

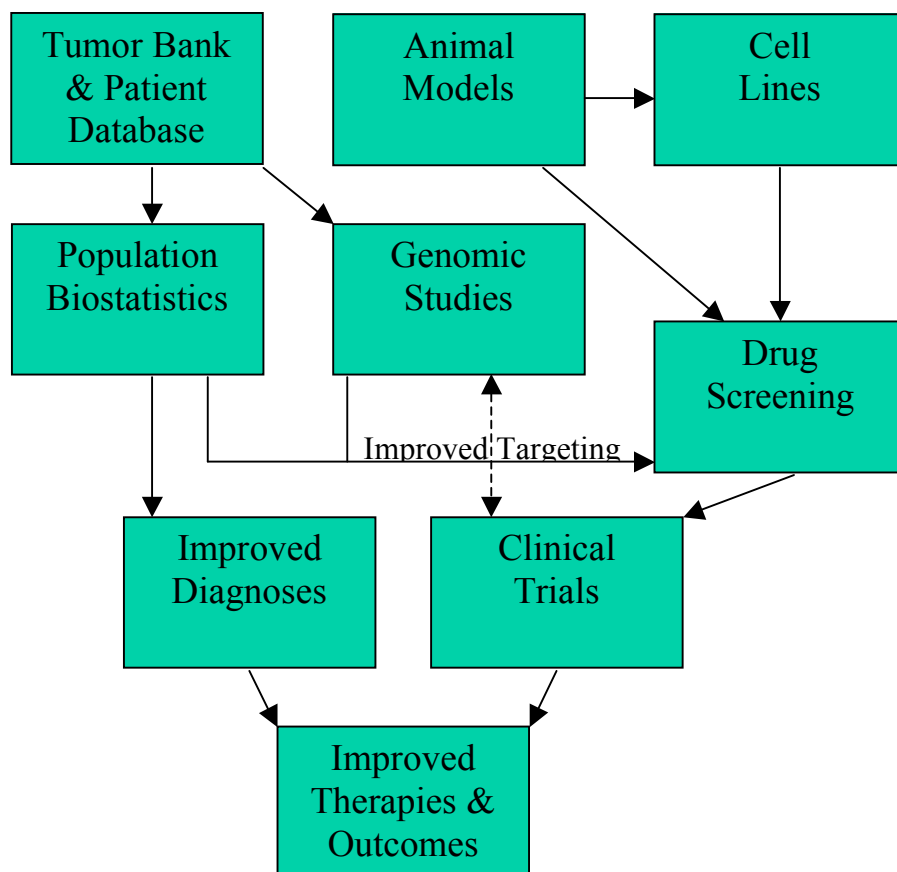


ACCRF – Research Agenda - June 2006

ACCRF's sole mission is to speed improved therapies to ACC patients. However, the best way to make quick progress involves a deliberate and thoughtful planning process that avoids duplicative or illogically-sequenced research projects. With the guidance of our Scientific Advisory Board and the input of many interested researchers, ACCRF has developed a Research Agenda that we believe will deliver new therapies to patients as quickly as possible. The Research Agenda certainly will change as new information and methodologies develop, but it represents the best efforts of the best minds across the best cancer institutions in the world.

As a rare cancer, ACC has received very limited research funding. Not surprisingly, the tumor banks, patient databases, animal models and cell lines available to researchers of more common cancers are not widely available to ACC researchers. Yet it is this infrastructure that is necessary to conduct the basic and translational research that will yield improved therapies and patient outcomes. ACCRF plans on making parallel progress in all these areas, establishing the building blocks of a coherent strategy.

Schematic Diagram of the Research Agenda





Current Project Proposals:

1. **Tumor Bank/Patient Database** – ACCRF is working with academic institutions to create a virtual tumor bank that will also detail the associated patient histories (while safeguarding patient confidentiality). The institutions will share information about their existing inventory and make samples available to worthy research projects. The first use of these tissues will be for genomic studies (see below).

2. **Animal Model and Cell Line Development** – ACCRF is coordinating the efforts of surgeons and pathologists to develop animal models of several ACC tumors (the most common animal models in cancer research are mice with implanted human tumors). In addition, these animal models will facilitate the development of new ACC cell lines (cell lines are human tumors grown in glass dishes). Both animal models and cell lines are necessary for pre-clinical testing of therapeutic drugs to determine their efficacy and toxicity. Drug screening that involves higher numbers of animal models and cell lines leads to more credible results. Currently, there is only one ACC cell line available to researchers in the United States and no centralized repository of ACC animal models. ACCRF plans on centralizing all animal models and cell lines at one institution and making them available to all interested researchers to carry out their own ACC projects.

3. **Genomics** – Cancer is caused by genetic mutations. Particular cancers are caused by mutations of particular genes or combination of genes. The process of comparing the DNA of normal tissue with cancerous tissue may lead to the discovery of potential genetic targets for drug therapies. ACCRF plans on funding genomic studies to help determine which genes should be targeted by therapeutic drugs.

4. **Drug Screening** – ACCRF is contracting with a non-profit research institution with expertise in the management of animal models and cell lines to screen drugs at low cost. Informed by the output of genomic studies, researchers will test the drug compounds and combinations that are most effective at shrinking or eliminating tumors cells in both glass dishes and mice. ACCRF does not intend to develop the therapeutic drugs. Rather, we aim to provide enough infrastructure and sufficiently promising results that the National Cancer Institute and pharmaceutical firms will find it worthwhile to carry on ACC-specific projects and human trials.

5. **Population Biostatistics** – Once the patient databases have been properly organized and updated, biostatisticians will be able to mine the data to determine if there are any correlations among patient characteristics, diagnoses, prognoses and the effectiveness of therapies. ACC patients may be diagnosed earlier or receive more effective therapies with such information. ACCRF will support the development of these databases as well as the analysis of their contents.

The ordering of these projects is important. The founding of the virtual tumor bank is a necessary precursor to obtaining sufficient tumor samples to begin the genomic studies.



Separately, the animal models must be developed and, from them, cell lines must be derived. These parallel tracks may take a full year, but then they will merge together as drug screening begins. The results of the genomic studies ought to be available in time to inform better the decisions about which drugs to screen in the cell lines and animal models. In a best-case scenario, sequencing may indicate that certain genetic mutations are involved in ACC for which existing therapies are likely to be effective (eg. particular kinase inhibitors). Pre-clinical tests might confirm that hypothesis, leading to ACC-specific clinical trials within 2 years from today. It is likely that the work of ACCRF will last well beyond that horizon. But the best-case scenario is a worthy goal for a carefully crafted Research Agenda.

The anticipated cost of this Research Agenda is likely to exceed \$2,000,000. There is considerable uncertainty about the precise cost of each project, but an approximation of the initial agenda's budget for the first three years follows:

Estimated Costs of the Research Agenda

1. Tumor Bank/Patient Database	\$150,000
2. Genomics	\$650,000
3. Animal Model and Cell Line Development	\$400,000
4. Drug Screening	\$500,000
5. Population Biostatistics	\$300,000
 Total Estimated Cost	 \$2,000,000

Each project might be improved considerably if additional funds were available. For example, DNA sequencing of more genes across more tumors might yield additional targets for therapy. Or novel drugs with high price tags may need to be tested on more cell lines or animal models. And the building of a patient database is an open-ended project that will increase in value as information accumulates. However, we believe that a very credible effort can be set in motion and sustained with the budget listed above.

It bears repeating that the Research Agenda is a work-in-progress. New inputs from the Scientific Advisory Board, the larger research community as well as ACC patients and their supporters will serve to improve it over time. Additional projects will certainly be considered and funded. ACCRF welcomes any and all suggestions that will help speed a cure for ACC.