



ACCRF Update – January 2008

Summary

The Adenoid Cystic Carcinoma Research Foundation (ACCRF) has been in existence for two years now. We are very excited that some of our early projects have come to fruition while others will do so over the next several months:

- A new national tumor biorepository will support and attract more ACC research projects.
- The first-ever mouse models with human ACC tumors have been created.
- Nine cell lines are available now to researchers, up from just one cell line two years ago.
- ACC will be one of the first cancers to benefit from a high-throughput RNAi study.
- ACC is one of the first rare cancers to be the focus of large-scale DNA sequencing.
- Screening of ACC mouse models with chemotherapeutic and targeted drugs has begun.
- ACCRF Co-Founder Marnie Kaufman has been named to a 3-year term on the National Cancer Institute's Head & Neck Steering Committee.
- ACCRF has raised over \$1 million to support ACC research.

These developments will make improved therapies and a cure for ACC much more likely and available on a shorter horizon.

Detailed Project Updates

1. Salivary Gland Tumor Biorepository – The availability of frozen tumor samples is crucial to the success of various genomic studies (see below) that may identify the factors driving ACC and lead to improved diagnostic, prognostic and treatment options. ACCRF assisted in the organization of the first-ever NIH Workshop on Salivary Gland Cancers in October 2006 (see [report](#)). As an outgrowth of that meeting, the National Institute of Dental and Craniofacial Research (NIDCR) addressed the need for high-quality tumor specimens in under-researched salivary gland cancers.

In 2007, NIDCR took the lead in the formation of the Salivary Gland Tumor Biorepository (SGTB) by funding a centralized facility at the M.D. Anderson Cancer Center. The SGTB will collect cancer specimens and associated histories from patients at the University of California at San Francisco, Johns Hopkins University, the University of Pittsburgh, and the University of Virginia. Additional institutions will join the consortium as their governing bodies approve their participation. Researchers with an interest in salivary gland cancers, including ACC, will apply to the SGTB to access specimens for their studies. ACCRF is pleased to have been participating in the organizational activities of this important consortium, a natural extension of ACCRF's funding of tumor biobanking at the M.D. Anderson Cancer Center and the University of Virginia.

2. Animal Models – Mouse models implanted with fresh human tumors (xenografts) are useful for the screening of potential therapies as well as for the creation of additional cell lines (see below). ACCRF-affiliated researchers at the University of Virginia, the Dana-Farber Cancer Institute, and Johns Hopkins University are actively creating the first-ever ACC mouse models.



Currently, nine xenografts have been created, with more in development. Patient donations of fresh tumors remain a critical element of success in these efforts.

3. Cell Lines – These tumor cells that grow in plastic dishes are useful in the screening of potential therapies as well as for studying the mechanisms of action that drive ACC progression (see RNAi Project below). ACCRF has accessed within the past few months an additional four cell lines for the use of affiliated researchers. We have now identified a total of nine cell lines available to researchers, seven of which have been consolidated at the University of Virginia. Less than two years ago, only the ACC3 cell line was being studied by U.S.-based researchers. Some of the cell lines are freely distributable while others require the negotiation of a Material Transfer Agreement (MTA) with the appropriate laboratories. As more cell lines are developed from ACCRF's xenografts, we will also make them available to interested researchers.

4. RNA Interference (RNAi) Project – RNA interference is a leading-edge technology in which the RNA products of individual genes are “knocked out” in order to determine their significance in tumor survival and proliferation. ACCRF recently approved a proposal from Dr. Ed Harlow, a world leader in high-throughput RNAi at Harvard Medical School, to find genes essential to ACC's progression. The project will generate and validate a list of genes that may represent promising drug targets for ACC. Without the collection of multiple cell lines by ACCRF, this exciting project would not have been feasible.

5. Genomic Studies – The Wellcome Trust Sanger Institute (Sanger), the leading provider of raw sequencing data to the Human Genome Project, has begun sequencing DNA samples from ACC tumors provided by the M.D. Anderson Cancer Center. This ACCRF-funded project will attempt to identify mutations in ACC tumors that may drive disease progression. The initial list of genes is heavily weighted towards those that already have effective drugs and those that are more easily “druggable”. The study will be the first project carried out on the Sanger's newest sequencing platform.

In addition, comparative genomic hybridization (CGH) studies are being carried out by ACCRF-affiliated institutions. These studies look for gross genomic imbalances at the chromosomal level that may be associated with ACC tumors. Findings from CGH studies will likely inform future sequencing studies as they help narrow down chromosomal regions that may harbor genetic mutations.

6. Xenograft Screening – ACCRF has begun screening drugs and drug combinations on ACC mouse models (xenografts) to determine their efficacy. Although mice and humans may have different responses to the same drugs, the results in mice may indicate more promising therapies to consider in human clinical trials. The initial screen includes a range of FDA-approved chemotherapies and targeted agents, and will serve as a baseline for evaluating new agents. ACCRF has begun discussions with pharmaceutical companies to access and evaluate novel agents for our xenograft studies. The eventual goal is to identify drugs and combinations that are sufficiently promising to warrant the initiation of clinical trials for ACC patients.

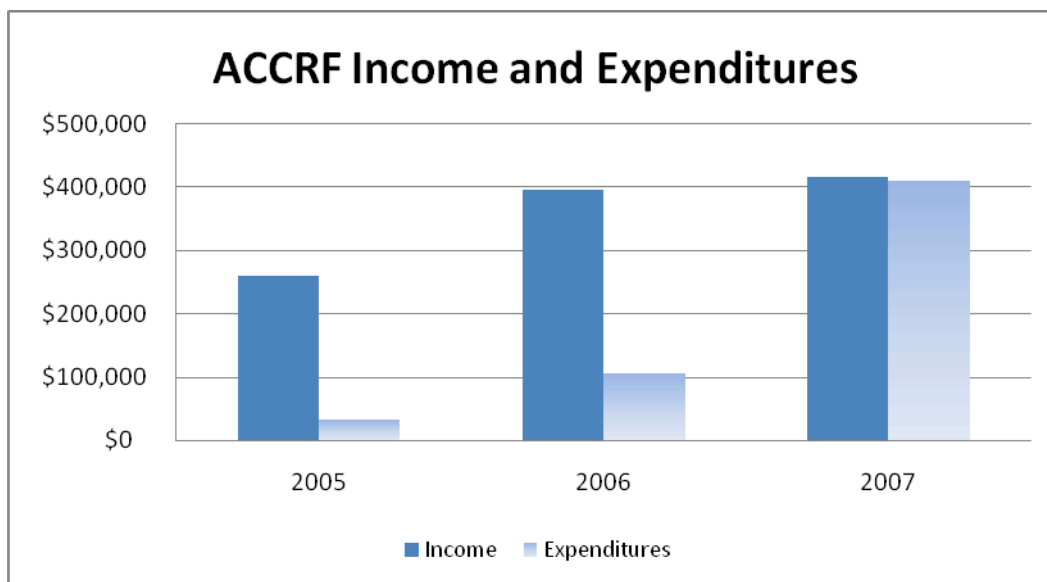
7. Clinical Trials – The National Cancer Institute (NCI) recently established a Head and Neck Steering Committee (HNSC) to coordinate the clinical trials of cooperative groups, Specialized



Programs of Research Excellence (SPOREs), academic medical centers, and community oncologists. The HNSC's role is to prioritize and design Phase 2 and Phase 3 clinical trials in cancers of the Head and Neck. The 22-member Steering Committee will benefit from the work of four Task Forces: (1) Metastatic/Recurrent Disease, (2) Rare Tumors, (3) Previously-untreated Locally Advanced Disease, and (4) Tumor Biology and Imaging.

ACCRF Co-Founder and Director Marnie Kaufman has been named to the HNSC as a Patient Advocate representative. As a voting member with a 3-year term, she is well positioned to learn of all new drugs and trials being considered for NCI funding. In addition, she will serve as a strong advocate for clinical trials in under-researched rare tumors like ACC.

8. ACCRF Finances – The remarkable progress witnessed in ACCRF's research efforts would not have been possible without the generous support of the ACC patient community, including families and friends. ACCRF recently passed the \$1 million mark in donations, a truly impressive feat in the realm of rare diseases. As expenditures rise with our expanding research programs, it is imperative that we maintain and expand our funding base.



Fully 95% of expenditures have been on research-related programs; the remaining 5% of expenditures represent legal, accounting, website and postage costs that have been more than covered by donations from ACCRF's founders. ACCRF is run by volunteers, none of whom receive any compensation.

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ACCRF remains dedicated to its mission of accelerating the development of improved therapies and a cure for ACC. As our Research Agenda makes parallel progress across a wide range of projects, we are optimistic that ACC patients will benefit from the amazing work of our affiliated researchers.