

Effects of circadian rhythm disruption on radiation-induced apoptosis

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Disruption of circadian rhythms may modulate the course of cancer. Epidemiological studies have suggested a link between working at night and increased incidence of breast cancer. One recent study reports that the *mPer2* gene functions in tumor suppression by regulating DNA damage-responsive pathways. In the present study, female Balb/c mice were used to examine the effects of disruption of rhythmicity on gamma radiation-induced apoptosis in the mammary and thymus glands. Ovariectomized mice received subcutaneous implants providing estradiol and progesterone one week prior to radiation. Half the mice experienced an 8 hour advance shift in the light/dark cycle (accomplished by shortening one dark period), and half were control unshifted mice (LD12:12; lights on 0700-1900h). Four animals from each group received 5 Grays (500rads) of radiation supplied by a ¹³⁷Cs irradiator at 1100h and 1900h and sacrificed at 1500h and 2300h, while 2 animals in each group were unirradiated controls. Mammary tissues and thymus glands were removed, formalin-fixed and paraffin-embedded in preparation for TUNEL, using the FragEL DNA Fragmentation kit. Preliminary results indicate that levels of apoptosis in unirradiated controls (~1% of mammary cells TUNEL-positive) were similar to levels described in previous reports. Both control and LD-shifted irradiated groups showed similar incidence of apoptosis (~15% of mammary cells TUNEL-positive). Further analysis of mammary gland results, as well as results from thymus gland will be reported. While our preliminary results suggest that there is little effect of acute light:dark cycle shifts, this does not preclude greater effects from chronic disruption of circadian rhythm entrainment.

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Note that after submission of this abstract, further analysis revealed significant effects of jet lag on mammary gland radiation-induced apoptosis. See Figure below.

