

RADIATION EXPOSURE OF MICE:

NOTES ON DOSE, STRAIN AND AGE by Mike McGarry Ph.D.

Hematopoietic cell transplantation has as the intended outcome the functional engraftment of exogenous blood-cell producing stem cells (**HSC** - hematopoietic stem cells) in a suitably prepared host. In mice, as well as other species, several variables need to be optimized to achieve this: a sufficient number of competent HSC in the infusion, a radio-insult of the prospective host sufficient to permit HSC to seed and conditions of husbandry that greatly reduce or eliminate exposure to pathogens.

Husbandry parameters and the differences that sublethal, lethal and supralethal doses of irradiation have on HSC engraftment and % chimerism were discussed in the extensive BMT protocol posted on this website. In this commentary, the effects of radio-insult and host age and strain variability are addressed.

It has long been known that radiation sensitivity is impacted by both age and strain in mice. The comparative parameter most frequently referenced is the **LD50/30**, which is the dose of whole body irradiation that is lethal to 50% of a target population by 30 days after exposure. Much of the seminal work regarding mouse strain and age sensitivity was done more than 50 years ago. A copy of one of the most relevant reports accompanies this commentary (1). The basic findings of their studies are relevant today. Most significantly, they reported substantial differences in the LD50/30 between **BALB/C** and **C57BL/6** strains, the former being more susceptible by > 100 cGy (r). This is particularly significant for those using BALB/C mice and seeking **radiation-induced immune suppression**. At doses of ~400 cGy, it is likely many mice will not survive >30 days. In fact, those that die will have a modal survival of closer to 2 weeks. Of similar significance is their observation that the LD50/30 increases with age. The estimated dose of irradiation leading to 50 % lethality at 30 days in 8 week old BALB/C mice is 50 cGy less than that for 3 month old mice of the same strain. A similar difference is noted for BL/6 mice, though the dose values for the BL/6 mice are greater by about 100 cGy.

Given these findings, it is incumbent on investigators today to assess the impact of recipient age, strain and of irradiation dose for studies. Genetic manipulations and substrain variability of prospective host mice can make this particularly challenging [see reference (2) below for a discussion of substrain variability]. Pilot studies to define optimal parameters for studies requiring irradiation may be necessary and, hopefully, institutional animal care and use committees (IACUC) will be responsive to such requests, given their potential impact on the conservative use of animals in any study.

Cited references:

1. Grahn, D. and K.F. Hamilton. 1956. Genetic variation in the acute lethal response of four inbred mouse strains to whole body x-irradiation. *Radiation Research* 4, 189-198)
2. Simpson, E.M., C.C. Linder, E.E. Sargent, M.T. Davisson, L.E. Mobraaten and J.J. Sharp. 1997. Genetic variation among 129 substrains and its importance for targeted mutagenesis in mice. *Nature Genetics* 16, 19 - 27.