Antiaging drug trials compel creative testing methods

The day when doctors prescribe pills to combat aging may sound a long way off. But medical researchers are already starting to test such drugs in clinical trials—and encountering scientific and regulatory obstacles along the way.

Over the last few years, biologists have identified a slew of compounds that prolong the life of animal models such as yeast, worms and mice. On the basis of these results, they have formed a handful of companies around the world and are embarking on clinical trials in humans.

Showing that a drug prevents aging in people, however, is proving almost impossible. The obvious test is to give one group of people the drug, and another a placebo, and wait to see which lives longer. But this would take at least a decade, be enormously expensive and spell bankruptcy for a cash-strapped biotech firm. "No companies have money to last that long," says David Sinclair at Harvard Medical School, Boston, whose studies on the antiaging compound in red wine called resveratrol led him to start Waltham, Massachusetts-based firm Sirtris Pharmaceuticals.

One way that Sinclair and other researchers plan to get around this problem is to show that a new drug delays or halts diseases associated with aging, without actually waiting for individuals to grow old. They hope to gain regulatory approval for slowing diabetes or arthritis, for example, and then carry out further trials to examine whether the drug also prevents these diseases from developing in the first place.

Catherine J. Jun/Detroit Free Press

Long wait: Proving that a medicine slows aging is a tough task for aspiring biotech companies.

This approach is being taken at Elixir Pharmaceuticals, a company based in Cambridge, Massachusetts, that is planning human trials of molecules associated with aging in yeast and the worm *Caenorhabitis elegans*. The company is attempting to get drugs approved for market by showing that they prevent type 2 diabetes, says Bard Geesaman, Vice President of Medical Development.

Neither the US Food and Drug Administration (FDA) nor its equivalent, the European Medicines Agency, has ever approved a medicine specifically to combat aging. But if a company can convincingly demonstrate that a drug prevents a specific disease, officials say that it should be approved for that particular use. "Much of preventive medicine is, in a sense, antiaging medicine," says David Orloff, an official in the FDA's Center for Drug Evaluation and Research.

But once such drugs hit the market, they raise the prospect that some people will use them as broad spectrum antiaging drugs even though their long-term side effects are unknown.

Indeed, some may already be swallowing prescription drugs, such as cholesterol-lowering statins and anticonvulsants, which have been shown to extend the life of animal models. "In the absence of human studies, it would not be advisable to take these medications to delay aging," says Kerry Kornfeld, who studies such therapies at Washington University in St. Louis, Missouri.

Those in the field believe it will be decades before a drug is approved specifically for combating aging. In order to do so, researchers will probably need to find genes or other biological molecules whose levels vary with a person's age and show that the drug stops this change. Until such trials are completed, it is irresponsible to label a drug 'antiaging', says Leonard Hayflick who studies gerontology at the University of California, San Francisco.

Emma Marris, Washington DC

Meager US budget fails to assuage drug safety concerns

Research and drug safety advocates expressed frustration at President Bush's budget plan for the 2006 fiscal year, which boosts funding for the Food and Drug Administration (FDA) but leaves other biomedical agencies with marginal increases at best.

The new plan, released on 7 February, proposes an overall cut in federal spending on science and technology by 1.4 percent, reflecting government attempts to rein in a budget deficit and bankroll the Iraq war. Advocacy groups say these reductions could chill medical and public health research and disease prevention services.

Under the new budget, the FDA would receive a 4.4 percent funding increase, or around $80 million. Of this, $6.5 million is earmarked for hiring new workers to monitor safety of drugs and medical devices in the Center for Drug Evaluation's Office of Drug Safety. This division has come under fire in recent months for not taking a more aggressive stance over emerging signs of side effects from antidepressants and arthritis drugs including Vioxx.

The FDA also announced in February that it would establish an advisory board of federal scientists to oversee the safety of drugs already on the market.

Some experts say the agency will need a far bigger cash injection if it is to adequately address drug safety concerns. "The new budget additions are OK for this year, but no one should assume that fixes the problem," says Georges Benjamin, executive director of the American Public Health Association in Washington, D.C.

Public health advocates also expressed concern about the proposed six percent cut, to $6.9 billion, in the budget of the Centers for Disease Control and Prevention (CDC), one of the biggest reductions proposed for the federal science agencies.

Many of the CDC cuts would affect disease prevention programs such as those fighting obesity and HIV, which some say is a shortsighted move that will ultimately create higher medical bills. "Decimation of prevention programs is particularly devastating," says Bill Leinweber, head of research advocacy group ResearchAmerica in Alexandria, Virginia.

The budget proposes a 0.7 percent increase for the National Institutes of Health, one that fails to match the estimated 3.5 percent needed to cover the rising costs of equipment and staff in biomedical research.

Science advocacy groups say that members of Congress, who must approve the new budget before it comes into effect, are likely to reject many of the proposed cuts for health and science agencies. "We're concerned the budget for the NIH will not sustain current research programs—and we'll work hard to get that message to Congress," says Jon Retzlaff, legislative director for the Federation of American Societies for Experimental Biology based in Bethesda, Maryland.

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