From Aug. 1, 2013, to July 31, 2014, the FDA has approved:

- **6 new anticancer therapeutics.**
- **5 new uses** for previously approved anticancer therapeutics.
- **2 new uses** for imaging agents.
- **1 new use** for a screening test.
THE BIOMEDICAL RESEARCH COMMUNITY

By working together, the stakeholders in the biomedical research community have made and continue to make lifesaving progress against cancer for the benefit of patients, survivors, and their families. Among these stakeholders are the following:

- patients, survivors, and their families and friends;
- clinicians;
- academic researchers from a wide range of specialties;
- biotechnology, pharmaceutical, and diagnostics companies;
- citizen advocates, and advocacy and philanthropic organizations;
- policymakers;
- regulatory agencies;
- funding agencies; and
- payers.

AACR CANCER PROGRESS REPORT 2014

American Association for Cancer Research
FINDING CURES TOGETHER™
CANCER HEALTH DISPARITIES IN THE UNITED STATES

Cancer health disparities are defined as differences in cancer incidence, prevalence, treatment, and outcome among certain segments of a population, including:

- Racial and ethnic minority groups;
- Individuals with low socioeconomic status;
- Individuals who lack or have limited access to healthcare;
- Residents in certain geographical locations, including rural areas; and
- The elderly.

Complex and interrelated factors contribute to disparities in cancer incidence and death among these medically underserved groups. These factors may include, but are not limited to, differences or inequities in:

- Access to and use of health care;
- Treatments received;
- Exposure to environmental cancer risk factors;
- Genetics;
- Social and economic status;
- Cultural beliefs; and
- Health literacy.

The interdependent nature of many of these variables makes it difficult to isolate and study the relative contribution of each to cancer health disparities. However, given that a significant proportion of the U.S. population falls into one or more categories of people at risk of experiencing a disparity, it is important that research into these difficult issues continues. Only with new insights will we develop and implement innovative interventions for the elimination of cancer for all (see Greater Efforts to Reduce Cancer Health Disparities, p. 81).
GENETIC AND EPIGENETIC CONTROL OF CELL FUNCTION

The genetic material of a cell is comprised of strings of four deoxyribonucleic acid (DNA) units called bases.

DNA bases are organized into genes, and the order, or sequence, of the bases provides the code used by the cell to produce the various proteins it needs to function.

The entirety of a person’s DNA is called the genome. Almost every cell in their body contains a copy of their genome. The genome is packaged together with proteins known as histones into structures called chromosomes.

Special chemical marks, called epigenetic marks, on the DNA and histones together determine whether a gene is accessible for reading. The sum of these chemical marks across the entire genome is called the epigenome.

The accessible genes within each cell are read to produce the proteins that ultimately define the function of the cell and the tissue in which the cell resides.
GENETIC MUTATIONS

Below are some of the various genetic mutations known to lead to cancer; however, genetic mutations do not always result in cancer.

Single base changes
- Some mutations can lead to new proteins that may cause cancer to develop.
- Deletion or insertion of DNA sequences can lead to new proteins or loss of protein function that can lead to cancer.

Extra copies of genes (gene amplification)
Higher quantities of certain proteins can lead to enhanced cell survival and growth, leading to cancer.

Large deletions
Loss of DNA can result in loss of genes necessary to stop or control the growth of cancer.

Genetic recombination
Exchange of DNA across different parts of the genome can lead to entirely new proteins that can drive the development of cancer.

Mutations that alter the epigenome
Mutations in the genes that produce proteins that alter the epigenetic marks on DNA or the histones around which it is packaged can lead to cancer.
CANCER GROWTH: LOCAL AND GLOBAL INFLUENCES

The matrix of proteins that surrounds the cancer cells can influence cancer formation, metastasis, and other processes.

Cancer cells can stimulate the growth of blood and lymphatic vessel networks, which supply the cancer cells with nutrients and oxygen required for rapid growth and survival and provide a route for cancer cell escape to distant sites (metastasis).

Systemic factors in the circulation, such as hormones and nutrients, influence the development and growth of cancer.

The immune system can identify and eliminate cancer cells, although in many cases this system is suppressed, permitting the formation and progression of a tumor. However, in some situations of chronic inflammation, the immune system can promote cancer development and progression.
**FUNDAMENTAL RESEARCH: THE FOUNDATION OF TODAY'S TREATMENTS AND TOMORROW'S ADVANCES**

45 FDA-APPROVED THERAPIES

A more comprehensive understanding of the genetic and molecular underpinnings of normal and tumor cell biology has led to the development of 45 FDA-approved therapies that target specific molecules involved in cancer.

5 FDA-APPROVED THERAPIES

An understanding that epigenetic factors influence cancer development has led to five FDA-approved therapies that work by targeting the proteins that modify the epigenome, with more under development, such as the therapy Jack Whelan received (see p. 36).

10 ANTICANCER THERAPIES

Identification of the factors and processes by which cancer cells stimulate the development of blood and lymphatic vessel networks has led to 10 anticancer therapies that impede this process.

17 ANTIHORMONE THERAPIES

Knowledge that the hormones estrogen and testosterone are systemic factors that drive many breast and most prostate cancers, respectively, led to the development of 17 antihormone therapies to treat patients with these diseases.

A more complete understanding of the immune system and its function has led to the development of a class of treatments collectively known as immunotherapies. These revolutionary treatment approaches harness a patient's own immune system to eliminate their cancer cells. They were highlighted in the AACR Cancer Progress Report 2013 (5), and they are discussed here in Treatment With Immunotherapeutics (see p. 64).
REASONS TO ELIMINATE TOBACCO USE

20 MILLION DEATHS
More than 20 million people in the United States died prematurely as a result of smoking and exposure to secondhand smoke between 1965 and 2014 (18).

18 TYPES OF CANCER
Eighteen types of cancer are causally related to tobacco use (see Figure 6, p. 16) (11).

0 EXPOSURE
No level of exposure to tobacco smoke is safe, including exposure to secondhand smoke (19).

6.5 MILLION SMOKING-RELATED DEATHS
Between 1965 and 2014, more than 6.5 million Americans died of a smoking-related cancer and more than 250,000 died of lung cancer caused by exposure to secondhand smoke (18).

Tobacco use during chemotherapy can reduce the effectiveness of treatment.

In addition to cancer-related deaths, tobacco exposure caused nearly 10 million cardiovascular and metabolic disease-related deaths between 1965 and 2014 (18).

Eliminating tobacco use after a cancer diagnosis can reduce the complications associated with treatment and improve overall survival.
REASONS TO MAINTAIN A HEALTHY WEIGHT AND KEEP ACTIVE

33% CANCER CASES
About one in every three new cases of cancer diagnosed in the United States is related to being overweight or obese, being inactive, and/or eating poorly (10, 16).

The adenocarcinoma subtype of esophageal cancer, colorectal, endometrial, gallbladder, kidney, pancreatic, and postmenopausal breast cancers have been causally linked to being overweight or obese (10).

7 TYPES OF CANCER
Regular physical activity can decrease an individual's risk of developing colon, endometrial, and postmenopausal breast cancers (23).

Sedentary behavior may increase the risk for developing colorectal, endometrial, ovarian, and prostate cancers (24).

RISK OF DEATH
Obesity, lack of regular physical activity, and sedentary behavior are linked to worse outcomes, including increased risk for death, for patients with a number of types of cancer.
PHYSICAL ACTIVITY GUIDELINES

The U.S. Department of Health and Human Services recommends the following minimum physical activity levels to improve the nation’s health; see http://www.health.gov/paguidelines/guidelines/summary.aspx.

FOR CHILDREN AND ADOLESCENTS

- Sixty minutes or more of physical activity like running daily.
- Muscle- and bone-strengthening exercises like pushups daily or at least three days per week.

FOR ADULTS

- All adults should avoid inactivity; some physical activity is better than none.
- At least 150 minutes per week of moderate-intensity activity like a brisk walk or 75 minutes of vigorous-intensity activity, like running, in a week.
- Moderate- or high-intensity muscle-strengthening activities two or more days per week.

FOR SPECIFIC POPULATIONS

- Older adults, those who are pregnant, and/or those with disabilities should consult their physician and the modified guidelines.
- Cancer survivors should consult their physicians and follow modified guidelines adapted for their specific cancer and treatment.
REASONS TO PROTECT YOUR SKIN

Exposure to ultraviolet (UV) radiation from the sun, sunlamps, sunbeds, and tanning booths is the predominant cause of the three main types of skin cancer.

Melanoma incidence rates have been on the rise for at least 30 years (1).

More than 85 percent of all skin cancers are estimated to be due to UV radiation exposure from the sun (31, 32).

Use of a UV indoor tanning device increases melanoma risk by 20 percent, and each additional use increases risk a further 1.8 percent (34).

In the United States, 8 percent of all melanoma cases each year have been attributed to indoor tanning (33).

Regular, daily use of sunscreen (sun protection factor [SPF] of 15 or higher) reduces an individual’s risk of developing squamous cell carcinoma and melanoma by 40 percent and 50 percent, respectively (35, 36).
SUN-SAFE HABITS

To reduce your risk of skin cancer, the Centers for Disease Control and Prevention recommend that you:

1. Seek shade and limit time in the sun, especially around midday.
2. Cover up with clothing that covers your arms and legs.
4. Wear wrap-around sunglasses.
5. Apply a sunscreen rated sun protection factor (SPF) 15 or higher at least every two hours.
CANCER-CAUSING PATHOGENS: PREVENTION AND ELIMINATION

**HELIcobacter pylori**
Helicobacter pylori infection can be eliminated by treatment with a combination of stomach-acid suppressants and antibiotics (51).

The Centers for Disease Control and Prevention (CDC) recommends testing and treatment for those with active or a documented history of gastric or duodenal ulcers, low-grade gastric mucosa-associated lymphoid tissue (MALT) lymphoma, or early gastric cancer that has been surgically treated.

**Hepatitis B virus (HBV)**
Infection with HBV can be prevented by vaccination, which has been part of the routine childhood immunization schedule since 1991 (52).

Treatment with antiviral drugs can eliminate HBV in those chronically infected with the virus (53).

The U.S. Preventive Services Task Force (USPSTF) recommends screening high-risk individuals—those from countries with high rates of HBV infection, HIV-positive persons, injection drug users, household contacts of HBV-infected individuals, and men who have sex with men—for HBV infection (54).

**Hepatitis C virus (HCV)**
The antiviral drugs sofosbuvir (Sovaldi) and simeprevir (Olysio) are two new HCV treatment options recently approved by the FDA.

Numerous antiviral drug combinations that exclude interferon, a mainstay of HCV treatment, are in clinical trials and show efficacy in more than 90 percent of patients (55).

The CDC and USPSTF recommend screening those born from 1945 to 1965 for HCV infection (56).

**Human papillomavirus (HPV)**
Two FDA-approved vaccines can protect against infection with HPV16 and HPV18.

Both vaccines are highly effective at preventing precancerous cervical lesions (57, 58).

One of the vaccines, Gardasil, was also found to prevent precancerous anal, vulvar, and vaginal lesions (58, 59).

According to the CDC, safe sex practices may lower the risk of, but may not fully protect against, HPV infection.
As part of the National Cancer Act of 1971, a three-person panel was created to report to the president of the United States on the development and execution of the National Cancer Program and make recommendations for improvements. Members of the President's Cancer Panel are invited to serve a three-year term, and at least two panel members must be distinguished scientists or physicians.

The "President's Cancer Panel Report 2012-2013" detailed progress against cancers caused by persistent infection with human papillomavirus (HPV), and recommended the following to increase vaccine uptake:

- reduce missed clinical opportunities to recommend and administer HPV vaccines;
- increase parents', caregivers', and adolescents' acceptance of HPV vaccines; and
- maximize access to HPV vaccination services.

The panel also recommended the following areas of research to promote global HPV vaccine uptake:

- investigating more convenient dosing schedules for current vaccines;
- developing next-generation vaccines that provide broader protection and/or are easier to store and administer;
- explaining the natural history of oropharyngeal HPV infections;
- developing more effective ways to communicate about HPV-associated diseases and HPV vaccines; and
- determining how best to integrate HPV vaccination with cervical cancer screening.
CANCER SCREENING

BENEFITS OF SCREENING

Reduced cancer incidence. Screening tests can detect precancerous lesions. Removal of the abnormal tissue can reduce, or even eliminate, an individual's risk of developing the screened cancer. For example, the Pap test can detect lesions before they develop into cervical cancer.

Reduced incidence of advanced disease. Screening tests that detect cancers that have already developed can reduce the individual's risk of being diagnosed with the screened cancer at a stage when it has spread to other parts of the body.

Reduced mortality. Diagnosis at an early stage of disease increases the likelihood that a patient can be successfully treated, and thereby reduces the individual's risk of dying of the screened cancer. For example, mammography can detect breast cancers at an early stage, when surgery may be curative.

POTENTIAL RISKS OF SCREENING

Adverse Events. Screening tests are medical procedures; as a result, they carry some risk. However, the chance that an adverse event will occur during a screening test approved by the USPSTF is low.

Anxiety. Screening individuals who are not at high risk of disease can cause unnecessary anxiety during the waiting period for the test results.

False-positive tests. Not all individuals who have a positive screening test have the screened cancer. The rates of false-positive tests are generally low, but a false-positive screen can result in additional unnecessary medical procedures, treatments, and anxiety.

False-negative tests. Not all individuals who have a negative screening test are free from the screened cancer. The rates of false-negatives are generally low, but a false-negative screen can lead to missed opportunities for early treatment.

Overtreatment and overdiagnosis. Not all cancers detected by screening will go on to cause symptoms and threaten life. Overdiagnosis, as this is called, leads to overtreatment, which carries its own risks. The rates of overdiagnosis and overtreatment vary between screening tests and are difficult to quantify.
USPSTF CANCER-SCREENING RECOMMENDATIONS

Below are the USPSTF recommendations related to population-based screening for early detection of several cancers as of July 31, 2014. Not listed are the screening programs for which the USPSTF believes there is insufficient evidence to make a recommendation. These recommendations do not take into account an individual’s unique medical history and risk; thus, everyone should always consult his or her physician prior to making any decision regarding cancer screening.

**BREAST CANCER**

As of November 2013, the USPSTF recommended*:

Women ages 50–74 have a screening mammography once every two years.

Women younger than 50 should make a decision in concert with their physician about when to start regular screening after taking into account their own personal situation.

*Breast cancer screening guidelines are currently under review and will be updated in the near future.

**CERVICAL CANCER**

Women ages 21–29 should have a Pap test every three years.

Women ages 30–65 should have either a Pap test every three years or a Pap test and human papillomavirus (HPV) testing every five years.

**COLORECTAL CANCER**

As of January 2014, the USPSTF recommended**:

Adults ages 50–75 should be screened through fecal occult blood testing yearly, sigmoidoscopy every 5 years, or colonoscopy every 10 years.

**Colorectal cancer screening guidelines are currently under review and will be updated in the near future.

**LUNG CANCER**

As of December 2013, the USPSTF recommended:

Adults ages 55–79 who have smoked one pack of cigarettes per day for 30 years, or the equivalent (two packs per day for 15 years, etc.), and who currently smoke or have quit within the past 15 years, should be screened annually through low-dose computed tomography.
HOW DO I KNOW IF I AM AT HIGH RISK FOR DEVELOPING AN INHERITED CANCER?

Among the factors to consider are whether, in your family, there is one or more of the following:

- many cases of an uncommon or rare type of cancer (such as kidney cancer);
- many cases of a particular cancer, such as breast cancer, among those on the same side of the family;
- members diagnosed with cancers at younger ages than usual (such as colon cancer in a 20-year-old);
- one or more members who have more than one type of cancer (such as a female relative with both breast and ovarian cancer);
- one or more members with cancers in both of a pair of organs simultaneously (both eyes, both kidneys, or both breasts); and
- more than one childhood cancer in a set of siblings (such as sarcoma in both a brother and a sister).

Adapted from:
WHO WE ARE

Biomedical researchers are often categorized by the type of work they do, although some individuals will perform several types of work and can be included in a number of categories. The types of biomedical researchers include, but are not limited to the following:

Basic researchers study animals, cells, molecules, or genes to gain new knowledge about cellular and molecular changes that occur naturally or during the development of a disease.

Population scientists, also known as epidemiologists, study the patterns, causes, and effects of health and disease conditions in defined populations. Epidemiological research is highly collaborative and can span the spectrum from basic to clinical research.

Clinical researchers conduct clinical trials, study a particular patient or group of patients, including their behaviors, or use materials from humans, such as blood or tissue samples, to learn about the way the healthy body works, disease, or response to treatment(s).

Physician-scientists care for patients and conduct research. They may perform population, clinical, translational, or basic research.
Researchers use a variety of models to mimic what happens in healthy and disease conditions. Below are some of the most common models used.

<table>
<thead>
<tr>
<th>Model</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cell lines</td>
<td>Cells of different origins that can be grown continuously in the laboratory.</td>
</tr>
<tr>
<td>Primary cells</td>
<td>Cells that are obtained directly from healthy or diseased tissues of either human or animal origin.</td>
</tr>
<tr>
<td>Tissues</td>
<td>Pieces of or entire healthy or diseased tissues from humans or animals. They are obtained through biopsies or surgery.</td>
</tr>
<tr>
<td>Organoids</td>
<td>Engineered 3-D structures generated from healthy or diseased components, which resemble an organ in cellular composition and organization.</td>
</tr>
<tr>
<td>Animal models</td>
<td>Many different animal models are used in biomedical research. Mice are the most commonly used models, but zebrafish and dogs are emerging as very good models for certain types of cancer. Less frequently used animal models include rodents other than mice, cats, fruit flies, nematodes (worms), pigs, and primates.</td>
</tr>
<tr>
<td>Yeast</td>
<td>Other models include yeast.</td>
</tr>
</tbody>
</table>
**THERAPEUTIC DEVELOPMENT**

- **Target validation.** Potential therapeutic targets identified in discovery research are confirmed to play a role in a given disease.

- **Target to hit.** Large numbers of chemical or biological agents are screened to identify molecules that "hit" the target.

- **Hit to lead.** Positive hits are further tested to determine which bind the target with the most specificity.

- **Lead optimization.** The properties of the lead compound are refined to enhance potency and drug availability and to reduce side effects.

- **Preclinical testing.** Animal models are used to test for effectiveness of the optimized lead, identify any potential toxicity issues, and determine an optimal starting dose for clinical testing. The final compound is called the clinical candidate.

- **Investigational new drug (IND).** Prior to clinical testing, one or more clinical candidates are submitted to the FDA for approval to be used in clinical trials.
PHASE I

Phase I studies are designed to determine the optimal dose of an investigational therapy and how humans process it, as well as to identify any potential toxicities. These first-in-human studies can also demonstrate early efficacy, or clinical results.

PHASE II

Phase II studies are designed to determine initial efficacy of an investigational therapy in a particular disease or selected group of patients, in addition to continually monitoring for adverse events or potential toxicities.

PHASE III

Phase III studies are large trials designed to determine therapeutic efficacy as compared to standard of care (placebos are rarely used in cancer clinical trials).

PHASE IV

Phase IV studies are also known as post-marketing studies. They are conducted after a therapy is provisionally approved by the FDA and provide additional effectiveness or “real-world” data on the therapy (see Figure 8, p. 33).
The best clinical trial endpoint for evaluating anticancer therapeutics is overall survival, which is defined as the percentage of patients still alive at a certain time point after they started treatment for a disease. However, determining overall survival may take too long and, in turn, delay access to potentially lifesaving medical products. Thus, the U.S. Food and Drug Administration (FDA) commonly uses the following surrogate endpoints or “direct measures of how a patient functions, feels, or survives” for approval of anticancer drugs.

**PFS**

*Progression-free survival (PFS)* is the length of time patients survive without their disease getting worse.

**DFS**

*Disease-free survival (DFS)* is the length of time after treatment that a patient survives with no sign of disease.

**pCR**

*Pathologic complete response (pCR)* is the absence of any detectable residual invasive cancer in a surgical specimen after presurgery treatment.

**ORR**

*Overall response rate (ORR)* is the percentage of patients in a trial whose cancer shrinks and/or disappears after treatment.
The FDA has developed four evidence-based strategies to expedite assessment of therapeutics for life-threatening diseases like cancer.

**Accelerated approval.** Accelerated approval is based on assessing the effect of a therapeutic at an earlier stage by using a surrogate endpoint. Any therapeutic approved in this way must undergo additional testing to verify that it provides clinical benefit following approval. Ponatinib (Iclusig) for the treatment of chronic myeloid leukemia (CML) was approved under this pathway in December 2012.

**Fast track.** This designation is given to drugs that fill an unmet medical need and can be granted solely on the basis of preclinical data or data from nonhuman studies. Fast track applications may be evaluated through a “rolling” or continual review procedure, rather than waiting until study completion. Ipilimumab (Yervoy) for the treatment of metastatic melanoma was approved through fast track in March 2011.

**Breakthrough therapy.** A drug that shows substantial improvement over available treatment in early clinical studies can receive breakthrough therapy designation, making it eligible for all features of fast track designation (see above) and additional guidance from the FDA throughout the drug development process. One example of a therapeutic that was FDA approved, in November 2013, after receiving a breakthrough therapy designation is obinutuzumab (Gazyva) for the treatment of chronic lymphocytic leukemia (see p. 53).

**Priority review.** Drugs that have the potential to significantly improve safety or effectiveness may be granted priority review after all clinical trials are completed. This allows the drug to be assessed within six months as opposed to the standard 10 months. Radium Ra 223 dichloride (Xofigo) was granted priority review and approved for the treatment of prostate cancer that has spread to the bones in May 2013.
RECENT ADVANCES IN CERVICAL CANCER PREVENTION AND EARLY DETECTION

A new HPV vaccine designed to protect against seven cancer-causing HPV strains is highly effective at preventing precancerous cervical abnormalities induced by these seven HPV strains (76). Currently approved vaccines cover two of the most common cancer-causing strains.

Current practice recommends three doses of either HPV vaccine for complete protection; recent studies demonstrate that two may be just as effective as three (77, 78).

The U.S. Food and Drug Administration approved a test to detect HPV for use as a single-method tool to screen women at high risk for cervical cancer.
Recent Advances Against Blood Cancers

Obinutuzumab (Gazyva) is a molecule targeted therapeutic and an immunotherapeutic that was approved by the FDA for the treatment of chronic lymphocytic leukemia (CLL) in November 2013.

Ibrutinib (Imbruvica) is a molecule targeted therapeutic that was approved by the FDA for the treatment of mantle cell lymphoma in November 2013 and CLL in February 2014.

Idelalisib (Zydelig) is a molecule targeted therapeutic that was approved by the FDA for the treatment of CLL, follicular B-cell non-Hodgkin lymphoma, and small lymphocytic lymphoma in July 2014.
THE CHALLENGE OF TREATMENT RESISTANCE

Diversity, or heterogeneity, among cancer cells within and between tumors, is ultimately what drives insensitivity to treatment, which in turn leads to treatment resistance. Some examples of heterogeneity are as follows:

Not all cells in a tumor may be rapidly dividing; those that are not are insensitive to treatments targeting rapidly dividing cells.

Some cancer cells in a tumor may contain mutations in the target of a given treatment that render the treatment ineffective.

Redundancies among signaling networks fueling proliferation can enable cancer cells to become resistant to a treatment.
COMPANION DIAGNOSTICS

The effective therapeutic use of most drugs targeting particular cancer-driving molecular abnormalities often requires tests called companion diagnostics. Companion diagnostics:

- are stringently tested for their safety, accuracy, sensitivity, and fidelity;
- are regulated by the U.S. Food and Drug Administration;
- accurately match patients with the most appropriate therapy;
- allow patients to receive a treatment to which they are most likely to respond; and
- allow patients identified as very unlikely to respond to be spared any adverse side effects of the therapy.
Many patients with breast cancer are treated with a traditional chemotherapy and/or molecularly targeted therapy before surgery, an approach called neoadjuvant therapy. The goal of neoadjuvant therapy for breast cancer is to shrink a patient's breast tumor, rendering inoperable tumors operable and thus allowing breast conservation. If, after completing neoadjuvant therapy, no residual invasive cancer is detected in breast tissue and lymph nodes removed during surgery, a patient is said to have a pathologic complete response.

Research has shown that pathologic complete response correlates with long-term survival (108). As a result, the U.S. Food and Drug Administration (FDA) decided to use pathologic complete response as a reasonable endpoint to assess the likelihood that a neoadjuvant therapy will improve disease-free or overall survival for patients with breast cancer (107).
HOW IMMUNOTHERAPEUTICS WORK

The way in which different immunotherapeutics work to benefit patients varies:

- Some release the brakes on the natural cancer-fighting power of the immune system, for example, ipilimumab (Yervoy) and pembrolizumab.
- Some enhance the cancer-killing power of the immune system by triggering the cancer-fighting T cells, for example, DCVax-L.
- Some boost the killing power of the immune system by providing more cancer-targeted immune cells called T cells; these are called adoptive T-cell therapies.
- Some flag cancer cells for destruction by the immune system, for example, obinutuzumab.
- Some increase the killing power of the immune system by enhancing T cell function, for example, Interleukin-2 (Aldesleukin).
- Some comprise a virus that preferentially infects and kills cancer cells, releasing molecules that trigger cancer-fighting T cells; these are called oncolytic virotherapeutics.
There are two main types of adoptive T-cell therapy.

Chimeric antigen receptor (CAR) T-cell therapy. T cells are harvested from blood or bone marrow and genetically modified before being expanded in number. This modification targets the T cells specifically to the patient's cancer and triggers them to attack when they get there.

Tumor-infiltrating lymphocyte (TIL) therapy. T cells are harvested directly from a patient's tumor and expanded in number in the laboratory. Many of these T cells naturally recognize the patient's cancer.
LIFE AFTER INITIAL CANCER TREATMENT ENDS

When an individual becomes a cancer survivor, his or her life is changed irrevocably. Cancer survivors often face serious and persistent adverse outcomes, including physical, emotional, psychosocial, and financial challenges, as a result of their cancer diagnosis and treatment. Some of these challenges may begin during cancer treatment and continue long-term, but others can appear months or even years later. These long-term and late effects include, but are not limited to:

- Bone density loss (osteoporosis);
- Lung (pulmonary) damage;
- Cognitive impairment sometimes referred to as “chemo brain”;
- Lymphedema, swelling, most often in the arms or legs, that can cause problems in functioning and pain;
- Diagnosis with a new form of cancer(s);
- Pain;
- Distress, which can interfere with a person’s ability to cope effectively with cancer and its treatment;
- Premature aging;
- Fatigue that is very severe and often not relieved by rest;
- Recurrence of original cancer; and
- Fear of cancer recurrence;
- Sexual dysfunction;
- Heart damage (cardiotoxicity);
- Infertility;
- Sexual dysfunction.

While all cancer survivors potentially face critical health-related problems, pediatric cancer survivors (ages 0–14 at diagnosis) are particularly at risk because their bodies are still developing at the time of treatment. Adolescents (ages 15–19) and young adults (ages 20–39) also have to confront a distinctive set of concerns, including adapting to long-term cancer survivorship while beginning careers and thinking about starting families of their own.
GUIDELINES FOR LONG-TERM FOLLOW-UP OF SURVIVORS OF CHILDHOOD, ADOLESCENT, AND YOUNG ADULT CANCERS

The Children’s Oncology Group “Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers” provide recommendations for screening and management of late effects that may arise as a result of treatments received by survivors who were diagnosed with cancer as a child, adolescent, or young adult. The guidelines were developed to help standardize and enhance the life-long follow-up care of these individuals.

Central to the guidelines is the idea that prevention and/or early identification of complications are vital if we are to decrease the long-term health risks associated with treatments for childhood, adolescent, and young adult cancers. As such, the guidelines indicate that the key services offered by a long-term follow-up program should include:

- monitoring for and managing physical late effects;
- providing health education to survivors regarding their diagnoses, treatment exposures, and potential late effects;
- providing referrals to specialists and resources as indicated;
- encouraging wellness and health promotion activities;
- addressing psychosocial needs of survivors and affected family members;
- assessing and providing intervention for educational and/or vocational needs;
- assisting with financial and insurance issues;
- guiding transition from pediatric to adult-focused health care;
- empowering survivors to advocate for their own health care needs; and
- facilitating survivorship research.

For more information on these guidelines, see http://survivorshipguidelines.org/
Racial and Ethnic Differences in Cancer Incidence and Mortality

The likelihood that a person in the United States will develop a particular cancer or die as a result of it varies depending on their race or ethnicity. Some examples are highlighted here:

- **30% Higher**
  - The cancer death rate among African-American men is 30 percent higher than among non-Hispanic white men, and for African-American women, it is 14 percent higher than among non-Hispanic white women (146).

- **34% Higher**
  - The cancer death rate among Hispanic men is 34 percent lower than among non-Hispanic white men, and for Hispanic women, it is 35 percent lower than among non-Hispanic white women (13).

- **45% Higher**
  - Compared with non-Hispanic white women, the breast cancer death rate among Hispanic women is 45 percent lower and is 36 percent higher among African-American women (139).

- **2X**
  - Asian and Hispanic Americans are about twice as likely to develop and die from liver cancer as their white counterparts (148).

- **More Likely**
  - People of Ashkenazi Jewish ancestry have an increased risk for several types of cancer, including breast, ovarian, pancreatic, and colorectal cancers.

- **African-American men and women are significantly more likely to develop colorectal cancer and are almost twice as likely to die from it as their white counterparts (148).**

- **African-American men are more likely to develop prostate cancer than men of any other race or ethnicity and are more than twice as likely to die from the disease (148).**

- **American Indian/Alaska Native men are nearly twice as likely to develop and die from stomach cancer as non-Hispanic white men (148).**

- **23% More Likely**
  - Hispanic children are 25 percent more likely to develop leukemia than non-Hispanic children (13).
ELIMINATING COLORECTAL CANCER DISPARITIES IN DELAWARE

The cancer control program was initiated in 2003 under the direction of the Delaware Cancer Consortium (150). As a result of this program:

**17% INCREASE**

Colorectal cancer screening among all Delawareans age 50 or older rose from 57 percent in 2002 to 74 percent in 2009.

**26% INCREASE**

Colorectal cancer screening among African-Americans rose from 48 percent in 2002 to 74 percent in 2009, matching the 2009-screening rate among non-Hispanic whites.

**ELIMINATED**

Disparities in colorectal cancer incidence and mortality between non-Hispanic whites and African-Americans were eliminated as a result of the equivalent screening rates between the two groups.
A PRESCRIPTION FOR INCREASING THE RATE OF PROGRESS AGAINST CANCER

To increase the rate of progress against cancer we must:

- Sustain growth in funding for cancer research.
- Develop the workforce of tomorrow.
- Enhance patient engagement and awareness.
- Advance regulatory science and policy.
- Promote evidence-based prevention strategies.
NIH: A CATALYST OF PROGRESS

The funding for research provided by the NIH can lead to:

- The discovery and development of new approaches for the prevention, detection, diagnosis, and treatment of cancer and other diseases;

- Improvements in the health of Americans and people around the world;

- Job creation and economic growth across the country; and

- Global leadership for the United States in the life sciences and biomedical research.

AACR CANCER PROGRESS REPORT 2014

American Association for Cancer Research
FINDING CURES TOGETHER™
To build the biomedical research workforce of the future we must provide:

- training in basic, translational, and clinical research;
- training in regulatory science;
- access to cutting edge tools and techniques;
- training in team science; and
- professional development training.
Regulatory science is the study of developing new tools, standards, and approaches to assess the safety, efficacy, quality, and performance of medical products, and it can help:

- determine toxicities of new therapeutics at an earlier stage in therapeutic development;
- determine optimal dosing strategies;
- design and implement more efficient clinical trials;
- develop novel tools and metrics to assess the safety and efficacy of new medical products more quickly (see New Path to Approving Breast Cancer Therapeutics, p. 64);
- leverage the power of new technologies, such as health information technology, to more efficiently evaluate new medical products;
- develop, evaluate, and regulate complex new medical products in a streamlined fashion; and
- evaluate the risks and benefits of new treatments in a more informed manner.

Adapted from: http://www.fda.gov/ScienceResearch/SpecialTopics/RegulatoryScience/default.htm?utm_campaign=Goo.
The 2014 Surgeon General's report, “The Health Consequences of Smoking—50 Years of Progress,” outlines the following strategies for eradicating tobacco use:

1. **Sustain high-impact anti-tobacco media campaigns for a prolonged period**;

2. **Increase cigarette taxes**;

3. **Provide access to proven tobacco use cessation treatments**;

4. **Expand smoking cessation efforts for all smokers in primary and specialty care settings**;

<table>
<thead>
<tr>
<th>Strategy</th>
<th>Icon</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sustain high-impact anti-tobacco media campaigns for a prolonged period</td>
<td><img src="image" alt="No Smoking" /></td>
<td>Increase cigarette taxes; provide access to proven tobacco use cessation treatments; expand smoking cessation efforts for all smokers in primary and specialty care settings; effectively implement the U.S. Food and Drug Administration’s authority to regulate tobacco products; increase tobacco control and prevention research efforts; fully fund comprehensive statewide tobacco control programs at levels recommended by the Centers for Disease Control and Prevention; and extend comprehensive smoke-free indoor protection to 100 percent of the U.S. population.</td>
</tr>
</tbody>
</table>