Analysis of low dose radiation induced epigenetic modifications in animal and human cell line models

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Over the last decade, it has become apparent that revealing the genetic sequence of anorganism is not sufficient to fully understand the development, physiology, or phenotype.Likewise, aberrant genetics cannot explain the onset or progression of many diseases. Thisrealisation has coincided with the exponential growth of the field of epigenetics which, aims toexplain the regulation of gene expression through mitotically and meiotically heritable changesthat are not caused by changes in the primary DNA sequence. To-date, three mechanisms ofepigenetic regulation have been described: DNA methylation, histone modifications and, mostrecently, small, non-coding RNA regulation. Although it has been widely accepted thatepigenetics play an indispensible role in regulating the life processes of an organism,thespecific mechanism by which intra- and inter-cellular signals manage to elicit the epigeneticchanges remains unclear.

This project has aimed to elucidate the epigenetic responses observed in higher levels ofbiological organization when organisms are exposed to low doses (<0.1Gy) of irradiation.Recent work in determining the exact effects of low dose radiation have shown that thebiological effects of low-dose are considerably more complex than the current linear nothreshold risk model suggests. Through the use of an inbred *in vivo* murine model and humancell cultures we have began to elucidate the epigenetic alterations that occur in various tissuesin response to low dose radiation exposure. Briefly, C57 black, 55 day old, male mice wereorganized into cohorts that received either: an acute dose (0.01, 0.1 or 1.0Gy), a fractionatedlow dose (10 days X 0.01Gy/day), primed and exposed (0.01 Gy + 1Gy) or sham treatment(control). Gene expression, DNA methylation, miR expression and histone profiles wereassayed at 6 hours—, 4 days— or 4 weeks post-irradiation. Similarly, human cell lines were assayed for epigenetic changes 24— and 48 hours after several acute doses.

The model of the role of epigenetic changes in low dose radiation responses will be presented and discussed.