Adenoid Cystic Carcinoma Research Foundation
20 Years of Groundbreaking Research

ACCRF Criteria for Grant Proposals Involving I*n Vitro* ACC Models

Developing reliable *in vitro* ACC models has been challenging. ACC cells grown in traditional 2D culture systems often lose high expression of the MYB oncoprotein, which results from recurrent MYB gene fusions and is a defining feature of ACC. Additional details on these technical limitations are available on our website.

Internal work, along with studies from academic collaborators, suggests that 3D culture systems may better preserve MYB expression and maintain both myoepithelial and epithelial cell populations found in ACC tumors with cribriform or tubular histology. However, these models are often short-lived, with cells capable of only a limited number of passages.

Given these limitations, ACCRF requires that the following criteria be addressed in the preliminary data for any project involving *in vitro* ACC cell models:

- **Molecular fidelity**: Evidence that the model retains key molecular features of the original tumor, including:
  - MYB protein expression (e.g., MYB IHC or Western blot)
  - Activating *NOTCH1* gene alteration and/or pathway activation (e.g., NICD1 IHC)
  - Presence of both p63-positive and p63-negative cell populations, where applicable (p63 is a marker of myoepithelial cells and a preliminary indicator of ACC molecular subtype - see reference)
- **Growth characteristics:** Data showing cell growth kinetics and stability across a reasonable number of passages.
- **Feasibility of genetic manipulation (if applicable):** For proposals involving genomic engineering, evidence that the cells can be successfully modified (e.g., via lentiviral transduction or other gene delivery methods)

While these requirements are rigorous, generating this data upfront allows ACCRF to prioritize projects with the highest likelihood of technical success and meaningful impact both for both the foundation and the academic investigator.