

Alzheimer's researchers call for clinical revamp

Current treatment options for Alzheimer's disease leave much to be desired. Existing medications, which either prevent the breakdown of neurotransmitters or modulate key receptors in the brain, can temporarily ease some of the cognitive decline associated with the disease, but they do nothing to halt or reverse its progression. And although scientists are developing new therapeutics that target the cause of the Alzheimer's more directly, even these latest experimental drugs might do little to help patients. To make headway, some Alzheimer's experts now argue that the research community must fundamentally change how it diagnoses the disease and designs clinical trials.

"The way we need to get at the disease is through prevention and through presymptomatic therapy, as opposed to classic therapy," says Dale Bredesen, a neurologist at the Buck Institute for Research on Aging in Novato, California.

According to the dominant dogma, Alzheimer's-induced memory loss is caused by a buildup of amyloid- β protein in the brain. The current thinking is that well before dementia manifests, protein aggregates

trigger a number of cellular changes that lead to irreversible neuronal injury. But the crux of the problem for drug development is that Alzheimer's is diagnosed long after this cellular damage occurs, so clinical trials of new drugs for the disease include only people for whom the underlying pathology is already beyond repair. According to this logic, treatments targeting amyloid protein—which are all at this point experimental, as none have been approved by drug regulators—might not do any good.

"What we really want to do is to prevent you from ever getting that head full of amyloid," says Todd Golde, a neuroscientist at the University of Florida College of Medicine in Gainesville. In January, Golde penned an opinion article arguing that drug makers and researchers need to adopt reliable biomarkers that predict Alzheimer's development on the basis of early cellular changes (*Neuron* 69, 203–213, 2011).

The Alzheimer's Association agrees: at its annual meeting in July 2010, the Chicago-based organization proposed new criteria—now being finalized—for diagnosing preclinical Alzheimer's using biomarkers.

Fortunately, tools for early detection might soon be on the market. For example, in January an advisory panel to the US Food and Drug Administration recommended approval of a new imaging agent called florbetapir, sold under the brand name Amyvid by Eli Lilly, which measures amyloid- β deposits in the brain during positron emission tomography (PET) scans.

Yet George Perry, a neuroscientist at the University of Texas–San Antonio, challenges the assertion that progress has been slow because of late diagnoses. Perry attributes the failure of most experimental Alzheimer's treatments—such as Lilly's semagacestat, which the Indiana-based drug maker announced in August worsened symptoms compared to placebo in large phase 3 trials—to the fact that drugs are being developed against the wrong target. Amyloid- β , he argues, may be a response to, rather than a cause of, the disease. "The amyloid theory was very appealing because it offered a therapeutic venue for intervention," Perry says. But "if amyloid was the sole cause of the disease, removing it should have had a beneficial effect."

Melinda Wenner Moyer

Facing budget cuts, Spain launches funding foundation

MADRID — In Spain, the government's overall spending on research is set to wither by about 8% this year, according to an analysis released last fall by the Confederation of Spanish Scientific Societies. Given the climate of budget cuts, it's perhaps no surprise that scientists there are turning to the public for funding.

Historically, Spain has fallen behind other nations in Europe when it comes to private giving for research. A Eurobarometer report published last summer said that 28% of people in the country reported having donated money to fundraising campaigns for medical research, below the EU average of 39%. By comparison, 78% and 70% of individuals surveyed in the Netherlands and UK said they had given money for these campaigns.

At a World Cancer Day event in Barcelona last month, Tony Kouzarides of the University of Cambridge, UK announced a new foundation called Vencer

el Cáncer (Vanquish Cancer), modeled after Cancer Research UK, a private not-for-profit nonprofit that distributed slightly more than £300 million (\$500 million) last year for research. "Even if we get, say, maybe just one tenth of this, this will allow us to start financing basic research in a very competitive way," says Vencer el Cáncer patron Miguel Beato, director of the Center for Genomic Regulation in Barcelona.

The duo say they will recruit external referees to evaluate research grant proposals and will also establish a translational arm, similar to that used by Cancer Research UK to help identify and evaluate commercial drug candidates that emerge from the research it funds. This type of translational vehicle is a "key instrument that is missing in Spain," Beato says.

Kouzarides, who serves on Cancer Research UK's science strategy advisory group, says that the organization will lend expertise, but no financial support, to

its Spanish counterpart. He has worked behind the scenes for the past three years, approaching prominent Spanish researchers to serve as advisers and recruiting over a dozen celebrities to record a television spot and shoot an ad campaign that will roll out across Spain this spring.

"We have a challenge to, first of all, convince the public that research leads to drugs, and to convince them that they can actually contribute to the running of this charity and solve cancer," says Kouzarides, who is not Spanish himself but is married to a researcher from Spain. Convincing people to dig into their pocketbooks might be tough, though: unemployment in Spain remains at more than 20%.

"Society and business must take part in supporting research," says Esther Diez Muñiz, spokesperson for the Madrid-based Spanish Association Against Cancer, the country's biggest cancer foundation. Beato agrees, noting, "we are also convinced that we cannot just lean on government money."

Lucas Laursen