

### **Box 1. Target theory**

The *target theory* of radiation induced effects [12] postulates that cells contain at least one critical site or *target* that must be hit by radiation in order to kill a cell or produce an effect. Therefore, radiation damage outside of the target should not cause cell death (effect). It is widely accepted that nuclear DNA is the critical target for radiation induced cell death as well as for not death related effects.

### **Box 2. Conventional biological effects of ionizing radiation.**

DNA damage occurs during or very shortly after irradiation of the nuclei in targeted cells. The potential for biological consequences can be expressed within one or two cell generations.

### **Box 3. Non-targeted effects of ionising radiation (NTE)**

NTE does not require direct ionizing radiation deposition in nuclear DNA to be expressed.

NTEs are predominantly low dose effects ( $\leq 0.1$  Sv) and typically have non-linear dose-response relationships.

Phenomenologically NTEs are distinguishable from direct effects due to differences in their spatial and temporal dependency.

NTEs do not contradict “target theory” but contribute to a concept of an “expanding target” related to underlying biological signalling triggered by physical dose deposition. For example, the bystander effect increases the target size spatially to a group of cells, the tissue, or whole organism. Genomic instability increases it temporally by prolongation of effect over many cell generations or transgenerationally.

### **Box 4. Radiation induced genomic instability (RIGI)**

RIGI is defined as a heterogeneous, delayed elevation in the rate of *de novo* appearance of genetic changes such as mutations, chromosome aberrations or micronuclei, cell death or mitotic failure etc. within clonal descendants of irradiated cells.

### **Box 5. Radiation induced bystander effect (RIBE)**

RIBE is characterized by cellular effects (cytogenetically and DNA-damage related, cell killing, mutations, transformation and differentiation) expressed in unirradiated cells in some vicinity to an irradiated cell or cells.