Reflections on the 2004 Meeting of the American Association of Cancer Researchers (AACR)

I was fortunate enough to be selected to represent the National Breast Cancer Coalition (NBCC) at the 95th annual meetings of AACR. This is a huge (about 16,000 participants) scientific meeting devoted to research about all sorts of cancers. I will not attempt to capture the many interesting findings that were reported at the meetings; for that I refer you to the AACR website—in particular:

- http://aacr04.agora.com/planner/ for abstracts
- http://www.aacr.org/PhotoAlbum/2004Webcast/webcast.asp for webcasts and slides of many talks.

Rather, I will attempt to provide some personal muses, contrasting this experience to that of attending other meetings, and reflecting on some of the themes I inferred.

AACR versus Other Meetings

The AACR meetings focused on basic science, but included many formats (e.g., distinguished lectures, panels, meet the expert tutorials, posters, etc.) that covered the full spectrum of scientific research—from lab science (bench) to clinical application (bedside). I was somewhat surprised by how many of the AACR presentations (probably around 30%) were translational or clinical. This is in contrast to American Society of Clinical Oncologists (ASCO) which also has a huge annual meeting, but is entirely focused on clinical application.

AACR, like ASCO, but unlike the San Antonio Breast Cancer meetings I attended last November, covered all cancers. This, of course, resulted in a very large and sometimes overwhelming meeting, with many parallel sessions. Although my primary interest is Breast Cancer, hearing about other cancers helped provide perspective on Breast Cancer in a way I had not anticipated (see “Beyond Breast Cancer” below).

Like the San Antonio Breast Cancer meetings, AACR provided scholarships to a number of cancer Survivor-Advocates, and hosted a number of special sessions for them. In the case of AACR, approximately 40 Survivor-Advocates participated, more than a third from outside the US. The scientists who presented to the Survivor-Advocates were especially skillful at making the science understandable and helping us understand the big picture. Additionally, a very nice feature of the program was the assignment of scientist-mentors to groups of Survivor-Advocates. These mentors helped us plan our schedules, walked us through some of the poster sessions, answered our questions, and introduced us to other scientists.

Meeting other Survivor-Advocates, both those with similar and different interests was a highlight of the meetings. Their roles varied from heath-care providers

(especially the foreign attendees), to organizational staff and volunteers from a wide variety of organizations. They were all impressive, and hearing about some of the similarities and differences among their concerns was both fascinating and helpful. One participant, a staff-lobbyist for a melanoma organization, was reading a book I should have known about—"*The Politics of Breast Cancer"* by Maureen Hogan Casamayou. It is, in large part, about NBCC. I hope to continue to network with many of the Survivor-Advocates in the future.

The 2015 Challenge

Another thing I should have been aware of but wasn't, is Andy von Eschenbach's (Director of National Cancer Institute) public challenge to "eliminate the suffering and death due to cancer by 2015." It is nice to have a concrete stake in the ground. While not as ambitious as some goals we might prefer (e.g., eliminating all cancer within five years) it does seem to have a realistic ring to it.

I heard von Eschenbach at a public forum available to local, lay folks interested in cancer, as well as at one of the scientific meetings. His messages were essentially the same. In addition to the 2015 challenge, he talked about the need for more multi-disciplinary work, and the role NCI will play as the provider of infrastructure to the scientific community. (See below under *"Selected Themes: Bioinformatics"* for additional information on this topic.) This includes, for example:

- Developing scientific computing resources
- Maintaining databases of information about genes, tumors, etc.
- Establishing standards for tissue collection and storage.

Beyond Breast Cancer

Although my primary interest is Breast Cancer, hearing about other cancers, both at the scientific sessions and during informal interactions with other Survivor-Advocates, was very useful. Still, more Survivor-Advocates had interests in breast cancer than any other cancer. This is not surprising given the statistics concerning breast cancer. On the negative side, breast cancer is among the most common cancers. On the positive side, many people affected by breast cancer go on to become long-term, Survivor-Advocates.

Other good news for the breast cancer community that we perhaps take for granted, is that there are numerous, often helpful therapies (albeit perhaps not often enough), as well as clinical trials. The situation is more depressing (but possibly changing) for pancreatic cancer and melanoma, where there are virtually no useful treatments or clinical trials. In regard to brain cancer, I had never really considered the added challenge of making progress against the blood-brain barrier.

The relatively happy story associated with childhood cancers was also enlightening. There is probably no greater success story in the field of cancer

research. Whereas childhood cancers were about 85% fatal twenty years ago, they are about 85% curable today. This is particularly interesting given the relatively small number of cases (relative to adults) and the diversity of cancers (most body sites). (See below under *"Selected Speakers: Kamen Brothers"* for additional information on this topic.)

Another interesting thought was shared with me by a melanoma survivor. Melanoma is currently quite curable when caught very early, but rarely is that the case. Yet, screening for melanoma is relatively simple—it just takes a thorough examination by a trained eye. Why isn't melanoma screening a standard part of every medical appointment, much like blood pressure screening? Perhaps it is due to the infrequency of the disease, but perhaps also because it entails a somewhat time consuming, non-reimbursable service, with no consumable product.

Rational, Integrative Science

Overall, I came away with the feeling that the science of cancer is really maturing. About five years ago I heard some very exciting talks about mapping the human genome and how that was going to change cancer research. Basically, the idea was that genetic analysis of tumor tissue would allow oncologists to prescribe effective, tailored treatments. Since then, however, I have had the sense that these genetic-based techniques are only proving how complicated things really are. Many studies seem more or less like random "fishing expeditions," often with suggestive, but not replicable results.

Although we still seem to be a long way from routinely prescribing effective, tailored treatments, the science seems to be developing. Much work reported at AACR this year was hypothesis-driven and focused on molecular pathways. More often than not, theory-based explanations were provided for why tumors with different genetic profiles had different prognoses or reactions to drugs. And there were many examples of multi-disciplinary, translational work which moved facilely from cell cultures to animal models to clinical trials, and then back again.

Selected Speakers

Although I will not provide detailed notes on particular talks, I must briefly mention a few I especially enjoyed.

Judah Folkman: Folkman is a legend in cancer research for his creativity and persistence. He was the lead speaker at a seminar titled: "*Angiogenesis: Biology and Therapeutics*." His presentation was a beautiful example of interdisciplinary, translational research that systematically analyzed angiogenesis--the concept that tumors attract, and are dependent on the vascular system— and identified usefully anti-angiogenesis treatments. Follow-up talks at this session presented work that is being directed at better understanding angiogenesis' role in cancer, and identifying treatment combinations that leverage this understanding.

Dennis Slamon: Slamon is another legend who did not disappoint. His talk, one of the early morning meet the expert sessions, covered many years of systematic research that moved from petri dish to rats to humans, and resulted in one of the first targeted cancer treatments based on a genetically engineered, monoclonal antibody—Herceptin--against Her2/Neu positive breast tumors. The work continues toward a better understanding of drug resistance, identification of synergistic drugs, and the application of the approach to other tumors.

Leland Harwell: Harwell is a Nobel Laureate of whom I had had not previously been aware. He gave a distinguished Lecture on "*The Potential of Molecular Diagnostics to Improve Cancer Survival.*" This was another summary of beautiful science that spanned a number of years, disciplines and methodologies. The common theme had to do with the value of identifying proteins produced by tumor cells to diagnose, prescribe and assess treatments of cancers. The promise of this work seems to be close to reality. (See below under *"Selected Themes: Proteomics"* for additional information on this topic.)

Bill Nelson: Nelson is someone I had not previously been aware of, but will follow in the future. He was very accessible, making presentations at the public and Survivor-Advocate sessions, as well as chairing a scientific seminar on "*Inflammation and Cancer*." This is a relatively new, hot topic--one that is likely to attract headlines over the next few years. While there is not yet a good causal explanation, there is converging evidence that most solid cancers are associated with long-term inflammation. (See below under *"Selected Themes: Inflammation"* for additional information on this topic.)

The Kamen Brothers: The special opening lecture—"*Inventor and Entrepreneur*"--was presented by Dean Kamen. He has developed many medical devices, as well as the highly-publicized "*Segway People Transporter*." His talk was meant to stimulate creativity, and focused on the value of cross-pollinating ideas from different disciplines.

Dean's brother, Barton Kamen is a pediatric oncologist at the Cancer Institute of New Jersey, who chaired one of the new concepts in organ site research" workshops titled "*Cancer Predisposition Pathways: Lessons from Pediatric Oncology*" and gave a related, interactive talk to the Survivor-Advocates that I found especially provocative. He suggested that the relative success in pediatric cancer is, at least in part, due to:

- Very aggressive treatment—much more aggressive than typically used on adults. (This, however, is resulting in more later-life secondary cancers.)
- The vast majority of childhood cancers are treated at Comprehensive Cancer Centers.

- About 85% of children with cancer are enrolled in clinical trials, both increasing the speed of scientific discovery and the likely quality of care they receive.

Selected Themes

I must also very briefly mention a few of the recurring topics that I found especially interesting and expect to hear more about in the future.

Metastasis: There was a great deal of work devoted to trying to understand metastasis, the aspect of cancer that makes it so devastating. Interesting questions included:

- What makes some cancers metastasize very rapidly, some more slowly, and others hardly at all?
- What therapies could interfere with the metastic transition?
- What makes certain sites hospitable to metastases and others not? (It was interesting to learn that following the shortest lymphatic or circulatory pathway does *not* adequately explain the pattern of metastases.)

Stem Cells: Cancer research using stem cells does not have the political baggage associated with embryonic stem cell research. Rather, it refers to site specific stem cells. For example, there are breast stem cells that have the potential to become multiple types of breast cells, but not other body parts. Some interesting findings I first heard about in San Antonio were elaborated on at AACR. It appears that:

- Only a small proportion of breast cancer cells are stem cells
- It is the only the stem cells that can establish new colonies
- Current therapies reduce or eliminate non-stem cells, but do not seem to impact stem cells.

Of course much work needs to be done to confirm and refine these findings, but if confirmed, they could have major impact on the way we think about and treat cancer.

Inflammation: Another area that is likely to have significant impact on future treatment—indeed, potentially prevention--is the finding that many, if not all solid tumors seem to be associated with long-term inflammation. Further, there seems to be increasing evidence that people who have been taking anti-inflammatory drugs (e.g., aspirin, ibuprofen, Vioxx, Celebrex) have a significantly lower risk of getting a variety of cancers. An understanding of the relationship between inflammation and cancer may shed light on the recently publicized finding that women who have taken many antibiotics are at high risk of get breast cancer. Inflammation is also probably relevant to the hot area of Cox2 inhibitors (chemically similar to Ibuprofen), which seem to have therapeutic value in a number of solid tumors.

Proteomics—Detection, Therapeutic Reaction": Finding simple blood tests for cancer is, of course, very appealing. Such tests would almost certainly lead to more, earlier detection, with better outcomes, and at reduced costs. Tracking molecular changes associated with cancer using simple blood tests could also be used to rapidly assess the value of various therapies. This becomes increasingly important as more drugs that are only sometimes effective become available. The challenge is for these tests to be both highly specific (i.e., few false positives), and sensitive (few false negatives). A significant amount of research is directed at these goals, and significant progress seems to be on the horizon.

Bioinformatics:
The amount of data that is becoming available as tumor cells are analyzed at the genetic level is massive. Further, the potential value of data available from previously stored tumor tissues, along with knowledge of their treatments and results have made the field of bioinformatics extremely important. NCI is playing a major role by:

- Establishing standards for collecting, coding and storing tissue
- Providing public access to genetic data
- Developing software tools for data mining
- Making it easy to integrate across data sets

The idea that much future biomedical research will be done on the computer, rather than in wet labs, seems to be a distinct possibility.

A Final Point to Ponder

Bill Haitt, who is the Director of the Cancer Institute of New Jersey, was assigned to mentor my Survivor-Advocate group. I'd like to share one of my interactions with him because it has haunted me since. He was explaining a poster summarizing work done in his lab--"*Use of DNA vector-based RNAi to modulate multi-drug resistance in cancer cells*"--about a fairly specific molecular reaction, and trying to make some general points about the progress of science. Quite frankly, I don't remember all of the details of the science, but a few of his general points stuck with me.

- He said that the poster had received quite a bit of attention because it had "RNAi" in its title, which was a hot topic this year. Yet, to Bill the really important aspect of the work had more to do with "modulating multi-drug resistance in cancer cells."
- He suggested that when advocates review scientific proposals we should ask: "What will you do if your work doesn't turn out the way you expect?" His point was that experiments should be designed to discriminate between interesting theories, with either result leading to additional questions. This is in contrast to designing experiments simply to try to confirm a favored hypothesis.

- The experiment reported on the poster confirmed an interesting hypothesis regarding the synergy of two therapeutic agents. Thus, I asked Bill a variation of his question: "What will you do now that your experiment did work out the way you expected?"
- It was his response that gave me pause. He assumed the relevant drug companies would notice the paper and follow-up. He was not, however, planning to do anything to ensure that this happened.
- I suspect that Bill's attitude is typical of most good scientists. Conducting good science and publishing the results is what most scientists view as their jobs.
- For quite some time now advocates have been asking whether progress toward eradication of cancer could be sped up by spending more money on good science. Perhaps more important is making sure that promising results actually see their way into treatments.
- I would welcome your reactions to this story, as well as any of the other points raised in these notes?

Thanks

In closing, I want to sincerely thank AACR for funding my participation in this year's AACR meetings, for putting together an excellent program for Survivor-Advocates, and for helping up feel so welcome. I also want to express my appreciation and admiration to the many scientists and Survivor-Advocates who participated and commit themselves to the common goals of understanding cancer and eliminating the suffering that it causes.