

The International Journal of Cancer enforces strict quality control of the cell lines used in biomedical research

Nicole Yvonne Souren¹, Konstantina Falida², Stefanie Heck², Franca Bianchini²

¹Department of Clinical Genetics, Maastricht Universitair Medisch Centrum, 6229, HX Maastricht, Netherlands

²International Journal of Cancer, 69120, Heidelberg, Germany

Correspondence: k.falida@dkfz.de

SLIDE 1

The slide contains the following information:

- Impact of misidentified cell lines:**
 - Misidentified:** cell line that no longer corresponds to original donor and may come from an entirely different species, tissue or disease
 - HEP-2:** 1955: believed to originate from a laryngeal carcinoma
 - INT 407 (Intestine 407):** 1957: believed to originate from embryonic intestinal cells
 - 1967:** geneticist Stanley Gartler unmasked both cell lines as HeLa
 - 2021:** Christopher Korch and Amanda Capes-Davis estimated:
 - 8497 articles** may have used HEP-2 inappropriately, producing an estimated **277,000 citations**
 - 1397 articles** may have used INT 407 inappropriately, producing an estimated **45,000 citations**
 - \$990 MILLION** estimated amount spent on articles published on HEP-2 and INT 407
- Cell line authentication at IJC: requirements from authors:**
 - Cell line authentication results of all human cell lines used in the manuscript must be provided
 - DNA profiles (i.e. short tandem repeat (STR) profiles) must be provided for each cell line
 - Purchase orders or invoices from a certified cell bank is necessary
 - All cell lines used in the study must be certified with the Research Resource Identifier (RRID)
 - A reference certificate of origin and flow cytometry analysis (FCM) must be provided
- Cell line-related problems at IJC:**
 - July 2016 - June 2021:**
 - 187 misidentified cell lines
 - 214 (25%) misidentified cell lines were identified
 - The cell lines were categorized into 16 cell lines
 - The highest percentage of misidentified cell lines were: HEP-2 (30%), INT 407 (15%), and HeLa (10%)
- Follow-up study:**
 - July 2018 - March 2023:**
 - 100% of 100 misidentified cell lines were identified
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- Recommendations:**
 - Cell line authentication should be mandatory for all human cell lines used in biomedical research
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My name is Konstantina Falida and I am working at the Editorial Office of the IJC. It's the first time I am attending an EASE conference and I am very excited to share our study on the importance of cell line authentication in biomedical research with you.

SLIDE 2

The slide contains the following information:

- Impact of misidentified cell lines**
- Misidentified:** cell line that no longer corresponds to original donor and may come from an entirely different species, tissue or disease
- HEP-2**
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A misidentified cell line occurs through cross-contamination, mislabeling, or other laboratory errors, meaning that it no longer corresponds to the original donor and may in fact come from an entirely different species, tissue or disease. The tremendous damage of the use of misidentified cell lines in biomedical research has been shown exemplarily by a study from Korch & Capes-Davis. It was estimated that almost billions of research dollars have been spent on studies using two commonly misidentified

cell lines, while at the same time data based on misidentified cell lines could misguide and delay therapy development, resulting in missed opportunities to improve human health.

SLIDE 3

**Cell line authentication at IJC:
requirements from authors**

- **Cell line authentication reports** of all human cell lines used in the manuscript (not older than 3 years)
 - **DNA profiles:** i.e. **short tandem repeat (STR) profiles** with high quality electropherograms
 - **Purchase orders or invoices** from a certified cell bank or commercial provider
- All cell lines must be listed using the **official cell line name and its Research Resource Identifier (RRID)**
- A **statement** confirming that all human cell lines have been authenticated using STR within the last 3 years

Soren et al. | The Cancer Journal 2022

To avoid publishing studies that are based on misidentified cell lines, the IJC has introduced a stringent cell line policy already since 2010. In the Editorial office, it's my responsibility to check all cell line-related issues of manuscripts submitted to our journal before the peer review process starts. We request:

- cell line authentication reports of all human cell lines used in a study
- listing of the official cell line name and its Research Resource Identifier and
- a statement confirming the authentication in the M&M section

SLIDE 4

Cell line-related problems at IJC

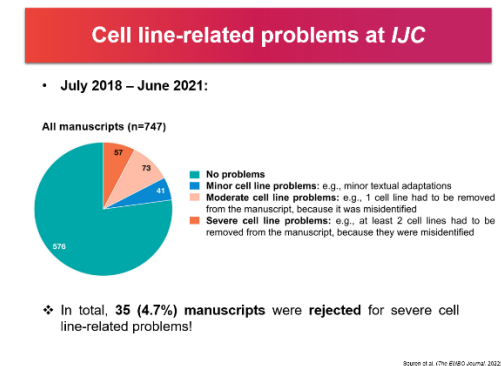
- **July 2018 – June 2021:**
 - **747** manuscripts containing **4,138** human cell lines were selected for peer review
 - **216 (5.2%)** misidentified cell lines were identified
 - The most frequent contaminant was **HeLa (44.4%)**
 - The highest percentage of misidentified cell lines was observed among **gastric cancer (25.4%)**, followed by **liver cancer (16%)** cell lines

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Last year we published a study providing an overview of issues pertinent to misidentified cell lines and discussing available solutions. More than 5% of the cell lines used in manuscripts submitted to our

journal were misidentified and the most frequent contaminant was the HeLa cell line. We also found that most of the misidentified cell lines were used in studies for gastric and liver cancer. These findings indicate that the literature on these cancer types probably suffers a lot from misidentified cell lines.

SLIDE 5

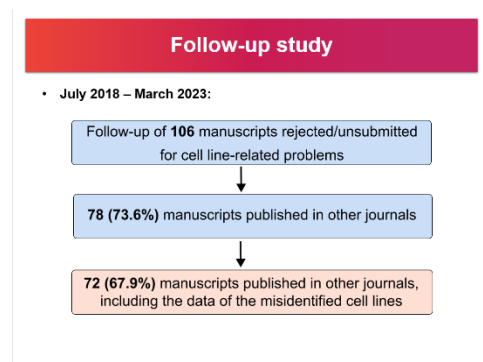


When we look at the manuscript level, then we see that based on the available information the majority of the selected manuscripts have no cell line-related problems.

However, in more than 100 manuscripts moderate or severe cell line-related problems were observed.

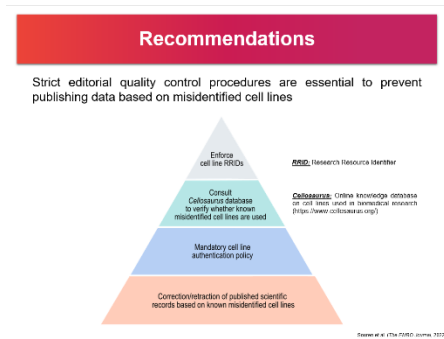
Finally, 35 manuscripts (almost 5%) were rejected for severe cell line-related problems.

SLIDE 6



In order to explore whether manuscripts rejected at the *IJC* with severe cell line-related problems are subsequently published elsewhere, we followed up 106 manuscripts that contained a large amount of data based on misidentified cell lines. In March 2023, 78 of these manuscripts were published in other journals, of which 72 manuscripts still included the data of the misidentified cell lines!

SLIDE 7



Based on our experiences, we have several recommendations for journals and publishers to avoid the publication of studies including misidentified cell line data:

- Journals should consider to enforce the use of cell line research resource identifiers (RRIDs); these can be obtained at the RRID portal or Cellosaurus database, where a warning is displayed when a cell line is problematic.
- Journals should verify all cell lines used in a manuscript in the Cellosaurus database, where many cell lines are recorded.
- In addition, journals should implement mandatory cell line authentication and occasionally check the documents, so that regular authentication of cell lines will become common practice.
- Last but not least, action should be taken to correct already published manuscripts that contain data on misidentified cell lines.

SLIDE 8

Before closing, I would like to mention that this study was performed by Nicole Souren and was supported by other members of our Journal as well as some external ones. For further information, you can check our paper by scanning the QR-Code at the right bottom of the poster or you could contact our Editorial Office or me personally.