



## **ACCRF ACCOMPLISHMENTS: August 2010 Update**

The pace of research progress in ACC has quickened over the past two years, providing the patient community with justifiable hope for improved outcomes in the coming years. Here we review some of the most significant advances as well as key goals for the remainder of this year and beyond.

### **Recent Accomplishments:**

- **Clinical Trial** - ACCRF's phosphoproteomics and xenograft screening projects formed the basis for fruitful discussions with a major pharmaceutical company on designing a clinical trial. We anticipate the opening of the clinical trial by the end of 2010, to be funded by the pharmaceutical company. This will represent the first-ever ACC trial with a clear scientific rationale supported by preclinical screening data.
- **Translocation Discovery** - ACCRF-funded investigator Dr. Göran Stenman published his findings that a recurrent translocation of chromosomes 6 and 9 is a hallmark of ACC. ACCRF convened a Scientific Advisory Board meeting with key investigators, including Dr. Stenman, to discuss the repercussions for ACCRF's Research Agenda. Soon thereafter, the Board approved multiple new studies of the MYB-NFIB gene fusion.
- **Sanger Sequencing Project** - ACCRF contracted with the Wellcome Trust Sanger Institute to carry out an ACC pilot sequencing study that is listed in the preeminent public database of cancer mutations. Follow-on exome and paired end sequencing projects are nearly complete and will make ACC one of the first tumor types with comprehensive genomic characterizations available globally. The project holds the promise of identifying multiple and/or low-frequency "hits" necessary for ACC tumorigenesis, providing high-quality leads on therapeutic targets.
- **NIDCR Relations** - ACCRF's collaboration with the National Institute for Dental and Craniofacial Research (NIDCR) led to that institute's support and expansion of ACCRF's biobanking, xenograft development and genomics projects. More than \$12 million in NIDCR funds has been allocated to the Salivary Gland Tumor Biorepository, the Salivary Gland Tumor Xenograft Bank and the Rare Disease Clinical Research Network. These investments will expand the pool of ACC researchers by making available specimens, mouse models, genomic data and funding to new investigators.
- **Cell Line Misidentification** - ACCRF initiated the discussions that led to the publication by Dr. Osamu Tetsu of an article on the misidentification of purported ACC cell lines. False conclusions about ACC will no longer be generated by these invalid models.
- **Genomic Studies** - ACCRF-funded investigators published articles on comparative genomic hybridization, methylation, mitochondrial mutations and the prevalence of c-kit mutations in ACC. These papers clarified some of the genomic drivers of ACC and demonstrate the high quality of ACCRF-supported research.
- **Phosphoproteomics** - ACCRF initiated the collaboration between the University of Virginia (UVA) and Cell Signaling Technology to generate phosphoproteomic profiles of ACC and identify druggable targets.



- **Bioinformatics** - ACCRF funded UVA to create a web portal of genomic, proteomic and drug screening data on ACC xenografts. Along with the Sanger sequencing projects, the UVA web portal will make available rich and robust ACC data sets for analysis by all interested investigators globally.
- **Xenograft Screening** - ACCRF contracted with South Texas Accelerated Research Therapeutics (START) for the 3<sup>rd</sup>, 4<sup>th</sup> and 5<sup>th</sup> baseline drug screening studies of its xenograft models. Approved and novel agents were evaluated for toxicity and efficacy in vivo, some of which showed significant promise and will be included in future clinical trials.

**Goals for 2010 and Beyond:**

PROJECT CATEGORY	PROJECT	2013 GOAL	2010 GOAL	CURRENT ESTIMATE
<b>Specimens &amp; Models</b>	Biobanking	500 frozen specimens	300	250
	Xenograft Development	20 established models	8	6
	Cell Line Development	20 validated models	2	0
<b>Basic Research</b>	Sequencing: Mutations	Whole genome across 50 specimens	All Exons x 25 samples	400 genes x 25 samples
	Sequencing: Rearrangements	10 fusion-negative samples	5 fusion-negative samples	0
	Fusion Gene Studies	Determine the fusion gene variants and their prevalence; establish transgenic mouse models		
	SNP 6.0 Arrays	50 tumors	25 tumors	0
	Phosphoproteomics	30 tumors & 4 normals	30 tumors & 4 normals	9 tumors & 4 normals
	Bioinformatics	Public dissemination and integration of all databases generated by ACC studies		
<b>Translational Research</b>	High-Throughput Screening	20 cell lines x 300,000 compounds	0	0
	Xenograft Drug Screening	616 protocols	250	170
	Clinical Trials Opened	6	1	0
	Therapies Approved Based on ACCRF-Supported Research	2	0	0
<b>Management Projects</b>	Website Update	Add sections on clinical trials and for researchers in 2010		
	Fundraising Goal	Revenues of \$1.275 million in 2010		