

Down syndrome-Alzheimer's connection set wheels in motion

Alzheimer's Center Ready to Roll

By Todd Neff

Alzheimer's disease and Down syndrome would seem to have little in common. One manifests with age; the other in the womb. But dig deep into cells and the connection couldn't be clearer: many patients with Alzheimer's disease have three copies of chromosome 21 rather than two – the same trisomy 21 as those born with Down syndrome. And those in the Down syndrome community know too well that half of those with Down develop Alzheimer's disease.



The arrivals of Huntington Potter, PhD, left, and Jonathan Woodcock, MD, have energized the research and clinical work related to Alzheimer's disease on the Anschutz Medical Campus.

Neuroscientist Huntington Potter, PhD, first suggested the Downs-Alzheimer's connection in the early 1990s while a faculty member at the Harvard School of Medicine. But it wasn't until 2010 that his team of researchers, then at the University of South Florida's USF Health Byrd Alzheimer's Institute, established the connection definitively.

Now, attracted by a combination of the nation's only Down syndrome institute and the clinical and research infrastructure needed to build a world-class Alzheimer's research and treatment center, Potter aims to advance the science behind – and care for – both conditions on the Anschutz Medical Campus.

The ultimate goal, Potter said, is to establish a National Institute on Aging-funded Alzheimer's Center at the University of Colorado School of Medicine. There are 27 of these nationally, the aim being to translate scientific advances into improving patient care and, ultimately, preventing and curing Alzheimer's.

Potter has experience with the process, having established the first such center in Florida. A \$1.1 million bequest from the estate of former University of Colorado professor Kurt von Kaulla, MD, and his wife, Edith – not to mention a recent \$100,000 gift from CU President Bruce Benson and his wife Marcy – have set the wheels in motion for the new Alzheimer's Center here. But long-term funding from the National Institute on Aging will be critical if CU's scientific and clinical Alzheimer's work is to realize its potential, Potter said.

Work to do. Potter arrived in Colorado in July 2012 to a joint appointment with the Linda Crnic Institute for Down Syndrome and the University of Colorado School of Medicine Department of Neurology. The Alzheimer's Center he envisions would be comprehensive, spanning basic research, translational research, clinical trials and patient care. Along the way, Potter and colleagues hope what they learn benefits Down syndrome as well as Alzheimer's patients. There are many of both in the United States: about 400,000 with Down syndrome and some 5.4 million with Alzheimer's. Colorado happens to be an Alzheimer's hot spot, with the number of patients expected to more than double here by 2025. It's not so much an epidemic as a function of age – half of those older than 85 have Alzheimer's.

"It's growing faster here than anywhere, because everybody who moves to Colorado discovers it's so wonderful that they never leave," Potter said.

The stakes for researchers searching for a cure are high, added Kenneth Tyler, MD, chair of Neurology at the School of Medicine. For one thing, Alzheimer's costs Americans \$200 billion a year alone, he said. But that's only part of the disease's burden.

Continued

“The problem is truly epidemic and will touch everyone, either directly, through their family or friends, or in a caregiver role,” Tyler said in an email. “We need to be part of the efforts to understand the basis of this disease, potential treatments, and the delivery of the best possible care to those afflicted.”

What’s more, Tyler said, the roots of Alzheimer’s are likely to shed light on other neurodegenerative diseases such as Parkinson’s disease and amyotrophic lateral sclerosis (ALS), not to mention Down syndrome.

“Discoveries related to Alzheimer’s disease are likely to have implications across a broad range of neurological specialties and for understanding the brain and its illnesses more globally,” he said.

New UCH clinic. The clinical side of Alzheimer’s care got a boost in November with the arrival of neurologist Jonathan Woodcock, MD. He leads the newly christened University of Colorado Hospital Memory and Dementia Clinic on the fifth floor of the Anschutz Outpatient Pavilion and is CU’s clinical director of Alzheimer’s Disease Research.

Woodcock, a neurobehavioral rehabilitation specialist, has enabled a seven-fold increase in capacity for patients with neurodegenerative diseases like Alzheimer’s, memory problems and other types of dementia. Prior to Woodcock’s arrival, behavioral neurologist Christopher Filley, MD, had been carrying most of the clinical load. His work as chief of neurology at the Denver VA Medical Center limited his time at UCH, though.

The boost in clinical capacity goes hand-in-hand with the expanding research enterprise Potter is driving. Physicians can do little for those with Alzheimer’s, and these patients and their families are hungry for clinical trials, Woodcock said. Although PET imaging is improving the ability to spot the beta-amyloid plaques that accompany the disease, it’s still not easy to draw sharp lines between patients with various neurodegenerative issues, he said. Having a larger clinical population will help providers differentiate patients and present more clear-cut cohorts for pharmaceutical companies wanting to test new therapies, he added.

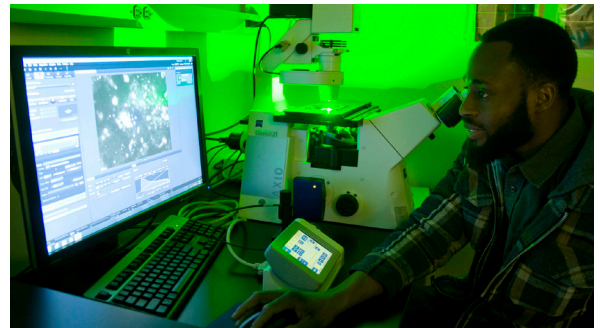
Having hardware like the Anschutz Medical Campus’s cyclotron close at hand means quick access to PET amyloid scanning, facilitating clinical research, Potter added.

Promising science. Potter’s first clinical trial at CU is slated to start this summer, with the Memory and Dementia Clinic and the USF

Health Byrd Alzheimer’s Institute targeting 40 participants in total. The trial will involve GM-CSF, better known as Leukine, a medication that increases production of infection-fighting white blood cells. The Food and Drug Administration approved Leukine in 1995 for bone-marrow-transplant patients. In Potter’s Tampa lab, research associate Tim Boyd, PhD, now at the Crnic Institute, found that mice preprogrammed with Alzheimer’s disease showed stark improvement when given the drug.

“It got rid of more than half of the amyloid within a week, and they all returned to normal cognition in a couple of weeks,” Potter said.

The idea to try Leukine emerged because of a curious disconnect: patients with rheumatoid arthritis are largely immune to Alzheimer’s. A study testing whether the body’s inflammatory response in these patients was driving resistance to Alzheimer’s came up empty, leading Potter’s team to look into the role of white blood cells.



Julbert Caneus uses a high-power microscope to examine chromosomes in the Linda Crnic Institute for Down Syndrome lab.

The new clinic and trial are two of many steps on the path to becoming a National Institute on Aging-funded Alzheimer’s Center. There also needs to be a neuropathology core, through which people who have been followed clinically can donate their brains for study; a biostatistics core; and a mouse neurobehavioral and neuropathology core to allow animal testing before clinical trials, Potter said.

While applying for the funding in 2014 is a possibility, it all might take three or four years, he added. The full-fledged center – and a firmer grasp of the Down syndrome-Alzheimer’s connection for the benefit of so many patients – can’t come soon enough, said Tom Blumenthal, PhD, the Crnic Institute’s executive director.

“We’re so far behind where we should be by now, and there are more and more people with Alzheimer’s,” he said.