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A CANCER diagnosis may not always be a death sentence, but cancers of various sorts still kill more than 6m people a year, and few can be cured reliably. The odds might, however, be improved if a model put forward at this week's meeting of the American Association of Physicists in Medicine, held in Montreal, Canada, proves itself in clinical trials.

Paul Keall, a medical physicist at Virginia Commonwealth University (VCU), in Richmond, has calculated that the cure rate could be improved by at least 15% using a novel combination of gene therapy and radiotherapy. X-rays have been killing cancers for donkeys' years. Increasingly sophisticated radiotherapy techniques have made the treatment more effective. But it is through the use of gene therapy to make cancer cells more susceptible to radiation that there lies an even better hope of a cure, according to Dr Keall. Radiation kills cells because it damages their DNA, creating errors in the genetic code and even breaking the double-helix. The accumulation of these faults eventually causes the cell, or its daughters who inherit the damage, to die. Both the rate and the way that a cell divides help to determine how fast radiation destroys its family line. So cancer cells, which multiply rapidly in an abnormal manner, are more affected than slowly growing healthy cells.

However, healthy cells--particularly those in tissues such as skin and hair-follicles that replicate a lot--are damaged to a certain extent by the radiation. The death of these cells causes nasty side-effects in the patient. Radiotherapists try to minimise such harm by aiming their X-rays carefully, but the best way to reduce side-effects is to lower the radiation dose. And this is where the gene therapy comes in.

Some of Dr Keall's colleagues at VCU have shown in laboratory experiments that they can "radiosensitise" cancer cells by blocking the function of a protein called epidermal growth factor (EGF). This substance encourages cells to repair themselves. When a cell is exposed to radiation, the number of EGF receptors in it soars in a protective response.

The researchers found that they could disable this mechanism by causing cells to produce dysfunctional receptors. These bind to EGF and so prevent it reaching receptors that work. To achieve this, a version of the EGF'receptor gene that produces a dysfunctional receptor is inserted into "Trojan" viruses, and those viruses are then injected into the cancerous tissue. When a virus

releases its DNA in order to infect a cell, it also releases the inserted DNA. The cell then uses this to manufacture dysfunctional receptor-molecules that in turn mop up EGF.

Laboratory trials in animals have found that cells altered in this fashion are almost twice as sensitive to radiation as are unmodified cells. This is more than enough to make a difference, according to Dr Keall's calculations. The other variable in his model is the fraction of cells in the tumour that are infected by the Trojan virus. The best improvement in tumour control is, not surprisingly, seen when all the cancerous cells are genetically modified. The actual efficiency of infection is hovering around 80%, but that should still be sufficient to weaken a tumour's response to radiation enough to kill it in some cases.

It will be difficult to increase the level of infection unless the virus can be made to attack cancer cells specifically. For now, the researchers rely on skill with the hypodermic needle and a little bit of luck, injecting the virus into the centre of the tumour and hoping that it will distribute evenly throughout the cancer without spreading to the tissues outside. This requires the tumour to be accessible--as, for example head, neck and breast cancers are.

The first human trials of the combined treatment should start within a year. Only when they are completed will Dr Keall know whether the predictions of the model are accurate. Has it raised false hopes or will genetic radiotherapy save real lives?

GRAPHIC: Gene therapy may make radiotherapy more effective

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