



# Cell Line Contamination and the Managing Editor

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Contaminated cell lines have been making the news in recent years and are blamed for millions of dollars' worth of wasted research dollars.<sup>1</sup> Retraction Watch has warned that one in six researchers are using the wrong cell lines,<sup>2</sup> which could call their findings into question. Although issues with cell lines were first uncovered in the 1960s, these have not been fully resolved and continue to cause serious problems with the reliability and reproducibility of studies.<sup>3</sup> What can a Managing Editor do to make sure his/her journal is on the right track?

To help answer this question, I interviewed Amanda Capes-Davis, chair of the International Cell Line Authentication Committee (ICLAC).

*Q: What is cross-contamination and why is it important?*

A: Cross-contamination happens when one cell culture is accidentally contaminated by cells from another culture. This can happen if two cultures are being handled at the same time, or reagents are shared (*e.g.*, if the same bottle of liquid medium is used to feed two different cell cultures). If you have two different populations of cells in the same space, one will

usually grow faster than the other—it's like your garden, the weeds grow faster than the plants you want! The end result is that, like weeds, the faster growing cells will overgrow and replace the other cells. Scientists who work with a cell culture may think it consists of "human cells" or "breast cancer cells." Instead, the cell culture may be completely different to what they expect—mouse instead of human, or brain instead of breast.

*Q: If the problems were first identified in the 1960s and 1970s, why have they persisted?*

A: It seems incredible that problematic cell lines are still used more than 50 years after the problem was first discovered. Often this is due to lack of awareness. Cell culture is a practical skill that needs to be taught. Young scientists need to learn how to handle cells using what we call "aseptic technique." They also need to learn about the common problems that affect cell culture, including the risk that one cell line can be cross-contaminated by another. Young scientists rely on the laboratories where they do their cell culture to teach them what they need to know. Some laboratories do this very well, but others do not—labs are either not aware of common cell culture problems or believe that their own research is not affected by them. We need training programs that are easily accessible to young scientists and teach them how to do good cell culture from the beginning of their careers.

*Q: What should a journal ask their authors to do to make sure that they are not submitting research based on corrupted cell lines? For example, should the journal ask authors to share information about cell lines in the Materials and Methods section of articles?*

A: The National Institutes of Health (NIH) recently issued "[Principles and Guidelines for Reporting Preclinical Research](#)." Based on the NIH's guidelines, authors need to report in their Materials and Methods section on the source

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- 1 Fung B. 'Oops, Wrong Cancer': How Contaminated Cell Lines Produce Bad Research. *The Atlantic*. Published April 23, 2012. <http://www.theatlantic.com/health/archive/2012/04/oops-wrong-cancer-how-contaminated-cell-lines-produce-bad-research/256246>. Accessed September 30, 2016.
- 2 Cape-Davis A. Hundreds of researchers are using the wrong cells. That's a major problem. Retraction Watch. Published December 8, 2015. <http://retractionwatch.com/2015/12/08/hela-is-the-tip-of-the-contamination-iceberg-guest-post-from-cell-culture-scientist>. Accessed September 30, 2016.
- 3 International Cell Line Authentication Committee. <http://iclac.org>. Accessed September 30, 2016.

of all cell lines and their authentication and mycoplasma testing status.

“Source” refers to the cell bank or colleague who supplied the cell line to the authors. If obtained from a cell bank, authors should list the catalogue number, which makes it easier for the reader to obtain the same material for their own work. “Authentication” is testing done to work out whether a cell line corresponds to the original donor of that material or is cross-contaminated by another culture. Mycoplasma is a bacterial contaminant that is difficult to see through the microscope. Mycoplasma contamination, and cross-contamination of one cell line by another, are common problems but they require specific testing to be detected.

An increasing number of journals are adding cell line requirements to their author guidelines and I urge all life science journals to consider this as best practice. For examples, editors can look up the requirements set out by the [Nature journals](#) and the [American Association for Cancer Research journals](#).

*Q: If I were the Managing Editor of a journal publishing research that uses cell cultures, what else could I do to help address this problem?*

A: Your first step is awareness—knowing that if your authors use cell cultures, this is a problem that may affect your publications. There are some freely available resources that every Managing Editor should know about. I particularly recommend the following:

1. The list of known misidentified cell lines from the [ICLAC](#). Journals can use the ICLAC list to see which cell lines are known to be inappropriate research models.
2. [Cellosaurus](#) is an online knowledge resource that editors and authors can use to look up cell line information. I use Cellosaurus myself a great deal and think it is a fantastic way to look up the essential information that is available about a cell line.

Your second step is to work with the Editorial Board on how to address the problem in a way that works for your journal. Adding authentication testing as a requirement can be difficult for an Editorial Board if they do not have much cell culture expertise to draw from. Addressing the problem is a step-by-step process and there is

always something that can be done to improve reporting.

*Q: Similarly, what should my Editorial Board do to be on the lookout for any issues?*

A: The Editorial Board needs to consider what impact this problem has on the journal’s publications. For example, the journal *Molecular Vision* found that one particular problematic cell line, RGC-5, was used in many papers. Their author guidelines now state that any papers using RGC-5 will be rejected without review. There are too many problematic cell lines to be aware of each one, but a few are extensively used and easy to spot in publications. These include KB, HEP-2, and INT-407. These cell lines are used as models for oral cancer, laryngeal cancer, and normal intestine; however, all three are actually HeLa, which comes from cervical cancer.

If the Editorial Board can ask authors to report on the source, authentication, and mycoplasma testing for all cell lines used (as per the NIH guidelines mentioned earlier) that would be a great help. Including cell line requirements in a journal’s author guidelines is best practice and really does help to address the problem.

*Q: How are cell lines authenticated?*

A: The scientist working with a cell line needs to prepare a DNA sample for testing. A genetic test is used to analyse that sample and compare it to results from other cell lines. There are online databases that scientists can use for comparison.

For human cell lines, the field of authentication testing worked together several years ago to develop a standard with a consensus test method for comparison. We decided on “short tandem repeat profiling” (STR profiling for short), which is a test method often used to identify crime scene samples in forensics labs. STR profiling works really well for human cell lines, and is usually done by core facilities or testing labs.

Non-human cell lines need a different approach, since there are many species used in cell culture and these species can be quite inbred. We recommend that scientists should, at minimum, check the species of the cell line—for example, to make sure that a “rat” cell line is not actually human or mouse. There is a very easy genetic test to work out species (DNA barcoding) that labs can do in-house or send out for testing.

## Discussion Forum Highlights

The [ISMTE Discussion Forum](#) is available to all registered ISMTE members and is a great resource to get and stay connected to a network of peers, publishers, vendors, and potential clients and employers. Here we highlight a question about authorship followed by further discussion.

1/5/2016 at 9:43:16 PM GMT



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**Submitting authors**

Hello, do any of you have any experience on a submitting author who is not included in the author list?

I have a single case where a person would like to submit on behalf of an author group, but I have no experience on this and usually we would refuse this possibility.

Thank you in advance for any suggestions you can share.

**Lucia Steele**

Posts: 0

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1/6/2016 at 2:21:19 AM GMT



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In my experience this is actually not that uncommon. Using someone who is not an author as a type of "submitting agent" should be OK (I would think) as long as you can verify that the corresponding author and co-authors are verified as being legit.

**A. Etkin**

Posts: 16

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1/6/2016 at 9:23:07 AM GMT



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It usually occurs when an author asks a secretary or departmental administrator to submit the paper on his/her behalf, and as Adam says it's quite legitimate. ScholarOne Manuscripts has the facility for a 'submitting agent', as distinct from an author, although I don't think a similar facility exists on Editorial Manager and don't know about other systems.

**M. Willis**

Posts: 23

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1/6/2016 at 11:51:28 AM GMT



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In terms of EM mechanics, what we do is create a temporary account with the true corresponding author's name but the emails of the submitting person and the corresponding author. That way the corresponding author is aware of what's going on but can leave the EM work to his/her designee. At final disposition we merge the temporary account into the real account so the manuscript is part of the corresponding author's history.

-Nijsje Doman  
Managing Editor, AJKD

**N. Doman**

Posts: 3

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1/6/2016 at 1:53:10 PM GMT



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Hi Lucia,

Do you know yet if the person who is submitting also wants to serve as the corresponding author? If the submitting agent will only submit and your system allows someone else to be the corresponding author, I don't think you will have any trouble. I agree with Michael, Adam, and Nijsje that it's ethical to have a submitting agent who is not an author, but I think Nijsje's workflow of ensuring at least one of the authors is notified of both the submission and the list of authors as input during the submission process is important.

**K. Overstreet**

Posts: 21

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1/6/2016 at 6:12:49 PM GMT



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Dear all,

thank you for your valuable opinions: they all make perfect sense and hit the ethics point too.

Lovely to count on you all!

**L. Steele**