Golfing at Pebble Beach

Aaron Kletzing, recipient of this year's donation prize, and three of his friends returned from their three day trip to Pebble Beach, California. He brought along with him two classmates from Harvard Business School (Andy Boudreau and Steve Bruch) and his uncle (Jim Christophersen). Also pictured in the photo are their two caddies (Larry and James). Aaron is a lymphoma cancer survivor, a West Point graduate, and an army veteran who served in Iraq.

RACING FOR CR&T

Nancy Crean, a dedicated and long-time CR&T donor, ran the More Magazine/Fitness Magazine Women's Half-Marathon on April 15 in New York City with family and friends. She raised money for CR&T from family and friends that sponsored her race. Over 8,000 women ran the race on a beautiful Sunday in Central Park. We are honored that Nancy thought of us and we hope to continue this wonderful friendship.

Prostate Screening in Queens, New York

For the second year in a row, CR&T co-sponsored a free prostate cancer screening at the First Presbyterian Church in Jamaica, Queens on Saturday April 14. Dr. Douglas Scherr of Weill Cornell Medical College, and a team of urologists, provided screenings and counseling to 180 men, ages ranging from 45 to 70 years old. Prostate cancer is the second leading cause of cancer death among men, but it is highly treatable with early detection. Reverend Patrick H. O'Connor, Pastor, stated, "The Prostate Screening day at First Church is an opportunity for us to help men save their own lives. We are grateful to our partners like CR&T who make it possible."

Cancer Research and Treatment Fund, Inc, is a non-profit group of physicians, nurses, and other medical professionals dedicated to research for the treatment of cancer and other blood diseases. Richard T. Silver, MD FACP founded CR&T in 1968.

Dr. Silver is Professor of Medicine and Director of the Leukemia and Myelpro - lferative Center at Weill Medical College at Cornell University. He is Attending Physician at New York Presbyterian Hospital/Weill-Cornell Medical Center.

Cancer Research & Treatment Fund
500 East 77th Street, Suite 1001
New York, NY 10162

Telephone: (212) 288-6604
Fax: (212) 288-7704

Web Site: www.crt.org

Richard T. Silver, MD FACP
Medical Director

Michael R. Wargo,
Vice President of Development

CR&T™ CANCER SURVIVORS HALL OF FAME™

CANCER RESEARCH & TREATMENT FUND, INC. WINTER 2012

Development of Therapies to Target Cancer Stem Cells

Malcolm Moore, D.Phil – MSKCC, CR&T Medical Advisor

The general public is familiar with stem cell transplants and the controversy over the production and use of embryonic stem cells. Stem cells are rare cells within a tissue or organ, endowed with the capacity to self-renew, i.e. providing one or two identical daughter stem cells upon cell division. There are many different types of stem cells— each with their own purpose. Stem cells can give rise to multiple different types of tissue. Embryonic stem cells that exist only at the earliest stages of development can differentiate into all the various cell types in the body.

NORMAL ADULT STEM CELLS:

'Tissue-specific' or 'adult' stem cells appear during early fetal development and remain in our bodies throughout life, for example hematopoietic stem cells (HSC) that the author showed over 45 years ago to originate in the yolk sac of early embryos and migrate via the blood stream to colonize the liver, spleen and ultimately the bone marrow and thymus. All of the billions of different types of blood cell produced each day in our circulation are the direct descendents of HSC that first appeared at 3 weeks of gestation. An understanding of HSC origins provided the logic for bone marrow transplantation, first begun in 1968. How do HSC find their way to their specific niche? Bone marrow transplantation involves injection of donor bone marrow cells intravenously yet the majority of stem cells leaves the circulation, and localize to their bone marrow niche within a few hours. Like a bloodhound following a scent, the stem cells follow a trail of a specific protein secreted by niche cells. Unfortunately leukemic stem cells can also follow the same trail.

Each major tissue type has its own specific stem cell- brain has neural stem cells even in adult life, liver stem cells can regenerate a whole liver, a single breast stem cells can regenerate a whole breast capable of lactating when transplanted into a mouse mammary fat pad. Stem cells are found at or near the base of the crypts of the large and small intestine and continuously proliferate to regenerate the intestinal lining cells. Stem cells are found in the hair follicles and have recently been identified in the lung and even in the heart. Mesenchymal stem cells (MSCs) were first identified in the mouse and we subsequently identified the human MSC in bone marrow and showed that its differentiation was restricted to formation of bone, cartilage and fat cells (Castro-Malaspina et al. Blood 56:289, 1980). Dr Dexter, a postdoctoral

continued on back cover

www.facebook.com/cancerresearchandtreatment

THE INFORMATION AGE & CANCER

Edward P. Ambinder MD
Department of Medicine, Mount Sinai School of Medicine, New York, New York

Clinical Professor of Medicine (Medical Oncology and Hematology

We are living in unprecedented times where oncologists and their patients are facing disruptive changes in healthcare, medical research and medical education brought on by the individual growth and merging of the fields of information technology, biology and physics. This dramatic increase in the quantity, quality and ease of finding information and the effortlessness of connecting everyone and everything brought on by the Internet, has changed our lives forever. However, many of us remain frustrated with our inability to control this information overload in a time-limited living situation.

In the last 7 years, the practice of medicine has changed dramatically with large, multi-disciplined and integrated organizations becoming predominant rather than small practices. Oncologists are beginning to document our patient care using electronic media rather than paper and have seen the doctor-patient relationship become more patient-centric to include wellness and patient-derived data. They are increasingly communicating electronically with all health care stakeholders including our patients using email for messages, reminders, data collection and education instead of mail, fax and phone.

Indeed, for the first time this new, disruptive digital world is fast becoming defined by information becoming electronically mobile, cheap, available to all and consumer-oriented to such an extent that almost all recent information technology advances in hardware and software begin with the consumer and not the computer professional or big business. Cancer doctors and their patients must begin to understand how we reached this point and where we are headed to better prepare for this new world.

Government grants to doctors are enticing them to use electronic health record (EHR) programs that are approved by a government acceptable certifying group and, in addition, be used in meaningful ways as defined by the Office of the National Coordinator (ONC) for Health Information Technology. Many meaningful use requirements center on electronic communication and documentation of medical data. All physicians will need to communicate electronically with patients and transmit individual patient encounters or the entire patient record to patients.

Only recently has the line between computing and biology begun to blur as the laws of the Information Age are applied to biologic processes and companies develop gene sequencers that rely on blending semiconductor chips, nanopore sequencing, robotics, chemistry, optics and computers to map the 3 billion base pairs that make up the human genome cheaply and rapidly. Oncology has been one of the first medical specialties that have taken advantage of this technology to compare gene sequences and activities of normal and cancer genes. We have begun to molecularly stage our patients for a more precise cancer diagnosis, prognosis and disease severity and to choose more effective therapies with minimal toxicities instead of just clinical and pathologic descriptors.

Cancer doctors in the past have been strongly criticized by the Institute of Medicine for not using health information technology effectively and not providing cancer patients with helpful information. In response, the American Society of Clinical Oncology has developed a patient and referring physician report that defines a Cancer Treatment Plan and a Cancer Patient Survivorship Plan that has been incorporated into many oncology electronic health records. Patients should request these reports from their oncologists.

Today, for the majority of our computer activities, we use Windows and Mac OS X computers that use windows, icons, menus, and pointers (WIMP) for human–computer interaction. These computers can do pretty much anything, but carry the burden of 30 years of rapid, unplanned change. However, many users remain frustrated because it is difficult to navigate through the different parts of the program, requires indeterminate training periods, and has poor learning recall without constant use. However, the introduction of the iPhone smartphone and later the iPad tablet changed everything. These devices introduced instant on, instant off, multi-touch, multi-sensor and multi-communicator cloud-based computing with a new conversationalist voice interface called SIRI and the App model of purchasing software for simple "plug and playing".

Consumers were the first to witness the future of integrated computer hardware and software coordinated through the cloud in which these inexpensive devices and their software became more humanly natural in operation. Medicine is also now beginning to adopt this technology in droves.

As a long time observer of health information technology and an oncologist who has used both the old and new computer interfaces created by the same company for identical functionality, I am a convert to the new system. I just pick up any of my devices, turn it on and instantly use the software with a smile on my face without reading help manuals, attending indeterminate classroom lectures and easily navigate to the appropriate places in the program from almost any location in the world feeling that the program is backed up in the cloud and easily updated so I always have the latest version of the software on any of my devices.

Patients will continue to take a more responsive role in health care as they pay a larger share of its cost, make known their values and wishes and help make key decisions. With the unlimited educational resources of the Internet our patients have access to the same medical literature and textbooks that we have. With meaningful use requirements for providing electronic patient reports to the patient, CMS proposing that patients have access to their laboratory test results, emailing between patients and oncologists becoming commonplace and reimbursable with some payers and most medical reports becoming available in digitized form, patients will be in control of their medical record. A pilot project making almost the entire medical record electronically available to patients has been successfully implemented at MD Anderson where the majority of patients are more than satisfied and most doctors, many of whom were skeptical initially, have become converted proponents of "open access" care and the healthcare system has become more cost effective and safer.

As patient information becomes digitized and is sent electronically to them by hospitals and providers they will need to create a personalized electronic patient personal health record (PHR) to hold this data and their own patient-derived data. However, the record collection process is still cumbersome especially when most of the medical data today still resides on paper. Aegis Review, a virtual cancer second opinion and navigator company, has an efficient method to use a case manager and medical scribe to collect and organize the cancer patient's record and create a secure and shareable electronic personal health record, (Disclosure: I am one of the founders of the company). Hopefully the future will see the seamless integration of the EHR with the PHR.

Only recently has the line between computing and biology begun to blur

With the advent of EHRs and PHRs it becomes obvious that there is a treasure trove of clinical data that is in these records that has the potential to benefit society by opening up what happens to the 97% of cancer patients who do not go on clinical trials. By learning about the comparative benefits or harm of our new treatments and procedures in non-clinical trial patients after their regulatory approval we can continually apply our findings and improve our treatments. ASCO and others have begun to define a Rapid Learning System for Cancer that will use the tools of the Information Age to develop a more thorough understanding of cancer biology, defining a cancer based on molecularly-driven diagnosis, and a therapeutic development system using oncology EHR registries to produce smarter and faster clinical trials. By having a more seamless integration of clinical and translational research it has the potential to ensure that every cancer patient's experience can inform research and improve care and help us take full advantage of the wonders of the Information Age.

Acknowlegement – I would like to acknowledge Steven Jobs for creating the hardware and software that permitted me to enjoy the Information Age, "think differently" about technology and make the Information Age understandable, approachable and fun for the rest of us.

Adapted from "The Information Age, Cyberspace and Cancer" (Oncology April 2012 pages 324-327) by Edward P. Ambinder

Cancer Stem Cells

continued from cover

fellow in my laboratory, showed that bone marrow MSC formed a confluent layer of cells supportive of the long-term proliferation of mouse and human HSC. This "stromal" layer had many of the properties of the bone marrow stem cell niche, providing growth factors for the HSC as well as protecting them from terminal differentiation. The method has been used to increase HSC number prior to stem cell transplantation. MSC have been transplanted into patients with genetic defects in bone formation and are increasingly used in regenerative medicine.

One unusual feature of adult stem cells is that they undergo asymmetric cell division and producing one identical daughter stem cell and one differentiate progenitor cell. A critical requirement for the niche is to ensure this asymmetric division resulting in maintenance of a stem cell pool of fixed size yet allowing enough differentiation to produce all mature blood cells in normal numbers. A normal adult has approximately a hundred million HSC in the bone marrow with ~95% in a non-dividing quiescent state. The remaining asymmetrically dividing HSC produce 2.4 million new red blood cells per second. These circulate for about 100–120 days to provide the 20-30 trillion red blood cells required in a normal adult, comprising approximately one quarter of the total human body cell number. White blood cells (granulocytes, lymphocytes, monocytes) comprise 25-50 billion circulating cells with life spans measured in hours to a few days. The bone marrow HSC also produce large megakaryocytes each up to 1000 platelets into the circulation and providing 100 billion platelets needed each day.

CANCER STEM CELLS:

In 1970, Don Metcalf and I first identified and characterized a cancer stem cell population in a mouse spontaneous leukemia (Metcalf D, Moore M.A.S. Factors Modifying Stem Cell proliferation of myelomonocytic cells in vitro and in viyo. J.Nat Cancer Inst 44:801,1970.) Leukemic stem cells (LSC) can undergo symmetric stem cell divisions as well as asymmetric and therefore outgrow the normal quiescent stem cells . Leukemia development can be likened to the Cuckoo who lays her egg in another birds nest, the egg hatches earlier than the host's, and the cuckoo chick grows faster and then outcompetes the host chicks for food and space. LSCs can also enter a quiescent state but this is generally after AML is clinically evident with suppression of normal blood cell production and appearance of immature leukemic cells (blast cells) in the blood. Leukemic stem cells were "rediscovered" 34 years later with the advent of special mice lacking an immune system and thus not rejecting a human tumor graft (Lapidot, et Nature 367, 645, 1994). LSCs were rare (one per 250,000 leukemic cells).

In solid tumors cancer stem cells were first reported in breast cancer in 1980 (Rudland et al Brit J Cancer 41:666, 1980) but it was not until 23 years later that they were rediscovered (Al-Hajj M et al. Proc Nat Acad Sci,100: 3983, 2003) . In the last ten years there has been an explosion of research into stem cells in all forms of cancer. The recognition that CSCs are resistant to most standard forms of chemotherapy explains in part why cancer is so difficult to cure. It is necessary to develop novel drugs designed to selectively kill the cancer stem cell. In collaboration with scientist at MIT, Harvard, the Broad Institute and Columbia we have screened tens of thousands of compounds for ability to selectively kill mouse leukemic stem cells while not killing normal HSCs. We have used a system that duplicates the bone marrow niche with co-culture of normal or leukemic cells on bone marrow stroma with addition of different concentrations of each compounds. Seventeen candidate drugs have been identified and validated for toxicity against a number of different types of primary human leukemia LSCs and for lack of toxicity against normal human HSCs. This program together with screening of additional compound libraries in the Moore lab has currently evaluated over 73,000 compounds and identified a number of novel drugs that have proved very effective in killing LSC and ovarian cancer stem cells.