Animal Program Policy

Title:	**Use of Cell Lines and Other Biological Materials in Mice**
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Biological Materials are defined as any material derived from or passaged through a living system; examples include established and primary cell lines, tumors, antibodies, blood or serum and saliva.

Any of these materials can be contaminated with rodent or human viruses or bacteria, with the potential for infecting laboratory mice or researchers. In the case of mice, some of these agents may not cause overt disease, but can produce physiologic changes that can affect research outcomes. A list of some of the potential hazards includes:

- Any cell line passaged in culture can be contaminated with Mycoplasma species. These species are not typically pathogenic in mice, but still should be avoided. They can also promote malignant transformation in vivo. Mycoplasma can be present in cell lines at low levels, particularly those grown in the presence of antibiotics.
- Tumors or cell lines that have been passaged in mice may have been contaminated with rodent viruses during their time as tumors. Even cells from a commercial repository such as ATCC may not have been properly screened.
- Monoclonal or polyclonal antibodies are derived from mouse or rabbit material, and could be contaminated with murine viruses.
- Any human derived material can be contaminated with human viruses including HIV and hepatitis viruses, and can be a risk to human health.

Therefore, any established or primary cell lines (continuously passaged) **must be tested for a series of mouse pathogens** prior to injection into mice. PCR is the recommended screening method, and Charles River offers screening services. We recommend the Charles River mouse essential panel . Information on this website includes how to submit samples, and how to place the order. For repeated experiments, cell lines should be retested every year, or stocks of frozen cells created at the time of testing should be used.

Studies using any human-derived samples must be either tested for a panel of human pathogens or performed in the BL2 room. This includes mice with humanized immune systems.

For protocol purposes, biological materials, including primary cells generated in-house, are considered non-pharmaceutical grade, unless they are specifically labeled as such. Protocols proposing to inject established cell lines should specify the screening to be carried out.

References:

Norman C. Peterson, From Bench to Cageside: Risk Assessment for Rodent Pathogen Contamination of Cells and Biologics, ILAR Journal, Volume 49, Issue 3, 2008, Pages 310–315, https://doi.org/10.1093/ilar.49.3.310

Zella D, Curreli S, Benedetti F, Krishnan S, Cocchi F, Latinovic OS, Denaro F, Romerio F, Djavani M, Charurat ME, Bryant JL, Tettelin H, Gallo RC. Mycoplasma promotes malignant transformation in vivo, and its DnaK, a bacterial chaperone protein, has broad oncogenic properties. Proc Natl Acad Sci U S A. 2018 Dec 18;115(51):E12005-E12014. doi: 10.1073/pnas.1815660115. Epub 2018 Dec 3. Erratum in: Proc Natl Acad Sci U S A. 2019 Jan 7;: PMID: 30509983; PMCID: PMC6304983.