A SCIENTIFIC UPDATE

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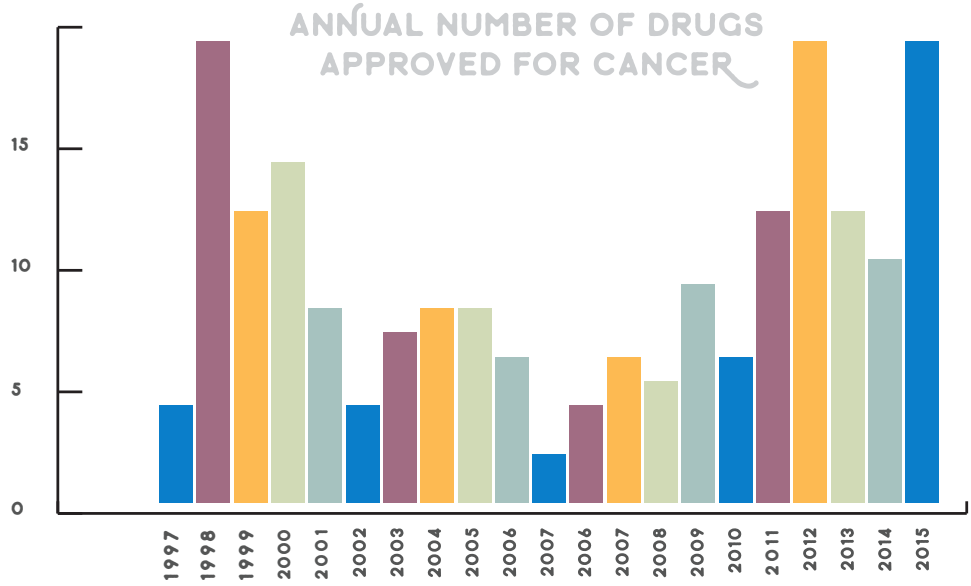
"...LOOKING FORWARD TO A FUTURE WHERE CANCER IS A DISEASE THAT CAN BE CURED..."

Since 1995, there have been 193 new drugs approved by the FDA for the treatment, diagnosis, and supportive care associated with cancer.



Over these past 20 years, there have been several important fundamental changes in the scientific paradigms used to understand cancer and the relationship between the malignant cell and those of the normal cell.

These changes have followed dramatic discoveries associated with the fields of cellular biology, including genetics, molecular biology, molecular mutations, cellular growth regulation, and immunologic interactions between a cancer cell and the healthy organism.

The ability to completely sequence the human genome, and then look for genetic mutations in aberrant cells, using sophisticated sequencing techniques, has led to discovering so-called driver mutations that are required to promote the inappropriate cellular proliferation of the cancer cell. Genetic sequencing has discovered the BCR-ABL mutation associated with chronic myelogenous leukemia, the EGFR mutation (epidermal growth factor receptor mutation) associated with some lung cancers, the ALK mutation (anaplastic lymphoma kinase) associated with some lung cancer and aggressive lymphomas, the BRAF mutation (B-RAF gene) associated with melanoma, non-small cell lung cancer, and hairy cell leukemia. Laboratory findings are leading to the discovery and delineation of important molecular pathways required by the cancer cell to promote division and cell growth; the mTOR pathway, the JAK-STAT pathway, and others are being categorized in ways that have and will certainly lead to new treatments that effect cancer cells in defined and specific ways, often with no or little toxicity—the so called "Targeted Therapies."

Drugs such as Gleevec, Spyrcel, or Tasigna, directly inhibit the BCR-ABL mutation associated with chronic myelogenous leukemia, leading to complete remission. Tarceva, Iressa, and Gilotrif affect the EGFR mutation associated with lung cancer and have induced dramatic responses in these patients; and Zykadia and Xalkori, which target the ALK mutation found in some lung cancer patients, can also induce remission. In melanoma patients whose disease carries the BRAFv600 mutation, drugs such as Mekinist, and Zelboraf directly target this mutation, and can place advanced melanoma patients into remission.

Molecular studies have also discovered the genetic changes associated with resistance to some of these drugs. This occurs with patients whose lung cancer has the EGFR mutation and suddenly progresses. These patients may have acquired a secondary mutation of the EGFR protein, the T790M mutation, leading to resistance; however, the newly approved drug Tagrisso (osimertinib) can overcome that resistance, and was developed specifically for this situation

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Basic understanding of cell biology—particularly of the cell membrane, cell surface receptors and the cellular messengers that induce and promote cell growth—have also been described and discovered over the past twenty years. The HER-2 neu molecule found on breast cancer cells, led to the important development of Herceptin, the monoclonal antibody directed at the HER-2 neu molecule, which effectively inhibits the growth of these cells found in breast and stomach cancer. Rituximab, another monoclonal antibody, directed again a cell surface protein, CD 20, was approved in 1998 for the treatment of patients with lymphoma, and has become one of the mainstay drugs in the treatment of lymphomas and some leukemias. This past year, another novel monoclonal antibody was approved, Daratumumab (Darzalex), directed against the CD38 cell surface molecule found on Myeloma cells.

Most recently, a greater understanding of the immune system has led to important therapies for cancer. The immunomodulatory agents Revlimid, Thalidomide, and Pomalyst are effective and important treatments for Myeloma.

One of the most exciting advances in the treatment of cancer is the understanding that many cancers shut off a patient's immune system through a unique mechanism that effectively kills immune cells attempting to attack cancer cells. A novel set of new agents, approved between 2011 and 2015, prevents cancer cells from protecting themselves from native immunity. Yervoy (ipilimumab) blocks the CTL4 membrane surface protein, and Keytruda (prembrolizumab) and Opdivo (nivolumab) both affect the so-called PD-1 molecule, allowing the immune system to effectively attack and destroy cancer cells; these drugs have received approval for melanoma and lung cancer, and are likely to be approved for many other tumor types including bladder, breast, and mesothelioma in the near future.

The explosion of new important advances in cancer treatment have resulted directly from the greater understating of basic biological mechanisms of normal cells and malignant cells elucidated in the scientific laboratories of investigators interested in understanding the processes of life.

The future also looks very exciting! Advances in stem cell biology, vaccine therapy, and genetic manipulation will have profound effects, not only in cancer care, but likely in preventing and predicating cancer, as well as other diseases.

Over the past 20 years, Tower Cancer Research Foundation's mission has been to provide research funds to those investigators who are asking and answering important questions relevant to understanding the biology of cancer. We have been successful in providing research grants to more than 40 researchers at important institutions throughout Southern California, including, Cedars-Sinai Medical Center, University of California Los Angeles, University of Southern California, University of California San Diego, University of California Irvine, Children's Hospital of Los Angeles, Wadsworth VA, and City of Hope. These funds come from patients, the families of patients, the friends of patients and the business community of Southern California. We have been honored and moved by their generosity and are looking forward to a future when cancer is a disease that can be cured or prevented, and is no longer affecting our families and friends.