Effect of low dose radiation on NF-kappaB-mediated transformation of pre-malignant MCF10A cells

Paul Yaswen and Bahram Parvin

Lawrence Berkeley National Laboratory

Inflammatory responses involving NF-kappaB have been strongly linked to promotion of carcinogenesis in a number of published in vitro and in vivo studies. In one recent study (Iliopoulos et al., Cell 139, 693-706), Struhl and co-workers used pre-malignant MCF10A cells bearing an inducible Src oncogene to demonstrate epigenetic transformation mediated by a positive feedback loop involving NF-kappaB and the inflammatory cytokine IL6. Importantly, once activated, the transformed state was self-sustaining in the absence of additional mutations in the parental line. Additional evidence indicated that this positive feedback loop is likely to play a role in maintaining the malignant growth of a variety of different human cancers. Since radiation has been shown to affect inflammatory responses involving NF-kappaB, we hypothesize that perturbation of these responses by low dose radiation may affect adaptive responses and thresholds of oncogenic transformation. Using the MCF10A system, we are determining the effects of low versus high dose X-irradiation on the epigenetic switch involving NF-kappaB and IL6. Our preliminary results indicate that the influence of low dose radiation on NF-kappaB-dependent transformation is qualitatively different from that of high dose radiation, suggesting the existence of non-linear or threshold effects.