An Investigation of Experimental Combinations of Radiotherapy and Chemotherapy in Cancer Treatment Using Immunodeficient Mice Bearing Human Tumour Xenografts

This hypothetical proposed project, prepared by *Focus on Alternatives*, illustrates how the general strategy shown overleaf would operate.

LITERATURE SEARCHES OF SUBJECT-SPECIFIC DATABASES

Search databases such as CancerLit or Medline using search terms such as: *neoplasms; radiotherapy; antineoplastic agents; combined modality therapy; experimental radiotherapy; experimental drug therapy.*

RESULTS OF SEARCH:

Armour A, *et al*. The effect of cisplatin pretreatment on the accumulation of MIBG by neuroblastoma cells *in vitro*. *Br. J. Cancer*, 1997, 75:470-476.

Casciari JJ, *et al*. Growth and chemotherapeutic response of cells in a hollow-fibre *in vitro* solid tumor model. *J.N.C.I.*, 1994, 86:1846-1852.

Cunningham SH, *et al*. Toxicity to neuroblastoma cells and spheroids of benzylguanidine conjugated to radionuclides with short-range emissions. *Br. J. Cancer*, 1998, 77:2061-2068.

Kearney T, *et al*. Radiotoxicity of Auger electron-emitting estrogens in MCF-7 spheroids: a potential treatment for estrogen receptor-positive tumors. *Radiation Research*, 1999, 151:570-579.

Santini MT, *et al*. Multicellular tumour spheroids in radiation biology. *Int. J. Radiation Biol.*, 1999, 75:787-799.

Sommers GM, Alfieri AA. Multimodality therapy: radiation and continuous concomitant cis-platinum and PKC inhibition in cervical carcinoma model. *Cancer Invest.*, 1998, 16:462-470.

CONTACT INDIVIDUALS WITH RELEVANT EXPERTISE IN:

- The Three Rs
- New techniques

For example, contact authors of the above papers, and individuals on mailing lists, newsgroups and discussion groups.

GATHER INFORMATION

Searches indicate that tumour cell spheroids and hollow fibres *in vitro* have been used in similar studies; guidelines on suitable cell types were found on the internet.

Is the project still relevant and necessary?
e.g. There is no information available on the particular drug/radiotherapy combination of interest.

YES

Can the project be done entirely without animals?

YES
The entire project can be conducted using cells *in vitro*.

CONDUCT WORK AND PUBLISH DATA, HIGHLIGHTING THREE Rs ASPECTS

SEARCHES OF SPECIALISED THREE RS RESOURCES

- To locate suitable cell lines for spheroids, some cell banks and collections can be searched via the internet. Species differences can be avoided by using human cells.

RELEVANT SITES INCLUDE:

The European Collection of Cell Cultures http://www.ecacc.org.uk

National Cancer Institute Tumor Cell Lines Database http://www.atcc.org/phage/ncisearch.html

Cell line collections available from institutes around the world can be searched at: http://www.biotech.ist.unige.it/cldb/indexes.html

- INVITTOX Protocol list (http://www.ivtip.org/protocols.html)

A protocol is listed which utilises tumour cell lines for drug screening in cancer research.

NO

Can a pilot study or other part of the project be done *without* living animals?

YES

YES
But part of the project still requires living animals.

YES

IMPLEMENT REDUCTION AND REFINEMENT

RELEVANT RESOURCES INCLUDE:

Hollingshead MG, *et al*. *In vivo* cultivation of tumor cells in hollow fibers. *Life Sci.*, 1995, 57:131-141.

Jennings M, *et al*. Refining rodent husbandry: the mouse. Report of the Rodent Refinement Working Party. *Lab. Animals*, 1998, 32:233-259.

The US National Cancer Institute uses an *in vivo* hollow fibre assay. Encapsulated human tumour cells are implanted in mice. http://dtp.nci.nih.gov/

UKCCCR Guidelines for the Welfare of Animals in Experimental Neoplasia, 1997.