Challenges to be met

Radiation-induced tumorigenesis is potentially an emotive issue particularly when cancers develop in children. They are caused by exposure of individuals to environmental sources of radioactivity, to material released at accidents or following military use to exposure in the workplace and to medical irradiation. It would be useful to determine whether signatures of radiation-induced cancers could be identified. An improved understanding of the molecular mechanisms and chromosomal changes induced by radiation would lead to a better understanding of the process of cancer formation. It is also important to establish whether particular sub-groups of the population are at increased risk of developing cancer.

Achievements

Radiation-induced childhood cancers from Belarus.
The consortium have painstakingly developed a tumour tissue bank from childhood cancers of the thyroid induced by radioactive iodine. Using this resource, it was possible to grow cells in tissue culture and thus study the chromosomes in the tumours. Specific hot spots in specific chromosomes where breakpoints occurred have been identified. Using molecular techniques, the DNA from specific regions can be amplified and checked for differences between normal DNA and tumour DNA. Characteristic rearrangements of the DNA were identified in the childhood tumours where the chromosomes are broken then repaired inappropriately leading to defects in the cells.

Radiation-induced human tumours induced in cell culture.
An alternative approach is to develop a laboratory model where normal human cells can be exposed to radiation and the stepwise process of cancer development followed. Using this in vitro approach tumours have been produced following exposure of cell cultures to gamma irradiation and alpha particle irradiation. Studies of the resulting tumour cells were able to establish characteristic chromosome changes and changes in gene expression.

Structural organisation of chromosomal regions in radiation-induced human cancers.
A genetic map of chromosome 10 has been constructed around the region where breakpoints occur in thyroid tumours. This was undertaken to try and explain why breaks occur at specific regions on the chromosomes and link this with DNA structure.

The programme has formed a useful transition into FP5 where new and established collaborations have developed. Using improved models of human epithelial cell cultures we have further established molecular and chromosomal changes in human cancers and will be applying this model to human breast cancer.

Partnership

The laboratories taking part in this programme have been collaborating for a long period of time and the EC funding has been essential in allowing good links to be maintained. The range of expertise being applied to this important issue of cancer induction in man could only be achieved by collaboration between laboratories experienced in this field. Future research will build upon the advances made in this project.
Selected references

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