLOGICAL THERAPY

1890
Demonstration of transferred immunity¹

1893
"Coley's Toxins" used to treat inoperable tumor

NATIONAL
CANCER
INSTITUTE

1934
National Cancer Institute founded by an act of Congress

1942
Freund's adjuvant used to bolster immune response

1951
First evidence of viral transmission of cancer²

1953
The nonprofit Cancer Research Institute established

1964
Epstein-Barr Virus (EBV) linked to cancer in humans

1970
Leukapheresis, a method for isolating leukocytes, is invented

1982
First successful treatment of lymphoma with mAb⁴

1993
Mouse strain engineered to generate fully humanized mAbs

2001
Immune surveillance hypothesis reborn

2002
Adoptive T-cell therapy shown to cause tumor regression⁵

2011
Approval of ipilimumab

2012
First pediatric use of T-cell therapy

2014
Mutational burden shown to correlate with CTLA-4 response⁶

BIOLOGICAL THERAPIES



MONOCLONAL ANTIBODIES (mAbs): mAbs are engineered antibodies with specificity for a single tumor-related epitope. They can be used to target the delivery of chemotherapeutic agents, disrupt growth signaling, and promote the killing and clearance of tumor cells.

IMMUNE STIMULATION: Immune stimulation generates a nonspecific increase in the overall functioning of the immune system, including its native anticancer activities. Agents used for immune stimulation include cytokines, toll-like receptor agonists, and attenuated or modified bacteria, like *Bacillus Calmette-Guérin* (BCG).

VACCINE IMMUNOTHERAPY: Vaccines train the immune system to quickly address known threats, and cancer vaccines are no different. Vaccines already exist for HPV-induced cervical cancer and HBV-induced liver cancer, and new vaccines are being tested that target tumor cell components and pre-activated T cells.

ONCOLYTIC VIRUSES: Oncolytic viruses find and infect tumor cells, effectively hijacking their replication machinery and causing the cell to explode. Cell lysis also generates a local immune response against cell components. As an added bonus, some oncolytic viruses can also encode for an immune booster, like GM-CSF.

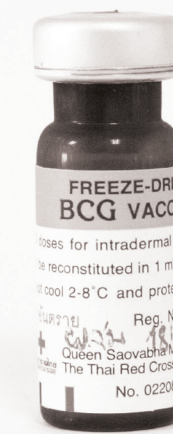
IMMUNOMODULATORY AGENTS: Some cancer cells express cell-surface proteins that can shut down an immune cell's response, improving the odds that a cancer cell will be able to grow into a tumor. By short circuiting the checkpoint, the immune response continues, killing the aberrant cell.

ADOPTIVE T-CELL TRANSFER: In some patients, tumor-infiltrating lymphocytes (TIL) are isolated from their tumor and expanded. In others, chimeric antigen receptor T cells (CAR-T) are leukapheresed and engineered to express new surface antigens. In both cases, the T-cells are returned to the patient to begin attacking their tumors.

1900



1909
Immune surveillance hypothesis proposed by Ehrlich⁷



1957
Interferon discovered

1959
Bacillus Calmette-Guérin (BCG) treats bladder cancer

1968
Nude mouse became a major lab research tool

1975
Monoclonal antibodies (mAbs) generated in vitro with hybridomas

2006
Preventive cervical cancer vaccine released

2016
Approval of atezolizumab

UNLOCKING CANCER'S SECRETS WITH NGS

BIOMARKER IDENTIFICATION: NGS is an essential tool in the discovery of new, reliable biomarkers to track the patient's response to therapies, monitoring cancer progression, response, or remission.

TUMOR IMMUNOGENICITY DETERMINATION: Neoantigen prediction, or the classification of relevant tumor-specific mutations, relies heavily on NGS and bioinformatics to learn and predict what signatures may spark an immune response.

TUMOR RESPONSE: A tumor's response to a therapy is multidimensional, and multiplexed

NGS enables the creation of a complex web of interconnections between facets of a tumor's response to treatment, including mutational load, epigenetics, microenvironment, and the microbiome.

EPIGENETIC ANALYSIS: NGS enables rapid screening of the epigenetic status of several loci or the entire genome, providing insight into how epigenetic modifications can up- or downregulate pro- or antitumorigenic states, shedding light on new therapeutic targets.

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¹ J. Behring E, Kitasato S. Ueber das Zustandekommen der Diphtherie-Immunität und der Tetanus-Immunität bei Thieren. *Deutsche Medizinische Wochenschrift* 1890; 22. Ehrlich P. Über den jetzigen stand der karzinomforschung. *Med Tijdschr Geneesk* 1909; 33. Gross L. "Spontaneous" leukemia developing in C57 mice following inoculation in infancy, with AK-leukemic extracts, or AK-embryos. *Proc Soc Exp Biol Med* 1951; 76:27-32. 4. Miller RA, Maloney DG, Warnke R, Levy R. Treatment of B-cell lymphoma with monoclonal anti-Idiotypic antibody. *N Engl J Med* 1982; 306:517-522. 5. Dudley ME, Wunderlich JR, Robbins PF, et al. Cancer regression and autoimmunity in patients after clonal repopulation with antitumor lymphocytes. *Science* 2002; 298:850-854. 6. Snyder A, Makarov V, Merghoub T, et al. Genetic basis for clinical response to CTLA-4 blockade in melanoma. *N Engl J Med* 2014; 371:2189-99.

“My hope for patients like me is for breakthroughs that lead to earlier cancer detection and effective treatments the first time.”

Francis, Battling cancer



There's nothing more personal than genomics

Powerful stories. New possibilities. Francis, and others like him, inspire us to create the genomic solutions that help researchers uncover new biologic insights that advance cancer's identification and treatment. Illumina next-generation sequencing and array-based solutions are designed to help researchers achieve deeper and more accurate analysis of a tumor's molecular profile. Our hope is to accelerate discoveries that will improve the entire cancer care continuum from earliest detection to companion diagnostics and personalized treatments.

Together we'll advance precision medicine and improve human health.
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Genomic solutions to transform possibility into progress.
Oncology | Reproductive Health | Inherited Conditions | HLA

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Shaping the future of individualized answers in cancer genomics

Advances in genomic sequencing and data analysis promise to revolutionize health care through precision medicine. Identifying individual variations in genes and correlating them to known outcomes and phenotypes allows for disease susceptibility, prediction of response to medications, preventive care, and therapeutic treatment to be more precisely tailored to the individual than ever before. Thanks to technological advances and efficiencies of scale, scientists and clinicians have an increasingly wide array of tools for uncovering genetic variants in patients.

Projects such as the U.S. federal government's Precision Medicine Initiative and the 100,000 Genomes Project (UK), the latter powered by Illumina sequencing technology, are building the evidence base to guide the clinical use of genomic data.

Oncology is at the forefront of precision medicine; already, a number of therapies are assigned based on the molecular and genomic qualities of the cancer. We anticipate a day where precisely tailored therapies based on an individual's unique genetic information will be standard-of-care. We need to ensure that the proper educational efforts in genomic medicine are in place today, in anticipation of the reimbursement and guideline setting activities required in the near future.

A global leader in DNA sequencing and array-based solutions, Illumina is dedicated to improving human health by unlocking the power of the genome. Serving customers in the research, clinical, and applied markets, Illumina technology is responsible for generating more than 90% of the world's sequencing data.* Through collaborative innovation, Illumina is fueling groundbreaking advancements in oncology, reproductive health, genetic disease, and beyond. By empowering large-scale analysis of genetic variation and function, Illumina is enabling studies that were not imaginable just a few years ago, moving us closer to the realization of precision medicine.

*Data calculations on file. Illumina, Inc., 2015.

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IMMUNO-ONCOLOGY: ADVANCING BIOLOGICAL THERAPY

“Since I was 5, I've had so many procedures. My wish is for better treatment. Never give up—let's kick cancer together.”

Jordan, cancer slayer



There's nothing more personal than genomics

Powerful stories. New possibilities. Every day Jordan wakes up to wage battle with her rare brain tumor, combating both the tumor itself and the treatment that left her in a wheelchair. Jordan and brave children like her, inspire us to create the genomic solutions that will make precision treatment for rare and childhood cancers possible. Our hope for the future is that children like Jordan can simply enjoy being children.

Together we'll advance precision medicine and improve human health.
www.illumina.com/immuno-oncology

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