Forty years on from Nixon's war, cancer research 'evolves'

SAN FRANCISCO — Ever since US president Richard Nixon declared war on cancer in 1971, scientists and physicians have launched a full-on offensive against the disease, seeking to cure cancer by eradicating the multiplying enemy cells. But, with few exceptions, treatments haven't lived up to expectations.

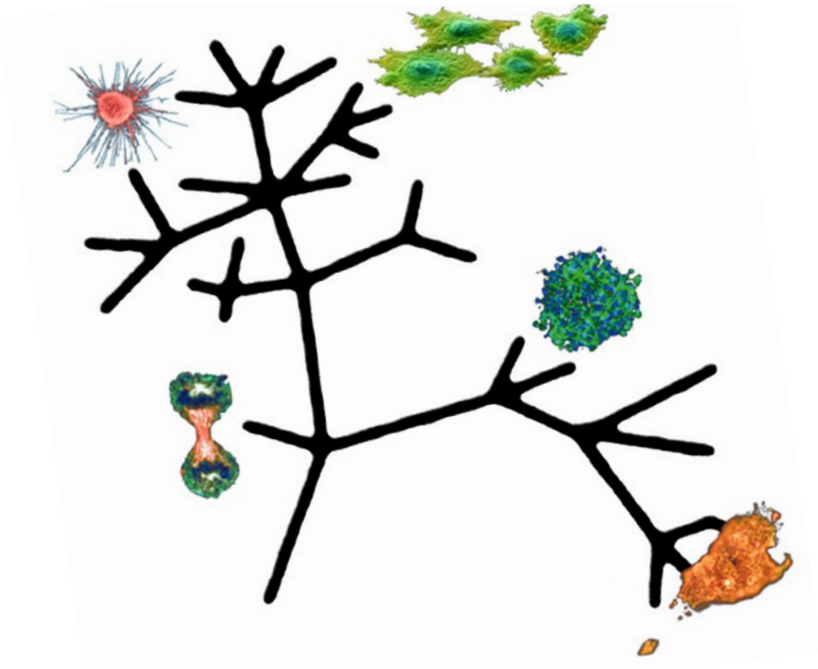
"We've been banging our heads against this cure thing for three, four decades now and really made almost zero progress," says Carlo Maley, a cancer researcher at the University of California–San Francisco (UCSF). "It's been a wash."

Now, Maley and others suggest that applying the principles of evolutionary biology to cancer research could do what that the existing paradigm has missed—and the idea is gaining traction. At the first biannual international Evolution and Cancer Conference, held here during the first weekend in June, around 125 scientists met to discuss how considering fields not typically associated with cancer—including evolutionary dynamics, comparative biology and even social psychology—might help turn the tide in the fight against the deadly disease.

"There's a quote people keep repeating: 'nothing in biology makes sense except in the light of evolution'," says Aurora Nedelcu, an evolutionary biologist at the University of New Brunswick in Fredericton, Canada, referencing the geneticist Theodosius Dobzhansky's 1973 essay bearing that title. "So, cancer shouldn't make sense except in the light of evolution as well."

The dominant cancer metaphor has, until now, been the concept of tumor as invading army, a barbarian horde attacking from outside city walls. But at the meeting, Steven Neuberg, a social psychologist from Arizona State University in Tempe, proposed a new way of thinking about the disease. Likening cancer cells to local residents gone bad who slowly exploit the environment around them for their own gain, he suggested "criminal gangs" as a more apt metaphor for cancer than "foreign invaders." "Cancers are not outside the body," Neuberg says. "They come from within us."

"I suspect this barbarian metaphor biases us toward overtreatment, using really aggressive approaches, and blinds us to thinking about the disease as a chronic illness," says Maley, who moved to UCSF last year to launch and head up the Center for Evolution and Cancer at the university's Helen Diller Family Comprehensive Cancer Center. The research center is the first such place in the world devoted to combining the two fields, and the June meeting was its first formal event.



Up a tree: Cancer researchers look to Darwin to improve tumor therapies.

Adaptive approach

Participants at the meeting agreed that approaching cancer as a manageable, chronic illness will require a dramatic restructuring of current treatments. But how to achieve this conceptual and clinical overhaul remains a matter of debate.

Robert Gatenby, a mathematical cancer biologist at the H. Lee Moffitt Cancer Center in Tampa, Florida, argues that the field should consider the somewhat iconoclastic idea of managing tumor growth rather than eliminating it altogether. Instead of conventional cancer treatments, which often end up selecting for populations of drug-resistant tumor cells in a 'survival of the fittest' type of contest, Gatenby proposes to treat tumors with lower doses of drug so as to intentionally salvage some of the drug-sensitive cells. According to evolutionary theory, after drug treatment stops these sensitive cells should out-compete the resistant ones, thereby keeping tumors alive but small and manageable (*Nature* **459**, 508–509, 2009).

In a similar vein, Gatenby also suggests exploiting tumor evolution by driving cells into an evolutionary corner where they are more susceptible to being hit with a subsequent agent. "It's like a chess game," he says. "You have to plan multiple moves ahead."

Others at the meeting considered the role that comparative biology could have in identifying important cancer pathways. For example, Andrei Seluanov, an aging and cancer researcher at the University of Rochester in upstate New York, compared life spans and cancer rates across 24 different rodent species ranging from gray squirrels and naked mole rats, which can both live for more than a quarter century without developing tumors, to house mice—95% of which typically die from cancer before the age of two. According to David Haig, an evolutionary biologist at Harvard University in Cambridge, Massachusetts, these types of cross-species comparisons can reveal natural defense mechanisms already present in the animal kingdom that are undermined during cancer development.

Despite the growing interest in the interface between cancer and evolution, however, not all cancer biologists are racing to embrace Darwin quite yet. "They understand the reasoning," Maley says, "but ask, 'so what?'"

Nonetheless, attitudes might be starting to change. "It's silly not to think about all that's been learned from evolutionary biology and apply it to studying cancer," says Tyler Jacks, director of the Koch Institute for Integrative Cancer Research at the Massachusetts Institute of Technology in Cambridge, Massachusetts, who did not attend the June meeting. "After all," adds Edward Benz, president of the Dana-Farber Cancer Center in Boston, "evolution is something that occurs as a result of dynamic changes in our genes and genomes, and that's definitely part of what's going on in cancer."

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