DEPARTMENT OF HEALTH AND HUMAN SERVICES
NATIONAL INSTITUTES OF HEALTH
NATIONAL CANCER INSTITUTE

MINUTES of the 54th DIRECTOR'S CONSUMER LIAISON GROUP MEETING
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Members Present

Ms. Gwen Darien, Chair
Mr. Everett Dodson, Vice Chair
Dr. Jeff Allen
Ms. Susan Braun
Ms. Joyce Wilcox Graff
Ms. Michelle McMurry-Heath
Dr. Deborah Morosini
Ms. Phyllis Pettit Nassi
Mr. Jon Retzlaff
Ms. Wendy Selig
Mr. Josh Sommer
Ms. Arlene Wahwasuck
Mr. Max Wallace

Speakers

Dr. Gregory Foltz, Director, Center for Advanced Brain Tumor Treatment, Swedish Medical Center
Dr. Martin A. "Mac" Cheever, Director, Solid Tumor Research, Fred Hutchinson Cancer Research Center
Dr. Peggy Porter, Associate Member, Divisions of Human Biology and Public Health Sciences, Fred Hutchinson Cancer Research Center
Dr. Nick Anderson, Department of Medical Education and Biomedical Informatics, University of Washington
Dr. Meg Mandelson, Public Health Sciences Group, Fred Hutchinson Cancer Research Center
Dr. Sunil Hingorani, Director, Pancreas Cancer Specialty Clinic
Ms. Maria Gonzalez, Cancer Research Manager, St. Joseph Hospital of Orange
Ms. Sarah Osen, NCI Community Cancer Centers Program Coordinator
Mr. Robert Mittman, Facilitator

National Cancer Institute Staff

Ms. Shannon K. Bell, Director, Office of Advocacy Relations (OAR)
Mr. Benjamin Carollo, Advocacy Relations Manager
Ms. Anne Lubenow, Special Assistant to the NCI Director

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Welcome and Opening Remarks

Rules governing potential conflicts of interest were reviewed, and a quorum was determined to be present.

The group welcomed three new members of the DCLG—Michelle McMurry-Heath, Josh Sommer, and Jon Retzlaff. The contributions of outgoing members Dr. Grace Butler, Ms. Kelly Cotter, Dr. Yvette Colón, and Mr. Alan Kaye were also recognized.

Tissue: The Critical Link to Genetically Driven Research and Personalized Medicine

Presenter: Dr. Gregory Foltz

Dr. Foltz welcomed the group to the Swedish Medical Center, where he is the director of the Center for Advanced Brain Tumor Treatment. His presentation focused on how patient engagement and tissue collection have provided a sound foundation for genomic studies in brain cancer. He also related how advocacy groups play a pivotal role in many facets of care. Technology is advancing quickly, but there are many pockets where people do not know what is available.

Glioblastoma is still one of the most quickly advancing, rapidly fatal cancers. Survival is still about 15 months after diagnosis. After surgery, it recurs in 7 months, on average, and then is rapidly fatal. Three treatments have been approved by the Food and Drug Administration, but they are mainly palliative and prolong survival by only a few months.

In Washington state, barriers such as finances, time, and distance make it difficult to engage glioblastoma patients in research. There are a few centers of excellence in the country, but travel is a real hardship for patients. Consequently, many patients never get to the big academic centers. The greatest chance to improve survival rates is to enroll these community patients in clinical trials. With the move toward genetically-based trials, it should become easier to enroll patients and collect genomic data—even in their local hospitals.

Working at the community level presents some challenges. Privacy concerns (e.g., Health Insurance Portability and Accountability Act [HIPAA]) must be addressed, and some effort is required to overcome legal issues to allow community hospitals to share records and tissue samples and to collaborate. Dr. Foltz also cautioned that intellectual property can pose a barrier, but collaboration agreements allow sharing of tissue samples and intellectual property among the research partners.

To collect samples, community hospitals have to put some basic infrastructure in place. For example, most hospitals do not have liquid nitrogen, and so they need to get a vat or a -80C freezer for specimen storage. The approximate cost of a tissue distribution system is $30,000 for infrastructure. A full-time staff person is generally needed to collect the samples and properly preserve them.

Just since September 2008, the Ivy Center has initiated tumor and serum banking, stem cell isolation, whole genome microarrays, stem cell culture, and xenobiotic culture. The transformation has required a tremendous investment per patient. Initially, it was entirely funded by advocacy groups, now it is supported by grant funding.

Dr. Foltz led the DCLG on a tour through the brain tumor clinic and research laboratory. One key to the success of biospecimen collection at the Swedish Medical Center is the proximity of the clinic and the surgical department to the laboratory. Having a person-to-person connection between researchers and patients is essential for the success of cancer care and the collection of samples for biobanking. A staff person is dispatched to the operating room (OR) when a patient is undergoing resection of a brain tumor, divides the sample, and transfers a portion to a liquid nitrogen container and another portion to media for culture of stem cells and xenotransplantation into mouse models.

DNA, RNA, and protein are extracted from the samples in the laboratory, where six senior (Ph.D.) scientists work. The scientists look at the entire genome for each patient by using a cartridge system (cost about $400). The test takes a few hours to run, and Dr. Foltz is willing to discuss the results with interested patients.

Dr. Foltz underscored the importance of advocates in explaining the value of tissue storage to their constituencies. The community is where the tissue and the patients are—not at academic centers. The community hospital is where initial diagnoses are made; more recurrences are seen at major cancer centers. Great progress can take place in community hospitals working on their own and in partnership with "big science."

Dr. Foltz answered questions from the DCLG:

- The researchers rarely get "normal" brain tissue, but blood samples are obtained to use as normal controls.
- It would be possible to collect tissue at every hospital; it is just a question of resources and time.
- Because it is difficult to convince patients to undergo serial brain biopsies, there is strong interest in the rapid autopsy program. Timing can be challenging, however, especially in remote hospitals. Another barrier is the lack of funding to transport patients' bodies for autopsy/brain retrieval. There could be a role for advocacy in solving such logistical problems and raising support for these important research activities.
- The economic model for the program is based on providing care for glioblastoma patients regardless of their insurance status. Because only about 200 patients per year are diagnosed with this cancer in Washington, it is possible to advocate and raise funds. Dr. Foltz underscored the importance of offering a value proposition to leaders in the field to help ensure that patients get access to new treatments.
- In glioblastoma multiforme, it is not critical for pathologists to examine the margins of the tumors because the disease infiltrates huge areas of the brain. Therefore, using part of the tumor for research does not present a problem for the pathologist or the patient (because removal of the entire tumor does not affect survival). It is also important to preserve pathology tissue blocks.

DCLG Response to Presentations and Site Visits

The DCLG discussed and summarized what the members observed and learned at the Swedish Medical Center and the FHCRC.

Biospecimen Collection and Storage in the Community Setting

- Advocates can make a real difference. At the Swedish Medical Center, the Chris Elliott Fund is underwriting tissue collection and genomic testing. Grassroots advocacy changed practice at this center.
- The DCLG noted that Dr. Foltz is actively raising funds to collect biospecimens. He has obtained support from advocacy groups and is aggressively seeking grant funds. He has developed an excellent model to get programs going.
- Biobanks are a good resource, but what is really needed is the information flowing from the samples. The focus should be more on analytes than on tissues.
- The DCLG observed that the cost of setting up liquid nitrogen storage in community hospitals is modest, only $30,000 according to Dr. Foltz.
- Some investigators have commented on the importance of preserving tissue and also grafting tissues into mice so that the tumor can be studied in murine models. Dr. Foltz is one of the first to immediately implant tissues into mice to test possible therapies for the patient from whom the tissue was obtained. Tissues engrafted into mice could generate more tissue to distribute to researchers.
- Patients' tissues should be saved not only for immediate research needs but also for testing emerging therapies to benefit that particular patient. Discarding tissues is troublesome. Some of the big centers are probably retaining tissue or DNA because they are stratifying patients based on molecular profiles.
- Community hospitals need to become the front line in biospecimen collection because that is where initial diagnoses are made.
- Stromal tissue in addition to tumor tissue should be biobanked.

Barriers

- One of the biggest barriers to clinical research is attitude. Patients should be considered partners, not research subjects. The patient-centered aspect of Dr. Foltz's work was striking.
- At the FHCRC, one barrier is the issue of biospecimen "ownership." Patients are reluctant to participate in research that does not share samples with other researchers. Investigators at major academic centers tend to be very restrictive about sharing because they feel proprietary about samples they collect and preserve.
- People with rare diseases are scattered around the country. Critical samples need to be collected from these patients regardless of where the tumor is resected.
- For rare cancers, it is bothersome that specimens are not being retained by some large cancer centers to accrue sufficient numbers of samples for meaningful research. Also, even common cancers may have rare subtypes. Therefore, long-term storage is important for all cancers.

Ethical Issues

- Some patients may not want their tissues to be xenografted into mice because of animal rights issues and other concerns.
- When tissues are stored, what is the usual approach for re-consenting participants for secondary research? One solution is to de-identify the samples so that the secondary research would not be considered "human subjects research." Therefore, there is no need

to re-consent participants. In such situations, however, de-identifying samples removes the link to clinical data and outcomes.

Enhancing Participation in Clinical Research

- Why is patient care considered to be at odds with research? The DCLG could help people understand that this is not a tradeoff.
- Keeping participants engaged with the research could be linked to ongoing benefit for that patient. The prospect of individual benefit will keep people in follow-up.
- EMR will be important for tracking patients in the national cohort and collecting patient-reported outcomes. Implementing EMR will require technology and political will. The Indian Health Service has set up EMR.
- Patients are seeking direct clinical benefit from research, but they also want the opportunity to contribute to something bigger than themselves.

Case Studies: Developing Biospecimen Resources in Community Settings

Presenters: Ms. Maria Gonzalez and Ms. Sarah Osen

Maria Gonzalez, Cancer Research Manager at the St. Joseph Hospital of Orange (Orange, California), said that St. Joseph is one of 30 centers participating in the NCI Community Cancer Centers Program (NCCCP).

Sarah Osen is the NCCCP Coordinator at the Billings Clinic Cancer Center (Billings, Montana). Because 40% of the people in the center's area are Native American, researchers and clinicians have to be very sensitive to their cultural and religious tenets. For example, many want to be buried in their entirety, which poses a challenge when it comes to biospecimen disposal. In addition, better education is needed about clinical trials and tissue banking. NCCCP funding provides the means to find out what is needed to reach out to communities affected by health disparities, such as Native American communities in the areas outside of Billings. To bring in more clinical trials and boost trial accrual, IT and EMR are critical.

Although participation in the NCCCP does not require setting up biorepositories, Ms. Osen said the motivation to establish one for the Billings Clinic stemmed from the results of a gap analysis. So far, there is no facility or funding for a biorepository, but the clinic is seeking to establish a partnership with other interested NCCCP sites that could provide some benefit to the population, which is largely Native American and rural. She mentioned the possibility of partnering with the Moffitt Cancer Center in Tampa, Florida.

A critical first step, according to Ms. Osen, is education. Patient advocates and clinical researchers have been hired who have appropriate backgrounds. It has taken 3 years to build trust with the community. A standard operating procedure (SOP) for biospecimen disposal was developed, and now the focus is on giving participants their tissues back. Some patients will refuse treatment or participation in studies because they want to be buried as a whole person.

The sharing of best practices, explained Ms. Gonzalez, is a key part of the St. Joseph Hospital NCCCP. Biospecimen collection is being integrated with cultural awareness activities.To diffuse St. Joseph's disposal SOP to other sites, Ms. Gonzalez said that it is necessary to seek assistance from legal departments and educate physicians about the importance of returning biospecimens

to patients. Another factor is that pathologists are custodians of the tissue and may not be at liberty to release it per the guidelines of the College of American Pathologists (CAP).

The DCLG members brought up several points for discussion:

- Community health representatives are an important conduit for educating and delivering messages to their people. There is a Website on which Native Americans tell their stories about living with cancer.
- In Native American populations, the family can be a strong ally.
- One suggestion was to offer continuing medical education programs on the integration of biospecimen collection and clinical care to educate the next generation of care providers (oncologists, primary care physicians, community health workers). This could be a tangible way for NCI to work with the American Association for Cancer Research (AACR).
- Cancer research is "married" to the pathology department.
- An NCI biospecimen template would be very useful for developing informed consent documents and protocols for community hospitals.
- A patient portal would allow collection of PROs, which could then be linked back to specimens and data. Some annotation needs to be done in near-real time by surgeons.
- A potential role exists for the DCLG in raising awareness about research going on in community hospitals.
- The NCI could tie center grants to collaboration with community hospitals. Community hospitals could focus on collecting biospecimens, or they could engage in research themselves. In addition, community hospitals could help cancer centers meet NCI's diversity expectations. Such collaborations are just a matter of structuring incentives properly.
- Researchers need assurance that tissues have been handled properly in community hospitals. Those involved in tissue collection must adhere to protocols and best practices.
- A discussion ensued about the possible commercial value of well-annotated tissues. Will the NCI issue guidelines on this? Some centers have asset managers who oversee intellectual property. Some consideration needs to be given in the informed consent about the possibility that commercial products could be developed using patients' samples.

A Message from Dr. Varmus

The session opened with a video message from the new NCI Director, Dr. Varmus. He plans to meet personally with the DCLG at its October meeting. During his tenure as NIH Director (1993–1999) he was very active with the Director's Council of Public Representatives (COPR); therefore, he realizes the importance of engaging advocacy organizations. Dr. Varmus concluded by saying that he counts on advocate groups to continue the fierce fight against cancer and by thanking the DCLG for all it is doing.

Board Action Planning

The board reviewed barriers not only to tissue collection but also to genomics research more generally. The challenges are classified into three areas. The DCLG was asked to modify the list of barriers so that they are better framed or juxtaposed.

- A new category was proposed: “high-quality samples exist but it is not known where they are.”
- Under “limited quantity of needed samples”:
    - Mention the need to accumulate rare tumors in sufficient numbers for study.
    - Lack of education.
    - Patients: what is in it for me?
    - Patient who failed conventional therapy: need posttreatment samples.
    - Rapid autopsy needed.
    - Pathologist might not be willing to release tissue.
    - Technology not available.
- Under “samples exist but are not of sufficient quality”:
    - Lack of standardized collection models.
    - Philosophy of “dispose of tissues and move on.”
    - Pathology verification.
- Under “quality samples exist but are not made available”
    - Lack of transparency about where tissues are.
    - Inaccurate annotation.
    - Patient: what is in it for me?
    - Need for collaboration with other agencies, e.g., Indian Health Service.
    - Cost of storage: how are priorities set?

Biospecimen Stakeholders

The DCLG members identified stakeholders that might be involved in addressing these barriers and explored what NCI or DCLG might do to engage each of the seven stakeholder groups.

Researchers

1. NCI could make grants contingent upon tissue collection. Many of NCI’s grants and contracts include funds for collecting samples, but mostly in the context of clinical trials. NCI has a role in creating an expectation of accountability and expectation for grantees.
2. With the cancer centers, NCI may have some flexibility in terms of sticks and carrots. For example, proposals that call for a biorepository attached to an investigator-initiated research project might be given priority. Incentives should be set up to get researchers out to the community to set up collaborations.
3. For a long time there has been a desire for more coordination among grant makers to reduce the wasting of resources and redundancy of effort. NCI could help orchestrate such a conversation.
4. NCI could work with the Centers for Medicare & Medicaid Services on a demonstration project to incentivize physicians to collect and store tissue specimens and work with NCI researchers.

Physicians, Surgeons, Other Clinicians

1. Additional support for training is needed; for example, offering specific continuing medical education (CME) or subspecialty certification directed at biosampling and genetically informed medicine. Also, fellowships and curricula for medical school were mentioned.

2. NCI could publish barrier-focused articles in journals to help clinicians in smaller hospitals understand the importance of tissues.
3. Getting Medicare to pay for certain procedures is a very strong lever and would rapidly expand biospecimen collection to all populations.
4. The AACR could set up training or make practicum workshops available.
5. Members of speaker bureaus for the pharmaceutical companies could talk about biospecimens.

Health Care Executives

1. Accreditation could be a lever. If biospecimen collection becomes a best practice in the field, health care executives will want to adopt and compete on this basis. Making this a perceived standard of care could be a basis for market differentiation.
2. Run "boot camps" for community hospital chief executive officers (CEOs) on biobanking. Make involvement prestigious, as a preceptorship is.
3. Reimbursement could be a way to fund studies on cost-effectiveness.
4. Biospecimen collection could be linked to Joint Commission accreditation.
5. More staffing is needed in laboratories to handle work associated with biobanking. NCI could help link hospitals with regional resources. Or, it may be possible to develop "Biospecimen in a Box," a turnkey kit for starting biospecimen activity.
6. Keep physicians' patient bases intact by keeping the patients with the community hospital and just bringing them to the cancer center for surgery and tissue collection.

Pharmaceutical Companies

1. Create a space, such as a journal, to publish on challenges and failures. Such knowledge would help steer NCI resources in the most promising directions.
2. Think about how this group could be a catalyst for dusting off investigational agents that were tested but, for unknown reasons, had limited success.
3. Patients are reluctant to allow their samples for the economic benefit of pharmaceutical companies. Ensure that the signed informed consent allows use of the tissue for commercial purposes.
4. Find ways to overcome the intellectual property and regulatory challenges of testing compounds and/or biomarkers in combinations.
5. Because many decisions are personally driven, DCLG members ought to look for where their groups have good contacts and feed them information.
6. If a company abandons work on a particular organ system (e.g., brain), NCI might be able to ask for such samples.
7. Engage trade associations.
8. Look at ways to modify informed consents to allow the broadest use of tissue.
9. Curate posttreatment samples.

Patients, Survivors, Friends, Family, Communities

1. Frame messages to engage specific groups (e.g., populations with low levels of literacy), especially those with strong family histories, to explain what could be learned and what might lead to effective treatment or cure.
2. Encourage NCCCP centers to collaborate with other agencies, e.g., Indian Health Service, Veterans Administration.

3. Look at organ donor consents as a possible model for biospecimen collection. How is the education for organ donation handled? Is there a corollary for tissue samples for education, consent, and advance directives?
4. Promote rapid autopsy programs as a means to obtain end-stage tissue samples.
5. Tell stories to convey the message that tissue collection is just a tool in research to help patients.
6. Our system of informed consent might be based on avoiding a harm that is not really a reality. It could be needlessly stifling research.
7. The DCLG could help craft realistic messages about what research can do.
8. Reach out to the National Library of Medicine for stories about patients donating their tumors for research. Stories could be honed by a professional writer.
9. Drive adoption by linking quality of care with research on biospecimens.

Advocacy Groups, Foundations

1. Foundations can provide and align incentives for researchers.
2. The NIH could become involved in funding the development of a standard infrastructure for the collection of data by registries for cancers and rare diseases so that one could look across all that data.
3. NCI could convene cancer advocacy groups to move beyond their focus on tumor sites and instead consider commonalities, e.g., *BRAF* mutations, which are present in 8% of all tumors. With such an approach, rare cancers could be aggregated into larger units. Emerging TCGA pathway data should be made available to the DCLG so that it can set up partnerships with relevant advocacy groups.
4. NCI could convene a lay conference about genetically informed research.
5. Advocacy organizations could exercise some control over where tissue is distributed. NCI could help drive the collection of tissues in partnership with advocacy organizations. By bringing all the groups together, NCI could help avoid a piecemeal approach.
6. There is a big difference between those who advocate on behalf of those who are well and persons who are advocates for those who are sick. Who will come to the table for these efforts?
7. Find ways to use social media to deliver messages.
8. Set up a clear path for those who want to donate tissue.
9. Get groups to share best practices and language for best practices.

Policy Makers, Politicians

1. Regarding the implementation of EMR, ensure that rare diseases are represented. DCLG could help ensure that all data is interoperable and inclusive.
2. As representatives of their own constituencies (not as DCLG members), advocates/leaders could meet with Congressional caucuses (e.g., the Cancer Caucus) and learn about their needs in terms of education and talking points. The DCLG does have an important educational component.
3. DCLG and NCI could identify a substitute for “biospecimens” that would be better than that term. Perhaps Dr. Varmus should be consulted on this matter.
4. DCLG could brief Congressional leaders on what is happening in their home districts.
5. Seek more information from groups advisory to the Armed Forces, the VA system, and the Department of Defense about their research, databases, and biospecimen repositories.

6. The NCI needs help to tell its own story. The DCLG could work with NCI staff to generate synergy and develop stories that could make a difference.
7. Develop an “elevator speech” so that DCLG members are prepared with educational information and common language. The text should be flexible enough so that people can customize it and build upon it.

Certification

I hereby certify that the foregoing minutes are accurate and complete.

_____	_____
Date	Chair, Director’s Consumer Liaison Group
_____	_____
Date	Executive Secretary Director’s Consumer Liaison Group