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The Challenge of Cancer

THIS SPECIAL ISSUE OF *SCIENCE* FOCUSES ON CANCER, A DISEASE THAT TAKES A TERRIBLE HUMAN toll. For scientists, preventing and curing this disease present an enormous challenge. We all know someone who suffers from cancer, and there is always pressure on researchers to focus on the immediate development of better treatments. But it is also essential to invest in innovative, longer-term efforts designed to generate more powerful approaches.

The Reviews and analyses in this issue reveal why the task of treating the disease is so frustratingly complex (see p. 1539). By the time most cancers are detected, a tumor has grown to contain more than a billion cells. Through a process resembling mutation and natural selection stretching over many years, these cells have become altered in ways that allow them to escape from the large number of failsafe mechanisms that normally protect the human body. For example, the rogue cells have evaded the elaborate system of growth controls that keep most of the 80 trillion cells that form a human in a quiescent state, disrupted the cell suicide mechanisms that would otherwise eliminate any aberrant cell, and evolved a resistance to immune system surveillance.

To make matters much worse, the cells in a cancer are constantly changing, having acquired a greatly enhanced ability to mutate and to alter the genes they express through other mechanisms. As a result, the population of cells in a tumor is quite heterogeneous, making it very unlikely that any single therapy can target them all. This presumably explains the repeated failure of powerful new treatments, such as those described on p. 1542, to permanently cure the disease: A small fraction of tumor cells resistant to the treatment continues to proliferate, eventually multiplying to a dangerous level. Attaining true cures for most cancers would therefore be expected to require that patients be treated with two or more drugs simultaneously.* The logic is simple: Whereas a tumor is likely to harbor some cells that are resistant to any one drug, it is unlikely that there will be cells resistant to two drugs that target different cellular pathways or multiple points within a single pathway.

But the cells in different individual tumors will be different. How can we hope to find a set of drugs that will effectively kill the cells in a particular patient's tumor without damaging the vast number of normal cells needed to keep us alive? Powerful new approaches seem possible, given the great advances made in our ability to study and manipulate cells. In a traditional scientific meeting, many experts in cancer come together to present their research and exchange ideas. More likely to generate the needed innovation is a newer model of small workshops, in which five or so experts on cancer spend several days with 25 outstanding scientists and engineers who have expertise outside the cancer field that is suspected to be relevant to new approaches. The effort begins with the experts framing the important unsolved problems for the nonexperts and answering their questions. Most of the remaining time is spent in a set of small breakout groups, each of which focuses on exploring a specific new approach, such as that emphasized in a previous editorial.** As a second example, what types of nanotechnologies might eventually be developed to allow a freshly excised tumor to be dispersed into many small groups of cells that maintain their normal physiological state, so that robotics can be used to rapidly administer many different combinations of drugs, growth factors, and antibodies, with automation used to monitor results?

Science's sister journal *Science Translational Medicine* will be cosponsoring a series of workshops of precisely this type in 2011, including workshops on Alzheimer's disease and a specific aspect of cancer. If successful, we hope that many more such efforts can be undertaken in future years.

– Bruce Alberts

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*A. D. Levinson, *Science* 328, 137 (2010). **B. Alberts, *Science* 325, 1319 (2009).