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ORIGINAL ARTICLE – TRANSLATIONAL RESEARCH AND BIOMARKERS

Society of Surgical Oncology Presidential Address: The War on Cancer—Shifting from Disappointment to New Hope

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First of all, it has been a singular honor to be your President for the past year. It has been a wonderful journey with the SSO since I first began working on the Program Committee in 1993. I have learned from outstanding mentors during this time and have watched our Society grow not only in membership, but also redefining itself as we seek to broaden our outreach across all surgeons across the world. We keep getting better and I am confident that our organization will continue on the paths set by my predecessors.

From a personal standpoint, I am grateful to all of the people who have helped me get here. The list is too large to show, and of course I would forget some, but I do want to thank a number of people who have guided me along the way. Dr. Warren Cole was my earliest mentor—meeting him in high school and benefiting from his wise counsel until his death in 1990 (Fig. 1). He was not only a consummate surgical oncologist who happened to retire to my hometown, but was a visionary, frank mentor. Early in my career, Dr. Hilliard Seigler helped nurture a lifelong love of the laboratory and was my first real-life demonstration of a surgical scientist. Probably Drs. Samuel Wells and Murray Brennan have had the greatest influence on my career (Fig. 2). There is simply no finer surgical scientist than Sam Wells and no finer teacher than Murray Brennan. From a research standpoint, two of our guest lecturers have had a profound impact on fostering the scientific portion of

FIG. 1 Dr. Warren Cole

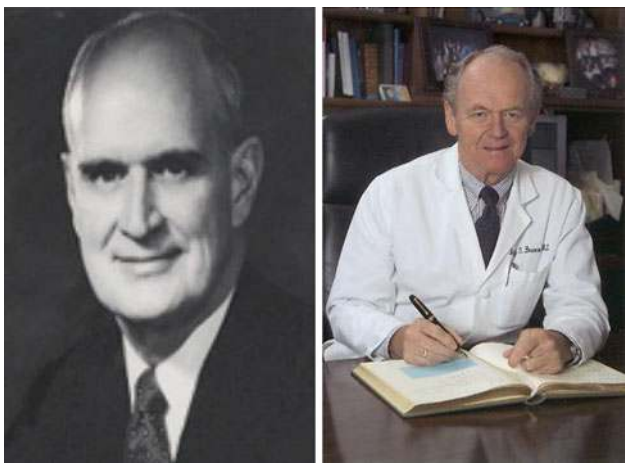

FIG. 2 Dr. Samuel Wells and Dr. Murray Brennan

Dr. Cance is a major stock shareholder with CureFAKtor Pharmaceuticals.

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my career: Drs. Ed Liu and Shelley Earp. They taught me to get back up when you have been knocked down and that study section pink sheets can actually be helpful! Most importantly, I want to emphasize that mentorship is a lifelong process, and it doesn't stop when you get your first job or your first grant. It needs to go on forever. Too frequently we forget this point—we all need mentorship and we need it throughout our lives. Mentorship isn't just advice on jobs or grants or the politics of your institution. It's being a true and honest colleague and friend. I am most grateful to people like Tim Eberlein, Dick Karl, and Ron Weigel who have been that to me. It is easy to reach out during the peaks of ones career but much more difficult during the valleys, and I especially want to thank them for their mentoring and support during a most difficult year. From a day-to-day standpoint, I am completely indebted to all my trainees and lab colleagues who have done the work each day, caring for patients and doing the experiments. A number of my laboratory colleagues and trainees are shown in Fig. 3. I am especially grateful for the efforts of Drs. Vita Golubovskaya and Elena Kurenova who have kept the laboratory endeavors rolling for the last 8 years.

When it comes to cancer, I haven't mentioned the person who has had the most profound effect on my professional life. I first met John when we lived in the same dorm as freshmen at Duke in 1975. He was a wildly funny engineering student with a raucous laugh who didn't hesitate to pick on my nerdy premed characteristics! Around Thanksgiving that year he wanted to show me a lump on his foot to see what I thought. Of course, I insisted I was just a premed, but he insisted I look, and I can remember that golf-ball sized lump on the sole of his foot as if I saw it yesterday. He assured me he would see a doctor over the holiday, and, of course, it was a fibrosarcoma. I guess that was my first surgical oncology consult. John left for the spring semester while he underwent chemotherapy, radiation, and surgery. He returned in the fall, looking fit, now with curly hair, and for a brief while, he was the old wild and crazy John. Then, around Christmas, again, he developed abdominal pain with widespread metastases. He died less than 2 years later, living in our dorm until a week before his death. I witnessed the unfathomable destruction of cancer firsthand. Why should a person of my daughter's age have to worry about not taking morphine so he could drink at a party? Why did he have to come face to face with death at such an early age, and I didn't? We all go through this with our patients, but those times and intimate discussions with John put me on an unstoppable course to try to understand and treat this devastating disease. Practically no day goes by when I don't think about John, and he died 32 years ago. So, John, this talk is about you, and it's about all of the Johns and Janes who we cancer surgeons know.

So, what have we done to help John? What would his outcome be today? Have we really made that much progress? Unfortunately, the answer is no. Even if John showed me his foot today, he would still die. To show you what I mean, let's take a look at sarcoma survival for the last 30 years. I am grateful to Murray Brennan for sharing this data on survival rates from sarcoma during different time periods. First, look at primary extremity sarcoma, like the one John had in 1975 (Fig. 4). As you can see, we haven't made much progress in overall survival. The results are even more dramatic when you look at survival of all sarcoma patients during five different time periods

FIG. 3 Laboratory trainees and colleagues. **a** University of North Carolina. **b** University of Florida

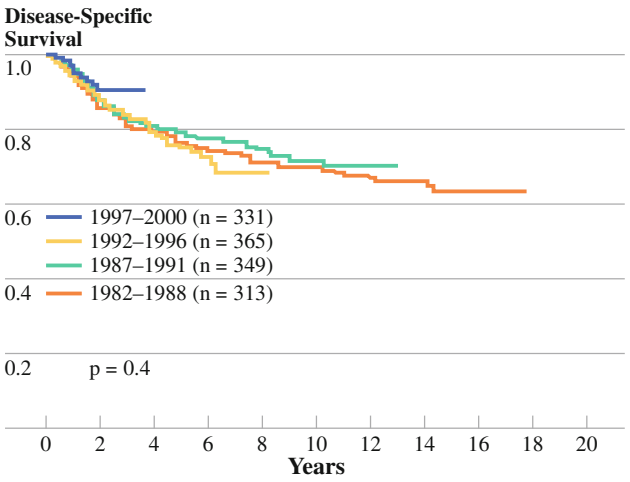

FIG. 4 Primary extremity sarcoma, disease-specific survival by 4-year intervals (Memorial Sloan Kettering Cancer Center Data, Courtesy of Murray F. Brennan)

(Fig. 5). Not much improvement either, although we have made progress with less invasive and less radical surgical approaches, we aren't changing survival that much.

What about some other cancers, such as pancreas? How are we doing there? As many of you know, one of my pet peeves is glamorization of the Whipple procedure. It's like that operation is the defining moment of a career: "I just did a Whipple…I have arrived." The Whipple procedure is one of the most technically overrated procedures while at the same time the most underrated for its complication rate. Residents and fellows base their career choices on the number of Whipples an institution does. Well, the 5-year survival for pancreatic cancer is approximately 3% (Fig. 6), and it hasn't changed over the years, despite our advances in surgical technique. Now, we have contests among us about how much or how little blood we lose or

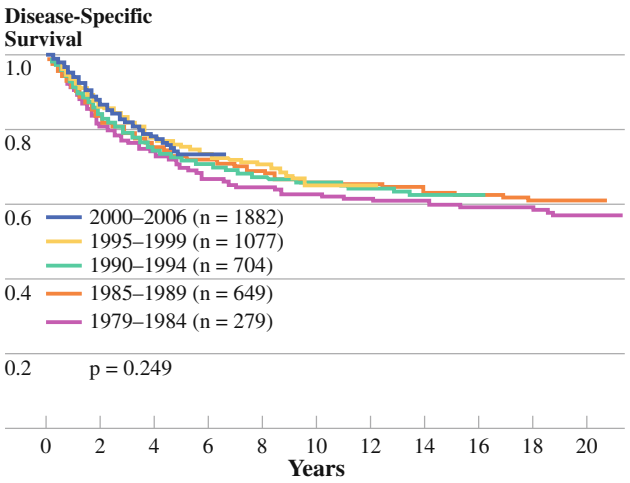

FIG. 5 Primary soft tissue sarcoma, disease-specific survival

how our length of stay is shorter, or whether we stent or whether we drain. But we don't talk much about the recurrences and we certainly don't talk about the patients on whom we don't operate because of extensive disease. We hear about them in the media, but like John, these patients are the ones whom biology has determined their fate early on.

So, why can't we stop cancer? The problem for you today is the same problem we had for John—the individual biology of the tumor determines the patient outcome, and we have had very little influence on that biology over the years. Although we have made significant progress in the surgical extirpation of cancer, we still have a long way to go. Today, I don't want to minimize our successes as surgeons, but I want to emphasize that we have much further to go. Ask yourself honestly, can we make a big impact on advanced cancer? Maybe sometimes, but it is not the norm, despite the massive resources we pour into treatment. To extend life a few weeks or a few months? Let's face it; we don't have very effective therapies…other than surgery. And surgery remains the most effective therapy we have. And in a large part of the world, it is the only therapy we have!

We desperately need better, easier, and cheaper adjuncts to complement what we do. The good news is that with some of the insights and new knowledge that we have recently gained into this biology of cancer, we are headed down the path to become the complete caregivers for the cancer patient. And that will be an extraordinary time for the Society of Surgical Oncology. Why? Because we are now at the point where we can molecularly dissect a tumor and tailor treatment to the patient with drugs that are less toxic and more effective. Never before has this happened and this is a transforming time for all of cancer therapy!! We are the gatekeepers for the solid tumor patients, and we must remain involved in all aspects of their care. But to do this, we have to think beyond the operation. It's the only way for us to maintain our status as oncologists and not become technicians. Best of all, I think our Society is uniquely poised to do this, but it will require ongoing investment in our members, their education, and their clinical practices. It will take a fundamental change in the SSO infrastructure. It also will require us to develop effective collaborations with industry. So today, let's take a look back on cancer and then take a look ahead to see why we can be the complete cancer doctor for our patients.

The term "war on cancer" has been used for a number of years. Strange how it has been put into military jargon…we have heard about cancer wars, magic bullets, stealth liposomes, and gamma knives. As if we don't hear enough war-talk! It always seems to be in the national press. I took a look back at *Time* magazine cover stories on cancer over the years. I was surprised the find the founding

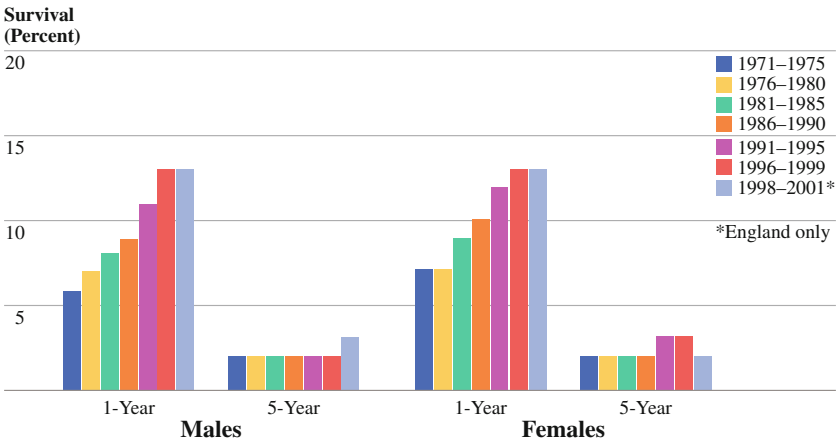

FIG. 6 One- and 5-year relative survival by sex, adults diagnosed with pancreatic cancer: England and Wales 1971–2001. Used with permission, Cancer Research UK (www.cancerresearchuk.org)

father of our society, James Ewing, on the cover of *Time* on January 12, 1931. In that issue, it was reported that "mankind's war of defense on cancer has only recently begun. The *Annals of Surgery* appeared last week with every one of its 54 articles devoted to discussion of cancer." Twenty-eight years later, we had a "new war on cancer." *Time* magazine reported in July 1959 about advances in antivirals and chemotherapy. "The NCI is mounting history's most intensive campaign against a human illness. Its budget is skyrocketing: from $14 million when Dr. Heller took over in 1948 to a probable $100 million in the fiscal year just begun." Now I'm sure Dr. Niederhuber wishes the NCI budget were skyrocketing now. Interesting to know that the NCI budget for FY 2008 was $4.8 billion, and we all know how fiscally constrained the NCI has been long before the recent economic downturn. But think about the growth: 100 million to 4.8 billion dollars…a growth of 50-fold over 50 years.

Now, let's fast forward again. Richard Nixon signed the National Cancer Act December 23, 1971. As he said at that occasion, "I hope that in the years ahead that we may look back on this day and this action as being the most significant action taken during this Administration." So, we have had a lot of national attention, but not the progress for which we had hoped. Now I could go on and on with these sort of illustrations. But let's fast forward to more recent results. Have we impacted cancer? Yes, there may be some magic bullets, such as gleevac; however, between 1950 and 2005, the cancer death rate in the United States declined by only 5%, much of that due to decreased rates of cigarette smoking. In contrast, the death rate from cardiovascular disease decreased 64% during that time! Globally, cancer is projected to become the leading cause of death worldwide in 2010. The burden of cancer doubled globally between 1975 and 2000, and it is predicted to double again by 2020 and triple by 2030. Seven million people will die from cancer worldwide this year. The burden also is increasing to a larger degree in China, Russia, and India, attributed in some part to adoption of western habits of tobacco use and higher fat diets. So, we are not winning the war on cancer.

But the root of the problem is even deeper and it has to do with our current approach to treatments. You all know that we have a number of options for our patients, particularly with drug therapies. When you look at pancreatic cancer studies you can see how far we have come with our treatments. In 1997, the trial that established gemcitabine as standard therapy for pancreatic cancer showed an increase in survival of 6 weeks compared with 5-FU.[1] Not very much, is it? I would argue that a more recent study from 2007 is one of the most dramatic illustrations of the disappointment that we have had. Here you have a phase 3 trial out of the Canadian NCI[2]; 569 patients were randomized to receive gemcitabine alone vs. gemcitabine plus erlotinib. The thought was that adding an EGFR inhibitor would augment the response to chemotherapy. When you read this article, it seems like this is a major discovery, particularly when the authors conclude "this is a new treatment option for the patients." But let's look at the data. The increase in survival was 11 days for the patients treated with the molecular target—11 days. *But*, the *p* value was highly significant! How did this happen? Well, there are a number of problems and they are nicely reviewed in a recent article from MD Anderson that was published this year.[3] The big problem is our bar is set too low—way too low. We have lost the focus on the big picture. We get involved with the appeal of the molecularly targeted therapy and proceed when the results are not very good. And then, we adopt the new trial as standard therapy when the *p* value is significant, or we abandon it when it is not. Let's think about this study—the lead author has invested a lot of time, secured resources and written protocols, collaborated with industry, hired data managers, and

so forth. This paper will be used for promotion…a high-impact publication, leader of a national phase III trial. All of that will appeal to University Tenure and Promotion committees. But what was accomplished?—a significant *p* value but only 11 days more of life.

In the article that makes the case for a higher bar, the authors also use battlefield analogies, here related to World War I.[3] Maybe it is appropriate to compare these types of studies to World War I trench warfare. During that time, many lives were sacrificed to hold onto a trench or advance to the next one a short distance away. It was not until the Germans had the idea to race around the trenches and capture distant territory that progress was made. The Allies adapted this strategy and won the war. Maybe this is the way to go with cancer? Forget about the small increment ahead and go for more significant battles. But how? The point I want to make is that we've spent many years and many dollars and we really haven't made much progress. We have had a number of new treatments from mustard gas to immunotherapy to novel targeted drugs, but we haven't had the dramatic successes for which we had hoped. Why not, and how can I convince you that we are on the verge of a transformation in cancer care?

Well, we can think of cancer in terms of an enemy army, but I would argue that we should think of it as a combination of Charles Darwin and Star Wars. I would reason that our patient's cancers are microcosms of classic Darwinian survival of the fittest. When you think about cancer cells, they have to adapt to survive. Why? Because Mother Nature has developed elaborate ways to execute any cell that lands where it shouldn't be. Steven Frisch coined the term anoikis to describe it…a Greek word for homelessness.[4] Any cell that detaches from its substratum is destined to undergo apoptosis or programmed cell death. But cancer cells don't become homeless—they make new homes and happily grow on. And this is where the Star Wars metaphor comes in…they have elaborate "force fields" to protect them from death. So the good news is that surgery can eliminate maybe 99.99% of the cancer cells, but the bad news is that the few remaining cells are the ones with the strongest force fields. The ones who can best grow, make new blood vessels, and set up shop in their new homes: survival of the fittest…that's basically it. And these force fields protect the cancer cells from the stresses of chemotherapy, radiation, and the overall stress of invasion and metastasis. This is the secret to the biology that we just can't seem to overcome and it is the reason why patients like my friend, John, still die today.

So, what have we learned that makes us better able to treat cancer? Why is there new hope? Well, we are beginning to understand the ways cancer cells activate these defense mechanisms, and, concomitantly, we are beginning to understand how to destroy them. It's basically

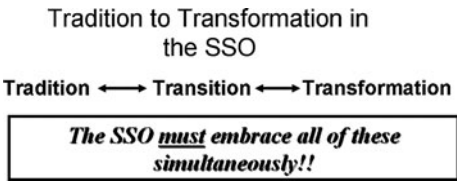

FIG. 7 Tradition to transformation in the SSO

a matter of enhancing our ability to effectively remove the force field while we use other modalities to kill the cells. Before I show examples of this, I want to state a few premises or assumptions for what I am about to say. But first, I want you to keep in mind the evolution in cancer care that I am talking about. We are moving toward a transformation in how we treat patients, and that is where the new hope comes from. To get there, we have to move from tradition through transition to transformation (Fig. 7). As a Society, we must be all three of these at the same time! We can't abandon traditional cancer care. In fact, we must teach it and practice it. But we must accept the transition as a path to transformation on how we care for our patients.

The first premise is that surgery will remain a mainstay of cancer treatment for a long time. Certainly we will get more effective therapies and probably will do more primary chemotherapy or radiation approaches, but operative therapy is here to stay. It makes sense scientifically and practically. Remember, most people in the world don't have access to the chemotherapy and radiation regimens that we take for granted in the United States. My next premise is that as cancer surgeons, we must be willing to understand genetic and genomic approaches and apply them to our patients. This is absolutely essential if we are to remain oncologists and not technicians. I'll get to some examples of this in a few minutes. Finally, this talk is based on the prediction that therapies of cancer will become less toxic and more able to be administrated orally. This will be transforming. Now we all know where some predictions go, but I am confident that we will have more and more drugs like gleevac that can actually be prescribed by surgeons. I don't think that surgeons will become interested in how many mg/m^2 we are prescribing or what the level of dose intensity will be or whether we have grade 3 or grade 4 toxicity or whatever. But I do think that we will be the natural caregivers when we can write a prescription like tamoxifen or gleevac and treat our patients. Think what gleevac has done…we can prescribe this drug to our patients with advanced GI stromal tumors, watch them shrink, then operate and get clear margins. And the leaders of this tremendous advance are SSO members in the audience today. With this disease, we are truly the complete oncologist. Think what will happen as we get newer and better gleevacs? Think what that will mean…for

patients, for health care economics, and for surgical oncologists. So this is where we have had traditional cancer care, and are in a transition toward a transformation in cancer care. And this transformation is already happening.

Let me give you some examples of the recent changes that cause us to have new hope. Let's get back to that Star Wars survival concept…the part about the force field. I'm going to tell a story about the protein that I have spent the last 19 years studying. It's called focal adhesion kinase, or FAK, and I must admit that I wouldn't be standing here today if it weren't for FAK. Ironically, we first found it by screening a large extremity sarcoma like John had. At that time, Ed Liu and I were on a hunt for novel genes that made cancers grow. We were searching for tyrosine kinases, those enzyme proteins that many of our modern therapies target, such as Herceptin, erlotinib, and Avastin. When we used our surgical niche to screen directly primary tumors, we found this protein that was called FAK because it localized to areas where cells contacted their matrix. This is the place where cancer cells must invade to metastasize. Now, it has taken us 19 years to figure out what FAK does, and although we still don't know everything about FAK, we do know that it is massively upregulated in cancer cells and acts as a survival signal. It was no coincidence that we fished this protein out of a sarcoma because FAK is massively upregulated in most solid tumors but expressed at low levels in normal tissues. This made us think that FAK must be doing something very significant for the cancer cell and should be a good cancer target.

Finally, we determined why FAK was expressed at such high levels in cancer cells, and to make a long story short, it is one of those force fields that I was talking about. In reality, it is very similar to the magnetic force field that surrounds Earth and protects us from radiation in outer space. Just as this field cocoons the Earth, FAK cocoons the cancer cell. It does this by binding a lot of other molecules, including many that we target today, such as Her-2, p53, and even one of the angiogenesis receptors, vascular endothelial growth factor receptor 3.[5] In fact, FAK sequesters many proteins that normal cells use to execute aberrant cells. It keeps these normal proteins from destroying cancer cells. One of the most profound things FAK does is bind and inactivate p53, leading to degradation of this protective p53 protein in cells.[6] So, we turned our attention on how to knock out FAK by targeting the binding sites for these oncogenic molecules. This was a different approach to the problem. Most people try to knock out tyrosine kinases by targeting the receptor, like Herceptin, or targeting the kinase enzyme, like gleevac. It was a novel approach, and a bit avant-garde, but generated a lot of intriguing data.

Initially, we targeted the FAK-VEGFR-3 interaction because we know that tumors can make new lymphatic vessels and metastasize by activating this tyrosine kinase. We knew that FAK bound to VEGFR-3 in a specific groove of the protein. Using x-ray crystallography, we virtually docked small molecule, drug-like compounds to this area and "in silico" measure their binding energy. This led us to a number of potential drugs, including one that we call C4. This drug disrupted the binding of the two molecules and reduced growth in breast cancer cells that overexpressed this lymphangiogenesis protein. We found that this drug worked in vivo in xenograft models of mice bearing human breast cancers or human pancreatic cancers. Furthermore, C4 sensitized the tumor cells to chemotherapy, allowing us to use dramatically lower amounts of chemotherapy with even better antitumor effects. Of course, these results must be proven in humans, but it seems that we were able to knock out that force field and sensitize the breast cancer cells to treatment. Think what that could mean to patients if we could give low-dose therapy before or after surgery. Furthermore, C4 is an old drug—a commercially available antihistamine, widely used and available off the internet, with the human equivalent dose just about the same dose of drug that you would take for hay fever. So look where we are beginning to be able to go. We will soon have more drugs that can pinpoint molecular interactions and effects and have less toxicity than conventional therapies. And even we surgeons can prescribe antihistamines.

I have talked about making cancer cells sensitive to chemotherapy, but what about making normal cells more resistant to therapy? Why not? They already have a leg up on the cancer cells that are living on the edge of life as they invade and metastasize. What if we gave normal cells a force field? As you know, the major toxicity we see from radiation and chemotherapy is related to the immune system, GI tract, and bone marrow. Maybe if they were more protected, we could have more efficacy and less side effects?

I want to tell a story about one such novel agent that was developed by Andrei Gudkov and his group at Roswell Park Cancer Institute. Andrei reasoned that if there were cells that had to be resistant to damage, it would be the intestinal epithelial cells. After all, they are constantly exposed to such things as bacterial toxins. So, he took Salmonella bacteria and screened them for substances that they secreted that protected intestinal cells. He called them "protectans" because they imitate the force fields around tumors to protect normal cells. At the same time, he found that normal cells and tumor cells died via different mechanisms.[7] This is an incredibly exciting observation and plays into where we are going from a cancer therapeutic perspective. We really are getting to understand why cancer cells and normal cells live and die. Interestingly, Andrei found that flagellin secreted from Salmonella was an effective radioprotectant. It did that by working through the

human Toll-like receptors on the host cells to activate NF-κB. Once they completed these studies, they engineered the protein to enhance its activity and have minimal immunogenicity and toxicity. This drug could completely protect a mouse from radiation toxicity, EVEN if it was given after the fact. Now my thoughts immediately went to rectal and head and neck cancer, but Andrei was one step further: biodefenses. Not a bad idea… Think about it…you could take this drug after a radiation accident or an exposure or a terrorist attack and be protected from the lethal effects. The drug protects against a lethal dose of irradiation and preserves normal cells in the bone marrow and the GI tract, for example. However, the really significant finding is when you take a tumor-bearing animal and give the drug with radiation, you can actually protect the normal tissues without protecting the tumor! Imagine that…putting a force field around the normal cells but not affecting the tumor cells. Perhaps that is a way to run around those World War I trenches…protect the normal cells and devastate the cancer cells: transitioning to a transformation in cancer care.

These are two examples of new potential drugs that represent very early days in the molecular revolution that will change cancer care. I hope that I have at least partially convinced you that with new generations of less toxic drugs, as well as new understanding of genomics and genetics, we are moving this war on cancer to an era of new hope for our patients. I have tried to make the argument that surgeons will remain as central figures in the ongoing war on cancer, and we have the potential to be leaders as we go forth down the molecular revolution. So what next for SSO? How do we deal with these changes as a Society? If you go back to the continuum between tradition and transformation, again, as a Society, we must be all three at once if we are to be successful oncologic leaders. For example, we must teach traditional educational methods of cancer surgery while we also teach the transformational. We must embrace and adapt to this changing oncologic world. The good news is that we have a head start. The SSO has a strategic plan, crystallized under Raph Pollock's leadership, and we have outlined our areas of focus. But we must take bold steps to move forward with definitive execution of this plan. A plan is wonderful, but execution requires resources and prioritization and this must happen to a greater degree in the SSO.

Finally, I want to update you on the progress that we have made and where our challenges lie. During the last year, we have made a number of new initiatives and allocated significant resources as part of this strategic plan. We are in the early stages of a complete web overhaul. I had hoped that we would be able to make faster progress and have it up for this meeting, but we are in the process of securing bids and defining the exact content. This is a huge project and is under Sam Singer and his website committee's leadership. The website will be a central piece of all we do as a Society and it is a major piece of our strategic plan. This year we have seen an exciting program emanate from the community surgeons. Under the leadership of Peter Beitsch, we have created the first of what we hope will be many programs designed especially to appeal to our community members who deliver most of the cancer care in this country. We have begun to put resources to reach out to our international colleagues and leaders to ensure that we keep a global focus. We have a group of international colleagues at this meeting whom we have specifically asked to come and advise us on how we can partner with other societies. In fact, we are meeting this afternoon to brainstorm on the next steps for broader partnerships. We also have expanded our funding of Clinical Investigator Awards. Ken Tanabe's committee has been extremely busy reviewing exciting proposals from our members across a broad array of topics. Finally, your SSO leaders have logged many miles meeting with industrial leaders to secure resources for this meeting and for these projects I have outlined. Although these are tough economic times, industry has been willing to help because they see us as gatekeepers of the patients and key partners as we move to transformation in oncologic care.

So, how do we take these initial steps forward as a society? What are the next steps? I think the most important thing we do is to really become an inclusive society. That is part of our strategic plan, reaching out to the three major groups of members. We must do it as one cohesive group, not three different subgroups within our organization. We must interact as one society with each of our different roots. So, what are the next steps? First of all, the SSO absolutely must become more of an educational machine. We are not keeping sufficient pace with the changes in educational requirements, although we are providing a huge educational function. We must invest in education as part of our strategic plan. I have mentioned some of our strategic investments this year in the website and the way we handle fellowship accreditation, but they are not enough. Nowhere near enough to provide the value to our members that we need. We must invest some of our reserves to create the ability to educate our trainees and our members in broader areas. We've heard about the new concept of "maintenance of certification," fondly known as MOC. We must have that capability on our website—better yet, a web portal where you can log in, learn about these changes in our specialty, and maintain your continuing education. But we have to get better from a CME and a website infrastructure. We need to make it easier to apply for membership for everyone—especially our international colleagues. This should be done online as part of our new website. As you may know, it is becoming much more

difficult to get accredited CME programs. The SSO must become adept at this, and to get there we must have more personnel at our administrative headquarters. We should proceed with these changes now.

As I have mentioned, we are delighted to see more of an international presence at our meeting, and your SSO leaders are committed to increasing our international outreach. To do this, we must invest our resources again. Next year, we should broaden our nascent career development awards. We also should seek to partner and collaborate with international societies, not compete with them. Charles Balch is committed to this partnership through the *Annals of Surgical Oncology*, and this provides a wonderful way to provide a two-way educational dialogue for our colleagues across the world.

We need to go further as we become inclusive. Why can't we broaden our training mission? Let me give you one statistic—in India, there are 16 surgical oncology fellowship slots for a country of 1.16 billion people! Why can't we broaden our training? How? Well, we have a lot of community surgeons who give outstanding cancer care—many of whom are in large groups. Could they take an international fellow for a year, train them, and have them take their experience back home? When international colleagues come over for the SSO meeting, why can't we arrange a series of visits to our institutions so we can learn from them? I will do this for Roswell Park, Murray Brennan will do this for Memorial, and I challenge others out there to participate as well. Network with our international colleagues! These sorts of approaches will cement relationships across all levels of our society and will help us become one group of cancer surgeons with a diverse set of roots. There are plenty of other examples, and I haven't even mentioned international clinical trials. But let's start small and work our way there.

We also need to enhance our support for research—research across all areas. We have a number of clinical investigator awards that have been funded, and we need to push for more. Let's look at areas where we might not typically have them. Diversities in cancer care, community training for clinical trials, along with the more traditional partnership approaches in breast cancer, pancreatic cancer, and so forth.

To do this, we need two things: people and resources. So first I want to encourage all of our members to get involved. You can and should bring ideas to committees. Seek out the committee chairs at this meeting and take an idea forward. We need people who can be "found pilots" who can figure out how to take ideas forward. Resources are more challenging. Of course, everyone today is challenged by resources. There is an economic downturn the likes of which most of us have never seen. The good news, thanks to the strong leadership of my predecessors in the SSO and an incredibly talented management team led by the Slawnys, we have sufficient reserves, even with the economy. It is impressive how the reserves have grown in the SSO over the last 16 years. We have about 1½ to 2 years of cash if we had absolutely no further income. We also have reached more than $900,000 in industrial support for this meeting thanks to the efforts of Eileen Widmer, many of your leaders, and the Corporate Relations Committee. At the same time, we lose money on this meeting. So, as I finish my President year, I challenge our Executive Council to develop a more methodical plan for our budget and prioritize our resource allocation for the strategic plan. We must invest now. Don't wait. I am not advocating that we spend down all our reserves. But with the transformation we are seeing in cancer care, we simply can't afford to wait.

I will close this talk by returning to where I started—Charles Darwin. One of his most profound observations was this: "It is not the strongest of the species that survives, nor the most intelligent, but the one most responsive to change." I leave this as my take-away message for you. If we are to maintain a leadership role in the treatment of the patient with cancer, we must respond to the changes I've outlined. We've done it before with minimally invasive surgery and sentinel lymph nodes, and I am confident we will adapt to the transformational changes in our field. And as a Society of Surgical Oncology, we must respond as a global leader. We must embrace changes, teach them to all our members, and partner with surgical oncologists in all practices, across the world. That's what we do best. So enjoy the meeting, learn from the diverse group in our Society, and get involved! Thanks for the honor of being your leader.

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