Low-Dose/Dose-Rate Low-LET Radiation Protects Us from Cancer

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Life on earth evolved in a low-level ionizing radiation environment comprised of terrestrial radiation and cosmic rays. Today we all reside in an ionizing radiation environment comprised of both natural background radiation and radiation from human activities (e.g., Chernobyl accident). An evolutionary benefit of the interaction of low-level, low linear-energy-transfer (LET) ionizing radiation with mammalian life forms on earth is adapted protection. Adapted protection involves low-dose/dose-rate, low-LET radiation induced high-fidelity DNA repair in cooperation with normal apoptosis (presumed p53 related), activation of an auxiliary apoptosis mechanism (presumed independent of p53), and induced immunity (Scott 2006a). These induced protective processes constitute a system of protection against genomic-instability-associated diseases including cancer.

Stochastic threshold radiation doses (which differ for each individual) are required for activating the indicated protective system components (Scott 2005a, 2006a; Scott *et al*. 2006). The high fidelity DNA repair when activated prevents the occurrence of cells with persistent genomic instability. However, severely damaged cells may undergo normal apoptosis rather than DNA repair, thereby also preventing the occurrence of genomically unstable cells. Mildly and modestly damaged cells may attempt repair of DNA damage and, depending on the repair fidelity, commit errors (misrepair) leading to genomically unstable cells that could contribute to disease development. A transient, auxiliary, protective-apoptosis-mediated (PAM) process (presumed p53 independent) when activated by an above-threshold, low-LET radiation dose can remove genomically unstable cells whether they arise spontaneously or as a result of environmental and other insults. High fidelity DNA repair also appears to require a stochastic threshold radiation dose. Fortunately, such thresholds can be exceeded by natural background radiation exposure over a relatively short time (Scott 2006b).

Our research has focused on quantitatively characterizing (i.e., modeling) the suppression of deleterious stochastic effects (mutations, neoplastic transformations, and cancer) via low-dose, ionizing-radiation-induced adapted protection. Our dose-response characterizations are based either directly or indirectly on our biological-based NEOTRANS$_3$ model (Scott 2004, 2005a,b, 2006a,b,c; Scott *et al*., 2006). The model accounts for two components of adapted protection [DNA repair/apoptosis (normal) and the PAM process]. For cancer induction by low-LET radiation, the relative risk (*RR*) at low doses has a hormetic character in that *RR* decreases as the dose increases above the background "*b*" radiation dose (Figure 1) up to a dose *D** (maximum threshold for activating protective processes) that is dose-rate dependent. Above *D**, *RR* remains suppressed below the spontaneous level at $RR = 1\text{-}PROFAC$ for a range of doses that also depend on dose rate. The *PROFAC* gives the expected proportion (0 to 1) of cancer cases that are avoided due to radiation induced adapted protection (also called hormesis) and accounts for protection associated with both the PAM process and induced immunity. Decreasing dose rate extends the dose range of suppression of *RR* (Redpath 2006). With further increase in dose, some of the protection is lost (PAM process is inhibited and immunity is not induced) due to exceeding stochastic thresholds for inhibition of these protective processes. At doses above where the inhibitory thresholds occur, *RR* is expected to be linear for a range of doses. This dose zone of linearity is where most of the epidemiological studies supposedly confirming the linear no-threshold (LNT) hypothesis have been conducted. The indicated LNT portion of the dose-response curve extrapolates to $RR = 1$ at the background radiation dose *b*. The dashed line in Figure 1 which connects the LNT branch shows the conventional low-dose extrapolation (based on the LNT hypothesis). We have published our view about the fallacy of this extrapolation (Scott 2005b) and point out in the indicated publication that *RR* is orders of magnitude more likely to decrease at low doses of low-LET radiation rather than to increase by a small amount as would be expected based on the LNT hypothesis when dose is increased above the background radiation dose *b*.

Our approach to risk modeling also allows evaluation of the impact of reducing background radiation doses to near absolute zero radiation. This is illustrated in Figure 1 as well. Because of the loss of adapted protection when the low-LET dose progressively drops below individual-specific thresholds for activating the indicated protective processes, cancer RR increases to a maximum *RR** as the radiation dose decreases to absolute zero radiation. For doses below the natural background radiation level, our modeling results indicate that only the low-LET component to the dose is needed for characterizing cancer *RR* (Scott 2006b). The shape of the dose-response curve for this dose zone depends on the form of the distribution of

the stochastic threshold for activating the protective processes. For a uniform distribution from 0 (i.e., absolute zero radiation dose) to a dose *D** (which is thought to exceed the natural background low-LET radiation dose), *RR* is expected to decrease linearly from its maximum, *RR**, at *0* dose to a minimum of *1-PROFAC* at *D**.

Evidence (from epidemiological and ecological studies) will be presented which supports our modeling prediction that reducing natural background radiation to near zero would be expected to lead to significant increases in cancers and other genomic-instability-associated diseases as well as reduced lifespan for humans and other mammals. These findings contradict the radiation-phobia-driven view often presented in the news media that any amount of radiation is harmful. To the contrary, low-level, low-dose-rate low-LET ionizing radiation appears to be preventing genomic-instability- associated diseases such as cancer and thereby saving many lives worldwide.

References

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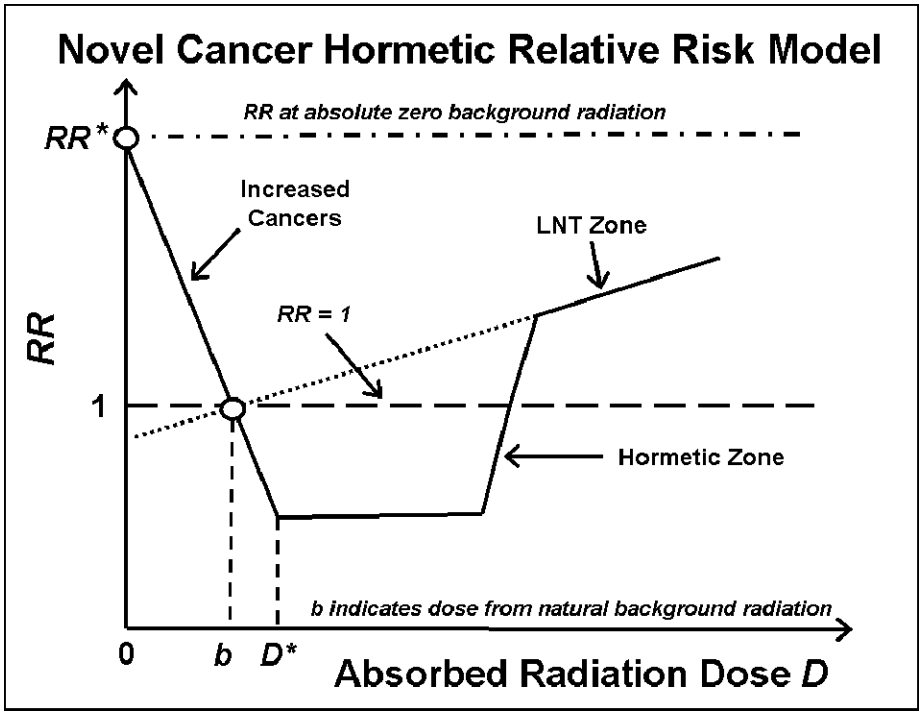

Figure 1