Guidelines for Screening Biological Materials and Cell Lines Prior to Administration to Rodents

BACKGROUND

Administration of biological materials to rodents carries risks with respect to research reproducibility and to animal health. Specifically, biological materials may be contaminated by adventitious and zoonotic pathogens (1, 2), and cell lines may be misidentified or cross-contaminated with other cell lines (3). Biological materials include cell lines, tissue harvested from other animals or humans, hybridomas, blood products and serum (including polyclonal antibodies).

Pathogens have the potential not only to infect an individual animal that has been administered the biological material, but may also spread throughout rodent colonies, even entire facilities. Rodents are susceptible to a large variety of viral and bacterial agents. Commonly encountered pathogens include parvoviruses and corona viruses, such as mouse hepatitis virus. Infectious agents may lead to clinical illness or death of animals, as well as fundamental perturbations in physiologic and immunologic homeostasis or microbiome, thus impacting animal health and representing a variable that may reduce research reproducibility. Further, some agents, such as lymphocytic choriomeningitis virus (LCMV) are zoonotic pathogens and pose risk to exposed personnel.

Importantly, cell lines may become contaminated with not only infectious agents, but also with other cell lines. This may happen as the result of serial passaging of such materials in animals or by inadvertent laboratory error. In either case, such contaminations likely complicate reproducibility over time within and between laboratories.

These guidelines are primarily intended for evaluation of materials that are not obtained from a vendor with stringent quality control procedures.

GUIDELINES

1. All use of biological materials in animals must be first approved by the Institutional Animal Care and Use Committee (IACUC).

2. Screening for rodent infectious pathogens should be performed prior to the initial use in animals at the University of Kentucky. It is advisable that biological materials obtained from other laboratories be screened prior to first use, regardless of previous testing results. PCR-based tests are available for testing of biological samples for mouse and rat pathogen contamination. More information, including sample submission, can be found at:

Charles River: Non-GLP Cell Line & Research Biologics Screening | Charles River (criver.com)

IDEXX BioAnalytics: IMPACT | IDEXX BioAnalytics

3. It is recommended that biological materials obtained directly from humans, such as tissue used for patient derived xenografts, be screened for human infectious pathogens. More information, including sample submission, can be found at:

Charles River: Non-GLP Cell Line & Research Biologics Screening | Charles River (criver.com)

4. To ensure fidelity of cell lines with the presumed identity, it is recommended that cell lines obtained from sources that do not regularly screen cell lines to confirm identity be authenticated appropriately. Typically, this requires genotypic conformity with a known control. More information, including sample submission, can be found at:

IDEXX BioAnalytics: CellCheck™ | Cell Line Authentication | IDEXX BioAnalytics

ATCC Cell Authentication: https://www.atcc.org/services/cell-authentication

5. Consideration should be given to periodic retesting of biological materials to ensure continued purity, and to retesting of cell lines to validate continued freedom from contaminating cells. For example, investigators might routinely retest cell lines after a specified number of passages.

REFERENCES

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2. From bench to cageside: Risk assessment for rodent pathogen contamination of cells and biologics. ILAR J. **49:**310-315, 2008.

3. Horbach SPJM, Halffman W. The ghosts of HeLa: How cell line misidentification contaminates the scientific literature. PLoS ONE **12 (10)**:e0186281, 2017.

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