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Michael Lesar,
Chief, Rulemaking, Directives, and Editing Branch, Office of Administration
Mail Stop T–6D59
U.S. Nuclear Regulatory Commission
Washington, DC 20555–0001

Dear Mr. Lesar:

I would like to express my significant concerns regarding the adverse impact that the proposed NRC regulations on cesium irradiators would have on our research program at the Division of Immunology New England Primate Research Center (NEPRC), Harvard Medical School.

Irradiation of cells plays a critical role in our research. Our work focuses largely on analysis of cellular immune responses in macaques infected with simian immunodeficiency virus (SIV), which is by all accounts the best animal model for the study of AIDS. Our research objectives include attempting to identify immune responses able to protect against AIDS virus infection and identifying novel means of protecting cells against AIDS virus infection. We use irradiated cells as feeder cells to help support the growth of T cell clones or T cell lines. These cell populations are then used to identify specific epitopes recognized by the immune system or to analyze the behavior of cells that have been modified with genes designed to inhibit SIV replication. Over the past 15 years our work using irradiated cells has appeared in over 25 publications, examples of which are listed below.

Prior to the installation of our irradiator at the NEPRC, we explored several alternatives to the use of irradiated cells, including the use of mitomycin-treated cells and irradiation of cells in Boston. None of these attempted alternatives yielded acceptable results.

Based on the National Academy of Sciences report, it appears several alternatives to the current cesium chloride sources are being considered, including: 1. alternative cesium sources or improved shielding; 2. cobalt sources; 3. X-ray sources. Implementation of any of these alternatives will require quite substantial logistic and financial support, as well as the requirement to demonstrate that these alternative means of irradiating cells will perform as well as those currently used in our lab. Cloning of T cells and generation of T cell lines is extremely technically challenging, and a host of minor technical details can result in a failed experiment. Therefore, it will be critical to do head-to-head comparisons of these alternatives to our current cesium irradiator, a process that would likely take several months.

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In closing, I would like to reiterate the fact that the implementation of the proposed irradiator changes could critically impact on our research capabilities, and ultimately on our research funding, which currently exceeds two million dollars per year. My personal view is that these proposed alternatives are likely to have a negligible effect on the safety of our cesium source, and I strongly believe that the best course would be to maintain the current cesium chloride irradiator in conjunction with the significantly improved security measures that have been implemented at Harvard University over the past several years.

Thank you for soliciting input on this critical matter. Please don't hesitate to contact me if I can provide any further information.

Sincerely,

R. Paul Johnson, M.D.

RPJ:cao
cc: J. Griffin, J. Wortham

Publications involving the use of irradiated cells from the Immunology Division, NEPRC:

1. Kaur A, Daniel MD, Hempel D, Lee-Parritz D, Hirsch MS, Johnson RP. Cytotoxic T lymphocyte responses to cytomegalovirus in normal and SIV-infected rhesus macaques. J Virol 1996; 70:7725-7733.

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5. Goodell MA, Rosenzweig M, Kim H, Marks DF, DeMaria M, Paradis G, Grupp SA, Sieff CA, Mulligan RC, Johnson RP. Dye efflux studies suggest the existence of CD34-negative/low hematopoietic stem cells in multiple species. Nat Med 1997; 3:1337-45.

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7. Allen TM, Sidney J, delGuercio M-F, Glickman RL, Lensmeyer GL, Wiebe DA, Pauza CD, Johnson RP, Sette A, Watkins DI. Characterization of the peptide binding motif of a rhesus MHC class I molecule (Mamu-A*01) that binds an immunodominant CTL epitope from SIV. J Immunol 1998; 160:6062-71.

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12. Kaur A, Hale CL, Ramanujan S, Jain RK, Johnson RP. Differential dynamics of CD4+ and CD8+ T lymphocyte proliferation and activation in acute simian immunodeficiency virus infection. J. Virol. 2000; 74:8413-8424.

13. Murphy CG, Lucas WT, Means RE, Czajak S, Hale CL, Lifson JD, Kaur A, Johnson RP, Knipe DM, Desrosiers RC. Vaccine protection against simian immunodeficiency virus by recombinant strains of herpes simplex virus. J. Virol. 2000; 74:7745-7754.

14. Sidney J, Dzuris JL, Newman MJ, Johnson RP, Kaur A, Walker CM, Appella E, Mothe B, Watkins DI, Sette A. Definition of the Manu A*01 peptide binding specificity: Application to the identification of wild-type and optimized ligands from simian immunodeficiency virus regulatory proteins. J Immunol 2000; 165:6387-99.

15. Kaur A, Alexander L, Staprans SI, Denekamp L, Hale CL, McClure HM, Feinberg MB, Desrosiers RC, Johnson RP. Emergence of cytotoxic T lymphocyte escape mutations in nonpathogenic simian immunodeficiency virus infection. Eur. J. Immunol. 2001; 31:3207-3217.

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