

Gene expression and molecular signaling responses to radiation

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Radiation has effects on biological organisms at different levels

- **Whole organism**
- **Cellular level**
 - Cell cycle arrest
 - DNA repair
 - Cell death
- **Molecular level**
 - Signal transduction - many pathways respond to ionizing radiation
 - Changes in gene expression levels - underly many cellular responses
 - "-omics" -- Such changes can now be measured across the whole genome

Microarray technology allows measurement of relative gene expression across the whole genome

- Irradiation of very diverse cell lines results in a coordinate down-regulation of cell cycle related genes in all cell lines
- Another common radiation-induced response is activation or change in specificity of transcription factors. For instance, the transcription factor p53 is activated by radiation exposure, and it is also the most commonly mutated gene in human cancers.
- P53 is required for the radiation-induced response of many genes involved in several different physiological processes:
 - Cell cycle regulation
 - Apoptosis
 - DNA repair
 - Senescence
 - Anti-angiogenesis

No pathway is activated alone, no signaling cascade acts alone

- The outcome of p53 activation is determined by the interplay of many other factors and signaling pathways
- The complexity of cell signaling pathways allows "fine-tuning" of cellular responses

Biological dosimetry would be needed if a large public radiation exposure were to occur

- Need to determine dose in population without physical dosimetry
- Need to perform triage to assign appropriate treatment
- Need to reassure people who were not actually exposed

Irradiation of blood samples in the laboratory has provided a number of potential gene expression changes that could be useful as radiation biomarkers

- **Gene expression changes:**
 - Are linear with dose
 - Last at least two days after exposure
 - May provide useful dose estimates without pre-exposure controls
- Studies with radiotherapy patients are providing further confirmation of these results, as well as additional gene responses not seen outside the body.
- Radiation responses must be distinguished from other stresses:
 - Inflammation or infection
 - Trauma (burns or other injury)
 - Drug treatments