



## **Adenoid Cystic Carcinoma Cell Lines: Research Update (March 2009)**

### Summary

- The scientific literature contains several cell lines that are purported to be derived from human adenoid cystic carcinoma (ACC) tumors. These include ACC2, ACCM (metastatic clone of ACC2), ACC3, SACC-83, SACC-LM (metastatic clone of SACC-83), ACCS, ACCNS and CAC2, among others.
- Through STR genotyping and other methods, ACCRF-affiliated researchers have discovered recently that many of these cell lines are not valid ACC models. Prospective research into ACC should not be conducted on these cell lines. And past conclusions about ACC that were generated from these cell lines ought to be viewed with skepticism and reconfirmed.
- ACCRF-affiliated researchers are actively developing new ACC cell lines that will be validated and distributed to interested researchers. Contact [jeffreykaufman@accrf.org](mailto:jeffreykaufman@accrf.org) for more information.

### Background

Cell lines are living cells that can grow outside the body in tissue culture given the appropriate nutrients and conditions. Scientists grow cancer cell lines from human tumors in order to conduct experiments into the biological events and mechanisms involved in the initiation and progression of cancer. In addition, cancer cell lines may be used to screen large libraries of drugs to find those that are most effective in killing or stopping the growth of tumor cells.

The first cancer cell line was developed in 1952 from the ovarian cancer of a Baltimore patient named Henrietta Lacks (nicknamed “HeLa” cells). Since then, hundreds of cancer cell lines have been created from human tumors, with approximately 1,000 cell lines on deposit at the American Type Culture Collection (ATCC), a resource repository for scientists. However, it is estimated that up to a third of all cell lines in common use are misidentified due to cross-contamination of cell lines ([Nature, 2009](#)).

Historically, the problem of misidentified cell lines has not been widely known. Researchers published articles in scholarly journals with the best of intentions, often spending years studying cell lines that they believed to represent a valid model of a particular cancer. More recently, the extent of the problem has become more apparent and the research tools to avert the problem have become available ([Nardone, 2006](#)).



Short tandem repeat (STR) analysis is used in forensics as “genetic fingerprinting” to determine if two sets of DNA are identical; researchers may search public databases of STR profiles to ensure that their cell line matches the cell line they intend to study. Such analyses have become inexpensive and provide an opportunity for researchers to effectively eliminate misidentified cell lines and the false conclusions generated from them. Two public databases of STR profiles are available through the [ATCC](#) and the [Japanese Cell Repository Bank](#). Comparable tests include isoenzyme analysis, human lymphocyte antigen (HLA) typing and SNP microarrays.

### Recent Findings on ACC Cell Lines

Following discussions with affiliated researchers who had raised concerns about the authenticity of several ACC cell lines, ACCRF arranged a conference call in October 2008 to discuss this issue. Twenty researchers participated. Various speakers reviewed the conclusions of their STR analyses of ACC cell lines and came to similar conclusions: most, if not all, of the existing “ACC” cell lines were not valid ACC models, but were either i) HeLa cells, ii) derived from mice or iii) identical to other cancer cell lines.

All of the cell lines discussed were created in China or Japan. U.S.-based researchers have not been successful in generating new cell lines, so they had to rely on models provided from overseas colleagues. Interestingly, different batches of cell lines that were received in the U.S. from different overseas labs showed similar STR profiles, indicating that the issue was not related to contamination in the receiving labs, but in the providing labs.

A correction already has been submitted for a recent article on three cell lines formerly considered to be ACC (Choi et al., Clin Cancer Res 14 (16) 5081-5089). The key findings are included below.

The research reported was conducted on three cell lines that the authors believed to be adenoid cystic salivary carcinoma cell lines. Because of reports of cell line contamination after publication, they have since genotyped the three cell lines used in the article -- ACC-2, ACC-3, and ACC-M -- by short tandem repeat (STR) analysis, and this analysis revealed that all three lines had identical genotypes. On comparison to the genotypes of the ATCC cancer cell line collection, they found that their genotype was identical to that of HeLa cells.

Another ACCRF-affiliated researcher has submitted for publication an article on a wider array of cell lines misidentified as ACC. ACCRF will provide further details as they become available. In the meantime, researchers should avoid the use of the previously-mentioned cell lines for ACC-specific projects.



### ACCRF Implications

ACCRF has initiated and funded research projects that used the invalid cell lines. However, such projects represented a relatively small portion of ACCRF's research portfolio. The vast majority of funds and efforts have been spent on primary tumor specimens, not cell lines.

Prospectively, it will be crucial for researchers to have access to validated ACC cell lines. High-throughput screens on ACC cell lines will help identify genetic targets and test the efficacy of drugs. And as genetic targets are identified in ACC, scientists will need to perform functional studies on cell lines to understand the mechanisms of action.

Fortunately, ACCRF has several investigators working to create new ACC cell lines with some promising results. Affiliated researchers are sharing the most promising protocols and a standardized set of validation criteria is being developed to ensure that researchers may be certain their studies are conducted on valid ACC models.