Buck Institute making progress on aging process

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Downhill from the I.M. Pei-designed, Ponce de Leon-inspired and worm-saturated Buck Institute for Age Research lies the rustically tony downtown of this Marin County, Calif., city.

There, in a three-block stretch, is brick-and-mortar retail evidence that the deep thinking and microscopic analyzing taking place up that hill is of utmost importance to the populace: Aesthetics by Claire, a skin-care salon; Strength Within, a fitness club; and Pharmaca, a veritable temple of antioxidant dietary supplements.

And every few months or so, the public is allowed behind Buck's gates for informational seminars and to see just what these bespectacled, white-coated geniuses are up to. On this December morning, more than 100 people filed into the auditorium to hear the latest on purported cell-restoring antioxidants and the efficacy of anti-aging drugs.

To these graying attendees, aging is not some abstract concept to be manipulated in a biochemical bouillabaisse. They are living it. But they also are eager to learn what scientific advancements may be on the horizon.

"I hear they're doing wonderful things here," says Adamarie Fernandez, a San Anselmo, Calif., resident who attended the lecture. "A lot of us here have things like arthritis and osteoporosis, and we want to know what the latest is."

OK, there's that.

But to sweeten the pot, Buck staff members raffled off an "anti-aging basket" featuring dark chocolate, green tea and red wine - the new holy trinity of the Baby Boomer Church of Antioxidants.

As the Buck event shows, Americans are nothing if not age-obsessed. No longer content to just look younger, they want to live longer and, more important, make more of those years healthier ones. Soon, seniors will hit a critical mass. By 2030, the population of older adults (age 65 and up) is expected to reach 70.3 million, double what it is now, according to census figures.

Living longer and better is a prime mission for scientists at Buck, a nonprofit, independent research center that opened in 1999. Originally funded from a gift by the estate of Marin County, Calif., pathologist Leonard Buck, the institute has since received grants from government agencies such as the National Institutes of Health and the California Institute for Regenerative Medicine, and private organizations such as the Ellison Medical Foundation.

Buck does no clinical trials or testing of specific drugs; it's as close to pure research as possible.

"As the country faces an unprecedented aging of its population, having a significant, free-standing, independent institute to study the basic connections between aging and elderly diseases is an enormous plus," says Dan Perry, executive director of the nonprofit advocacy group Alliance for Aging Research in Washington, D.C. "It may not be UCSF, not Duke or Harvard, but it is a unique, stand-alone institution. Its stature has risen in recent years."

The biomedical findings that Buck researchers have published include

discovering a chemical compound that could extend the life span of nematode worms as much as 40 percent. And last month, Buck researchers say, they identified gene biomarkers that can accurately predict the true physiological age of the worms.

The center's work on age-related illnesses includes finding a natural protein that grows new neurons and increasing dopamine in mice induced with Parkinson's disease.

While the results haven't made a splash - don't hold your breath, no "Fountain of Youth" pill is in the immediate offing - Buck research has helped scientists understand more about life span at the cellular level in simple animals, and how certain genes and protein compounds affect age-related diseases such as Alzheimer's, Parkinson's and stroke.

Might the research by Buck and others lead to breakthroughs that someday will lead to a genetic test doctors can give patients to determine their true physiological age, see what diseases they are prone to develop and take biochemical, nutritional or environmental steps to combat it?

In other words, if you're 40 but your cells are aging like a 70-year-old, it's time to change your lifestyle.

"I'm not going to make any predictions, because whenever a scientist makes predictions, it turns out to be wrong," says Simon Melov, director of genomics at Buck, with a broad smile. "Scientists are always promising to have a pill or treatment within five years, but that's just to get renewal on funding.

"But I'd like to think that in my lifetime we'll get significant advances in figuring out the genetic nature of aging."

Melov and fellow Buck professor Gordon Lithgow are renowned in the

field for research using the nematode worm (C. elegens) - which in the past 20 years has become the invertebrate of choice among scientists.

Why? Because, as Lithgow explains, "it's a simple animal, grows easily in the lab, (is) transparent, and you can see every step of the development and track the life span."

All 20 days of it. Or 60 days or longer, given the chemical compound manipulation Lithgow and Melov first detailed in a 2000 study showing that a single stress gene can lead to a longer nematode life span.

Not all of Buck's research leads to hopeful results. In the case of much-hyped antioxidants, Lithgow's research on worms showed that only four of the 40 antioxidants tested extended life span. Some actually did harm.

"There are a lot of baseless claims you can read on the labels of these antioxidant (supplements)," says Lithgow, whose study was released two months ago. "The ones we found that are effective aren't effective in the ways you'd expect. This is what happens sometimes in research."

Melov's latest anti-oxidant work involves studying a type of mouse that has no natural protein to fight the oxidation by free radicals in the mitochondria (energy producers in the cells) that break down tissue and lead to aging. He's found that treating the cells with certain antioxidants can retard aging.

That's great news for nematodes and mice, of course.

But what about everyone's favorite mammal - humans?

"Good question," Melov says. "People have shown you can extend nematodes' life tenfold. It's not that difficult anymore. But you move that to mice, you may get only a 10 or 20 percent expanded life span.

The magnitude greatly diminishes with the number of cells you're dealing with.

"And when you deal with a much more complex individual like a human, you may not get any change. That's what a skeptic would say. But an optimist would say that you might get some (increased) longevity with humans, but certainly nothing like lower vertebrates. Then there are those science-fiction/fantasy people out there who think we can all live to be hundreds of years old."

Though not the stuff of sci-fi fans, Melov's research published in 2007 on human subjects has shown that regular strength training can rejuvenate muscle tissue in healthy older adults.

Melov and co-author Mark Tarnopolsky of McMaster University Medical Center in Canada took tissue samples from the quadriceps of older adults (average age: 70) and compared them with samples from a younger group (average age: 21).

The gene "fingerprint" showed that the older adults had significant mitochondrial dysfunction, resulting in a loss of muscle mass. But after six months on knee-flexation weight training, the subjects were able to nearly fully reverse the decline and show molecular fingerprints similar to the younger group.

"It was important to validate a way that older people can improve their quality of life and reverse aging just by exercising," says Melov, who in the future will look at whether strength training can affect organ tissues and how aerobic training affects cells.

There has long been a push-pull at Buck between the basic research, such as determining biomarkers for worms, and more practical applications, such as the human strength-training study.

Former Buck CEO Dale Bredesen, who left his post this year to return to research, wrote in the spring 2007 newsletter that Congress has instructed the NIH to fund research that provides "practical solutions to our health care problems."

But he added that the pure research on genes and proteins that determine life span in worms, fruit flies and mice - and, potentially, humans - "accelerates the rate at which we can discover new therapeutics that lengthen the health years of life (and) delay or prevent virtually all of the diseases of aging."

All of this leads back to what some people think the scientists are trying to do up on the hill overlooking Highway 101.

Thumbing through the pages of the 2007 annual report, you can read the bios of staff scientists. Each is asked his or her "Big Hairy Outrageous Goal" in the job.

Christopher Benz, the program director, modestly wrote, "To age with increasing contentment and grace and with preserved mobility and mental acuity."

And then there's professor Jan Vijg's goal: "To cure aging."

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