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In some future Star Trek century, doctors cure using an intelligent probe. In the 21st Century, medicine, though far from that fictional world, is itself poised for major advances in an emerging area of science called Systems Biology. In turn Systems Biology has major implications for cancer therapy.

At its core, Systems Biology focuses on the integrated interplay among the thousands of molecules within and between cells that underlie health and disease. Central to this molecular dance is the genetic regulatory network that coordinates the activities of some 30,000 genes and their products into the choreography that leads from the fertilized egg to the adult human. Different cell types -- liver, kidney, pancreas, nerve -- are due to different patterns of activity among these genes. Different combinations of genes make their unique proteins in the different cell types. In the genetic network that coordinates these processes, genes turn one another on and off in complex ways. When this process goes awry, cancer can result.

Systems Biology is advancing rapidly in the U.S., U.K., Europe and Japan. Canada has mustered only marginal efforts to date and will either compete on a global scale or lose an enormous opportunity. The Institute for Biocomplexity and Informatics at the University of Calgary, where my colleagues and I work, is one of the few Canadian venues for this emerging arena. Canada needs a nationwide effort. Among the primary outcomes of this new science will be the discovery of the structure and behaviour of genetic regulatory networks. Much of our Institute's work is focused on this complex task.

In my view, the major health implication of Systems Biology and understanding genetic networks lies in the hope for dramatically enhanced therapies for cancer, for it is now clear that cancer is typically due to the accumulation of mutations in cells that skew the behaviour of the genetic regulatory network.

We all know the ravages of cancer, and the consequences of surgery, radiation and chemotherapy. There now appear to be glimmers of a bold new approach to therapy, perhaps for most cancers, and possibly without resorting to surgery, radiation, or chemotherapy. The approach rests on new and old facts about cancer.

Strikingly, cancer biologists have recently discovered that many cancers are driven by a very small subset of the cells within the cancer called cancer stem cells. For example, this appears true in brain, prostate, skin, and breast cancer. These cancer stem cells are cousins of familiar embryonic and adult stem cells. In an increasing number of cancers, cancer stem cells and their immediate progeny, called cancer progenitor cells, appear to

be the only two proliferating populations of cells. Some of the proliferating progeny then sometimes change, or differentiate, into non-dividing cancer cells. Thus, therapies that remove the non-dividing progeny of the cancer progenitor populations do not cure the cancer. Removal of the proliferating cancer stem and progenitor cells is necessary, otherwise the disease recurs.

Moreover, for the maintenance of stem cells of a normal tissue and cancer stem cells of the same tissue, it is beginning to appear that the same genes are necessary, suggesting that the two kinds of stem cells are very similar. Since normal stem cells can change, or differentiate, into a variety of normal cell types, this suggests that cancer stem and progenitor cells can also differentiate into normal cells. And indeed they can. Mutated cancer cells can give rise to normal cell types.

These features of cancer suggest the bold new approach. It may be possible to find molecules that induce cancer stem cells and progenitor cells to change, or differentiate, into normal, benign cell types. We call this “cancer differentiation therapy”. Vitamin A is already used in this way to treat some leukemias. If such molecules could be discovered more generally, this could allow therapies for many cancers, targeted to tissue specific cancer stem and progenitor cells causing them to change into benign cell types, thereby stopping the cancer. This is a pinpoint attack, not on all dividing normal and cancer cells as in most chemotherapy, but on the specific cancer stem and progenitor cells which are the ones that make the cancer grow.

Fortunately, the search for molecules that might induce cancer cell differentiation on a very large scale is now possible. “High through-put” screening methods now allow rapid search through very high diversity “libraries” of molecules, seeking those that induce cancer stem and progenitor cell differentiation which render them harmless. In short, high through-put screening is a fast way to find candidate drugs. It allows vastly more candidate molecules to be screened than conventional methods.

Despite the enormous promise of high through-put screening for molecules inducing such “cancer differentiation therapy”, an extensive search reveals no use of high through-put methods in the search for such a cancer cure. At the Institute for Biocomplexity and Informatics, we will soon initiate this work using robotics, but the effort must be far broader nationally and internationally. The stakes are too high to do otherwise.

It is proper to be cautious. Cancer is extremely complex and many seemingly wonderful ideas have not worked in practice. The screening approach described above may not easily find molecules of high efficacy and safety. Many cancers have more than one proliferating cancer cell type. Here one can hope that cancer differentiation therapy can work on each of these cell types as well. In addition, each case of a type of cancer may have a unique set of mutations to its genes, rendering any single differentiation therapy problematic. It may turn out that "cancer differentiation therapy" will mature as a powerful member of a range of therapies applied in the most effective combination possible.

The approach above is bold, it is new, and it simply must be tried. With its unique array of national and provincial funding agencies, Canada is well poised to undertake and collaboratively lead the broad research that is required.

21st Century medicine will be increasingly subtle compared to the medicine of today. The Star Trek fictional image of the healing intelligent probe may be a glimpse of where we are headed in reality and we aim to explore this intriguing possibility.