FROM THE DIRECTOR

# The Origins of Cancer

**Over the decades,** we've been fortunate to participate in a revolution in cancer treatment. Jonsson Cancer Center scientists and physicians played key roles in the testing and FDA approval of Herceptin for breast cancer, Gleevec for chronic myeloid leukemia, Iressa for lung cancer and Avastin for colon cancer.

Data presented at the American Society of Clinical Oncology conference this year showed the stunning results of the first set of Phase III trials using Herceptin along with chemotherapy in patients with metastatic breast cancer. The addition of Herceptin reduced the risk of recurrence by 52 percent. The venerable *Wall Street Journal* led with "*Almost overnight, one of the worst forms of breast cancer has become potentially one of the most curable.*" Of course it wasn't "almost overnight." Dr. Dennis Slamon and his colleagues pioneered the ultimate development of Herceptin almost 20 years ago. We eagerly await the results of the worldwide Phase III trials, likely to conclude this fall.

At the same meeting, Dr. Charles Sawyers accepted the Karnofsky Prize with a lecture entitled "The Age of Molecularly Targeted Cancer Therapy has Arrived." He concluded his comments by saying, "This is truly the golden age for experimental cancer therapy and we have an unprecedented opportunity to make real progress." Many, many of my colleagues have called to tell me that this was the best Karnofsky lecture in the 35-year history of the award. Congratulations, Charles.

This has been a gratifying decade to serve as director of the JCCC. Our partnership with the Jonsson Cancer Center Foundation provided funding for the recruitment and retention of many of our outstanding faculty. It also has provided early funding for individuals and teams of faculty to pursue this as well as the next generation of cancer prevention, detection and treatment advances. Nonetheless, progress is always bittersweet. The list of friends, family, faculty, staff and volunteers lost to this disease continues to grow every year and much remains to be done.

1. Why do cancers metastasize to specific locations in the body, such as the bone marrow or liver?

2. Why do cancers frequently recur after seemingly successful treatment?

3. Why does it often take years for the tumor to recur?

4. When it does recur, why is the tumor more aggressive and unresponsive to treatment?

I believe that the answers to these questions below will provide the foundations for the next generation of targeted therapies.

1. Cancers metastasize to specific locations in the body because that is where they find the physical structures and soluble factors that support their growth.

2. Presumably cancers recur because they were never completely eradicated.

3. The tumor takes a long time to recur because it comes from a small number of slow-growing cells.

4. When it does recur, the tumor is more aggressive because the susceptible cells have already been killed, more mutations may have occurred and/or the remaining cells don't use the same pathways to control their proliferation.

The answers above describe many of the properties of adult stem cells found throughout our bodies. Adult stem cells reside in specialized niches surrounded by supporting cells and structures. Stem cells grow slowly, with each division giving rise to one daughter cell, which retains the ability to self-renew. Stem cells aren't regulated by the same intracellular signaling pathways controlling the growth of more differentiated cells.

There is now solid scientific evidence for the existence of "cancer stem cells" in leukemia, breast, prostate and brain cancers. In retrospect, it seems obvious that mutations occurring in normal adult stem cells would pass on to their progeny. Does this account for the "origins of cancer?" You'll read about the many scientists working on cancer stem cells in this issue of Discoveries. Ironically, normal bone marrow stem cells have been used to treat certain types of cancer for the past four decades. We need to develop more effective ways to produce healthy stem cells to replace those damaged by chemotherapy and radiation.

The importance of stem cells as the potential causes and cures for cancer dictated that the JCCC would play a prominent role in stem cell research at UCLA. In March, Chancellor Albert Carnesale announced the formation of UCLA's Institute for Stem Cell Biology and Medicine (ISCBM). This effort represents the first truly campus-wide initiative bringing together experts from medicine, engineering, law, public policy, public health and the College.

We are fortunate to have prominent JCCC scientist Owen Witte as the director. Owen's work paved the way for the development of Gleevec.

At the JCCC, we are working with the ISCBM to recruit new faculty to UCLA. Our first recruit, Hanna Mikkola from Harvard, is already on campus and launching her career in stem cell research. We also have funded the first wave of high throughput screens, using model systems to screen thousands of compounds for potential inhibitors of stem cell signaling pathways.

Same as it's ever been: The End of Cancer Begins with Research. ✶

Judy Salsson

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