

Robots and Laser Beams:

High-Tech Weapons in the War Against Cancer

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Researchers and scientists at the Princess Margaret Hospital (PMH) and its research affiliate - the Ontario Cancer Institute (OCI) - are developing new, high-tech weapons in the war against cancer, complete with robots, laser beams, and gene chips which can isolate, read, and compare tens-of-thousands of genes stored on a chip the size of a postage stamp, to quickly differentiate between normal and cancerous cells.

Ten years ago, researchers examined genes one at a time, an excruciatingly slow task considering that each cell houses between 50,000 and 100,000 genes. But today, thanks to advances in technology, scientists can do in hours or days, what their predecessors took months or years to accomplish.

To speed up the process of gene comparison, researchers at OCI/PMH, working with a team from the University of Toronto, are perfecting a special robot that will allow them to compare gene cells thousands and thousands at a time. And being able to examine the differences between normal and cancerous genes very quickly and accurately will hopefully lead to the discovery of ways to inhibit the growth of cancer cells without damaging normal, healthy cells. The robot, called a microarrayer, uses a tiny glass tube to uniformly cover a small slide with minuscule dots of human DNA, each dot representing one human gene. The DNA dots - one-hundredth of a millimeter - are then interpreted for patterns of colour using a laser micro-scope, called a gene chip laser. When the genes are examined by the laser, they are projected onto a computer screen in various colours. According to Dr. Jeremy Squire, Associate Professor in Laboratory Medicine, Pathobiology and Medical Biophysics and Acting Director of the

Cancer Cytogenetics Program at OCI/PMH, it is the ratio of that colour which tells researchers whether a gene is over - or under - expressed. The colour patterns change between normal and cancer cells. In short, scientists can determine the genetic changes that drive the development and onset of cancer. "Using gene chip technology allows us to better analyze solid tumours to learn more about abnormal patterns of gene expression," says Dr. Squire. "We will be able to improve the diagnosis for patients and find ways of preventing tumours from forming." Once researchers have an inventory of the human genome - the full genetic code of our species - they will then be able to compare a person's genetic composition to the way things should look, allowing doctors to diagnose genetic weaknesses and susceptibility to diseases that result from gene defects. Once scientists know which genes are defective in an individual, they can find ways to replace them with good genes, or simply "turn off" the bad ones. Each human cell contains blueprints for over 100,000 genes, but only a few thousand of the genes are active. The active genes define the behaviour and identity of that cell. Through miniature arrays of the genes, scientists can rapidly determine which genes are active and controlling certain functions.

According to Dr. James Woodgett, Head of the Division of Experimental Therapeutics at OCI/PMH and Professor of Medical Biophysics at the University of Toronto, comparing "genetic fingerprints" allows researchers to quickly identify genetic changes in early stages of cancer malignancy and identify candidates for new treatments.

Gene chip technology represents a new way of looking at tumours and robotics is a new wave in cancer research. The new microarrayer in use at OCI/PMH is the first prototype for the actual robot, the final version of which will cost over \$1 million, once it is completed. OCI/PMH's robot is the only one in Canada. Researchers in the laser lab are using lasers to develop indexes of how cancer cells differ from normal ones. They are working to develop optical fingerprints of tissue. Using a range of light colours - green, blue, red, and violet - scientists are developing lasers that will help in the early diagnosis by detecting changes in genes before they grow into a tumour. Laser light can detect changes in cells that occur as a result of disease. As intensity of the colour spectrum changes, researchers can detect whether tissue is normal, pre-cancerous, or cancerous.

Gene chip technology may also allow a researcher to examine the effects of a certain drug or therapy on genes and cells immediately, rather than having to expose a cell to the drug and wait to observe the reaction. It allows scientists to screen drugs 100-times faster than normal. This new high-tech weapon will allow scientists to increase their confidence in diagnosis by looking at hundreds of independent signs of a particular disease at the genetic level.

Researchers at the OCI/PMH expect to complete testing the gene chip robot and begin examining actual cancer cells next month. That step, they say, will mark an exciting new era in cancer research. "This is an exciting time for researchers in our field," says Dr. Squire. "With the advent of gene chip technology, we've turned a corner in cancer research. We're expecting great things from this."