ACCRF Overview

Nicole (Nikki) Spardy Burr, PhD, Scientific Program Officer
The Roots of ACCRF

ACCRF was founded by Marnie and Jeff Kaufman. Marnie was diagnosed with ACC at 38 years old when she had four boys under the age of 10.

ACCRF is a public charity established in December 2005 in Needham, Massachusetts, USA
ACCRF Overview

**MISSION**
Accelerate the development of better treatments and a cure for ACC patients

**GOAL**
Develop a pipeline of clinical trials based on the best available science

**STRATEGY**
Create a community of researchers following a coordinated plan that is driven by supportive and supported patients
ACCRF Research Agenda

**ACC Patient Community**
- Donation of Specimens & Records
- Funding
- Input on Key Challenges & Unmet Needs
- Clinical Trial Enrollment

**ACC Research Community**
- Building Blocks of Research
  - What can researchers work with to find answers?
  - Biorepository & Registry
  - Cell Lines
  - Mouse Models
- Mechanisms of Action
  - What biological processes make ACC possible?
  - Genomics
  - Pathway Identification
  - Target Validation
- Translational Research
  - What will hit the Achilles’ heels of ACC?
  - Functional Studies
  - Drug Discovery
  - Preclinical Screening
- Clinical Research
  - What will work in actual patients?
  - Approved Drugs
  - Novel Drugs
  - Radiation/Radiology

**Better Therapies and Outcomes for Patients**
ACCRF Research Network

Academic Institutions
- MD Anderson
- University of Virginia
- Sahlgrenska Academy (Sweden)
- Massachusetts General Hospital
- Sanger Institute (UK)
- University of Alabama
- Johns Hopkins
- Dana-Farber Cancer Institute
- University of Michigan
- University of New Mexico
- University of Oklahoma
- Yale University
- Memorial Sloan-Kettering
- University of Munster (Germany)
- University of Miami

ACCRF
- Specimens & Models
- Genomics & Proteomics
- Drug Discovery
- Clinical Trials

Government
- National Institute of Dental and Craniofacial Research (NIDCR)
- National Cancer Institute (NCI)

Private Industry
- South Texas Accelerated Research Therapeutics (START)
- Bethyl Labs
- Cell Signaling Technology
- Novartis
- Pfizer
- Eli Lilly
- Merck
- Bristol-Myers Squibb
- Abbott Labs
- Bayer
- Astra Zeneca
- Glaxo Smith Kline
- Oncomed
- Cyclacel
<table>
<thead>
<tr>
<th></th>
<th>2005</th>
<th>2018</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Biobanking</strong></td>
<td>Limited</td>
<td>Repositories with hundreds of frozen tumor specimens</td>
</tr>
<tr>
<td><strong>Cell Lines</strong></td>
<td>Multiple invalid models</td>
<td>Misidentifications discovered; valid models in development</td>
</tr>
<tr>
<td><strong>Animal Models</strong></td>
<td>None</td>
<td>20+ mouse xenografts developed; first transgenic models</td>
</tr>
<tr>
<td><strong>Genomics</strong></td>
<td>Sporadic reports of translocations</td>
<td>• Discovery of recurrent t(6;9) and MYB-NFIB fusion gene</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Identification of additional molecular targets with potential</td>
</tr>
<tr>
<td></td>
<td></td>
<td>therapies: NOTCH, FGFR, IGF-1R, HDAC</td>
</tr>
<tr>
<td><strong>Preclinical Drug</strong></td>
<td>None in valid models</td>
<td>• Open xenograft platform for academia and industry</td>
</tr>
<tr>
<td><strong>Screens</strong></td>
<td></td>
<td>• Strong relationships with biopharmaceutical companies</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• 100 anti-cancer compounds screened in xenografts</td>
</tr>
<tr>
<td><strong>Mobilizing Patients</strong></td>
<td>Limited</td>
<td>Tissue donations, clinical trial accrual and $15 million in donations</td>
</tr>
<tr>
<td><strong>NIH Commitments</strong></td>
<td>Negligible</td>
<td>Over $25MM for salivary gland tumor research (NIDCR)</td>
</tr>
<tr>
<td><strong>Clinical Trials</strong></td>
<td>Few, small &amp; haphazard</td>
<td>Multiple science-driven trials with improved designs, enrollment,</td>
</tr>
<tr>
<td></td>
<td></td>
<td>data quality and patient outcomes</td>
</tr>
</tbody>
</table>
How we think ACC works

Grade 1
No solid component

Grade 2
<30% solid

Grade 3
>30% solid

**MYB/MYBL1**
fusion or overexpression
(90-95% of cases)

Secondary alterations in other genes
*(NOTCH1, FGFR, IGF, PI3K and chromatin modifiers)*
drive disease progression

**Therapies:**
Research grants focused on finding **MYB/L1 inhibitors**

**NOTCH inhibitors** show early signal in NOTCH-mutant ACCs
Clinical trials are investigating other targeted and immune therapies in ACC
ACCRF Funds in Action

ACCRF grants to the University of Virginia…

• Jump-started mouse model development

• Blossomed into genomic studies and preclinical drug screening, and

• Led directly to the first science-driven clinical trials of targeted drugs in ACC patients

Dr. Christopher Moskaluk
University of Virginia

Dr. Patrick Dillon
University of Virginia
ACCRF Funds in Action

ACCRF grants to MD Anderson…

- Jump-started tumor banking that eventually gained NIH funding
- Blossomed into the identification of drug targets in aggressive cases of ACC, and
- Is leading to the development of clinical trials for ACC patients with NOTCH-altered tumors

Dr. Adel El-Naggar
MD Anderson

Dr. Renata Ferrarotto
MD Anderson
ACCRF Funds in Action

ACCRF grants to Dana-Farber Cancer Institute…

- Jump-started immunologic profiling of ACC tumors
- Blossomed into the identification of PD-1 and PD-L2 markers expressed in ACC, and
- Is leading to clinical trials for ACC patients with PD-1 inhibitors in combination with radiation, chemotherapy and targeted drugs.

Dr. Glenn Dranoff
DFCI, Novartis

Dr. Jon Schoenfeld
DFCI

Dr. Nicole Chau
DFCI
ACC Targeting Approaches

- Multikinase (FGFR, VEGFR) inhibitors
- NOTCH inhibitors
- Immune checkpoint inhibitor combinations with radiation, chemo
- MYB inhibitors and DNA vaccine
- MDM2 inhibitors
- HDAC inhibitor combinations
- PSMA radiopharmaceuticals
- …and more in the pipeline…
Keep yourself updated…

- Sign up to receive ACCRF research updates via email…

- Check the “Clinical trial- current studies” section on our website!
Summary

• ACCRF has jump-started the field of ACC research through:
  – World-class Scientific Advisory Board driving a directed agenda
  – Creation of biobanks, preclinical models and research network
  – Target discovery and validation leading to clinical trials

• ACCRF is prioritizing therapy discovery and innovative clinical trials, with several promising concepts in development

• We ask for your support to achieve our goal of having the first FDA-approved therapy for ACC by 2020
Thanks to ACC Research Heroes!

Adel El-Naggar
Chris Moskaluk
Göran Stenman
Andy Futreal
Michael Wick
David Sidransky
Lillian Siu
Bruce Chabner
Robert Haddad
Ned Sharpless
Gigi Lozano
Irwin & Joan Jacobs

ACCelerate the CURE