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Seven-fold clinical growth

Alzheimer's Center on the Upswing

By Todd Neff

As recently as 2012, University of Colorado Hospital treated a trickle of patients with Alzheimer's disease and hosted little in the way of Alzheimer's research. Just two years later, the hospital's Memory and Dementia Clinic sees seven times more patients – roughly 1,200 a year – and University of Colorado School of medicine researchers are kicking off a promising drug trial with more clinical and laboratory studies underway and in the works.

Huntington Potter, PhD, and Jonathan Woodcock, MD, have been the principal engineers of this growth. Potter, who came to CU from the University of South Florida (USF) in July 2012, is a University of Colorado neuroscientist and director of Alzheimer's disease research for both the CU School of Medicine and the Linda Crnic Institute for Down Syndrome.

Huntington Potter, PhD, left, and Jonathan Woodcock, MD, have sparked an upsurge in interest in Alzheimer's disease at UCH and the CU School of Medicine.

Woodcock, a neurologist, is clinical director of the UCH Memory and Dementia Clinic, and leads Alzheimer's disease research. He arrived in November 2012, creating the clinic and expanding the hours available to patients with memory and neurodegenerative problems ranging from Alzheimer's disease to frontal temporal dementia to vascular dementia to head trauma. Clinic hours have grown from four hours to 28 hours a week (Christopher Filley, MD, a CU neurologist working mainly at Veterans Affairs Medical Center in Denver, had been seeing UCH patients a half day a week, which he continues to do).

Potter aims to fuel continued growth with the establishment of a National Institute on Aging-funded Alzheimer's Disease Center at CU and UCH. In late May, Potter filed a 598-page application for the creation of a Rocky Mountain Alzheimer's Disease Research Center. There are 29 such centers in the United States, each aiming to translate scientific advances into improved patient care and, ultimately, prevention and cure of Alzheimer's disease. It's highly competitive: Potter anticipates the NIA will fund 12 to 14 centers this round; 12 existing centers are up for renewal and he knows of three new applicants, he said.

"It's zero-sum in terms of finances," Potter said. But he has been successful before, having applied for and established an Alzheimer's disease center at USF.

Down connection. The new center would have a special focus on the relationship between Alzheimer's disease and Down syndrome. Everyone with Down syndrome exhibits Alzheimer's disease neuropathology by age 40. But many – nearly 40 percent – never develop Alzheimer's-related dementia. Potter first suggested a mechanism for the Down-Alzheimer's connection in the early 1990s while a faculty member at the Harvard School of Medicine; in 2010, his research team detailed the relationship definitively. Put simply, many brain cells of patients with Alzheimer's disease show the same trisomy 21 aneuploidy (three, rather than two, chromosome 21s) as underlies Down syndrome. Moreover, Alzheimer's-related brain-cell death seems to be concentrated among these neurons.

The upshot, Potter said, is that those with Down syndrome offer a unique window into potential protective mechanisms that may one day help those with Alzheimer's pathology to avoid dementia.

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The proposed center would also have a special focus on American Indian and Hispanic/Latino populations. It would build on an expanding clinical and research core at CU, a process well underway.

Many trials. An upcoming trial involving Leukine *(see accompanying story, this issue)* is one example of new research into Alzheimer's at CU. A second clinical project, in collaboration with Tom Blumenthal, PhD, Director of the Linda Crnic Institute for Down Syndrome, is using a technology from Boulder-based SomaLogic, Inc. to screen roughly 3,300 proteins in plasma samples. The project is assessing biomarkers in subjects with and without Down syndrome and with and without Alzheimer's-associated cognitive impairment. The goal, Potter said, is to develop a blood-based fingerprint to identify people at risk of dementia.

Another research project, led by Mark DellAqua, PhD, is assessing the link between calcineurin signaling and the impact of beta-amyloid plaques in the brain that are the calling card of Alzheimer's – in animal models of the disease and in human brain samples. The hypothesis is that a particular protein helps beta-amyloid deposits interfere with calcineurin signaling, leading to diminished cognitive function. Should this prove true, the interaction could become a future therapeutic target.

In addition, CU neuro-ophthalmologist Victoria Pelak, MD, continues to develop virtual reality tools with the aim of early Alzheimer's disease diagnosis based on flawed visual processing.

Synergies. The clinical program's growth is "right on course," Woodcock said, to the point that the UCH Memory and Dementia Clinic now has a wait list of patients. He said the program aims to add a clinical-support person who can help patients connect with caretaker-training providers, day programs, home-care programs, residential facilities, and other services in the community.

The hospital is also planning to hire an additional nurse, and Woodcock said he would like to bring in a medical fellow starting in July 2015. With continued growth, an additional neurologist may also be in the cards, he said.

The boost in clinical capacity goes hand-in-hand with the expanding research enterprise Potter is driving. Alzheimer's patients and their families are hungry for clinical trials. Having a larger clinical population is helping present clear-cut patient cohorts for pharmaceutical companies wanting to test new therapies, Potter said.

"Obviously the NIA grant application is the big one, but there will be others also designed to increase clinical studies and services in the outpatient clinic," Woodcock said.