

## Profile

### Tom Bird: one of the world's first experts in neurogenetics



Speaking to *The Lancet Neurology* from his home in Seattle, Tom Bird has much to be proud of in a career stretching back more than half a century. Bird set up the first neurogenetics clinic for adults in the USA at the University of Washington (Seattle, WA) in 1974, and since then has worked tirelessly to unravel the genetic secrets of many neurological diseases.

Born and raised in western New York state, USA, he wanted to emulate his grandfather who was a respected country physician. He studied psychology at Dartmouth College (Hanover, NH, USA) before completing his medical degree at Cornell University's New York City campus (NY, USA). "When working a summer job as an orderly on a locked psychiatric ward, my experience with schizophrenia and depression left me fascinated with the brain", says Bird. This further extended to neurology after working with eminent neurologist Fred Plum on sleep disorders and coma during his time at Cornell University. Bird then did his internship and residency at the University of Washington, which suited his Northwest-born wife Rosaline, with whom he has just celebrated their golden wedding anniversary. Apart from two years with the United States Navy in San Diego (CA, USA), Seattle was to be Bird's home. "I love the natural beauty and cannot imagine living anywhere else", he explains.

As a fellow in Seattle, he studied with Arno Motulsky, seeing for the first time many genetic disorders in adults, including Charcot-Marie-Tooth disease and Huntington's disease. Bird completed a 2-year fellowship with the medical genetics group, during which he established the first adult neurogenetics clinic—still in existence today—with a particular focus on Charcot-Marie-Tooth disease, ataxia, and Huntington's disease. He was also a general neurologist at the Veterans Affairs Hospital in Seattle (now known as VA Puget Sound Health Care System), later becoming chief of neurology for 12 years. In his research, he continued to plough into neurogenetics, using genetic linkage analysis to move his theories forward. "Back then no-one knew what genes looked like", Bird explains. "There were only methods to estimate where genetic problems lay, on which chromosome."

In the days before the availability of modern DNA analysis, he teamed up with a genetic statistician and a genetic biologist to perform a linkage study on Charcot-Marie-Tooth disease. "Although this condition affects peripheral nerves and muscles, it's not fatal, making it ideal for a linkage study having several generations of the family alive at the same time." His team identified linkage to chromosome 1 in the early 1980s; this discovery was later confirmed in 1993 when technological advances led to discovery of mutations in the *MPZ* gene for Charcot-Marie-Tooth disease type 1. This discovery accelerated Bird's career, and he extended the multidisciplinary approach to other conditions, including

frontotemporal dementia and familial Alzheimer's disease. Working with Gerard Schellenberg, Ellen Wijsman, and Ephrat Levy-Lahad at the University of Washington, Bird did another linkage study on Alzheimer's disease in which they identified families with early-onset Alzheimer's disease confirmed by autopsy. "There were sometimes 15 to 20 people affected in three or four generations", explains Bird. While other researchers found the *APP* and *PSEN1* variants underlying early-onset Alzheimer's disease, Bird's team discovered *PSEN2* in 1995. "The families affected were Germans who had settled in the Volga River region of Russia. All of them were distant cousins of one another, connected by the [*PSEN2*] gene." In 1998, Bird's team and two groups in the UK co-discovered mutations in *MAPT*, the tau protein gene responsible for one form of frontotemporal dementia.

Using the same collaborative strategy with more sophisticated technology and working with University of Washington geneticists Wendy Raskind and Dong-Hui Chen, this team discovered mutations in the *PRKCG* gene responsible for spinocerebellar ataxia type 14, mutations in the *SAMD9L* gene causing ataxia with pancytopenia, and mutations in the *ADCY5* gene responsible for an intriguing combination of chorea and dystonia. "After reporting our findings that the *ADCY5* gene was responsible, we suddenly discovered that there were many other cases, not only in the USA but worldwide", says Bird. He continues to be delighted to discover the genetic causes of diseases in families that he has been following more than 30 or 40 years.

Today, Bird's focus is on Alzheimer's disease since the three dominant genes discovered thus far only represent around 2% of cases. "Science needs to sort out the other 98%", he says. "There are likely many other genes, each contributing only a very small amount to risk. The human genome has so much variety it's hard to distinguish what's benign from what could be causing disease. It's a key problem in today's research." Despite his busy schedule, he also spends considerable time mentoring fellows and junior faculty members to help jumpstart their careers. While he remains dedicated to research, he is attempting to have more down time visiting his children and grandchildren all living on the East Coast of the USA.

"Tom Bird is unique in having made discoveries related to several major areas of neurogenetics," says Roger N Rosenberg, Professor of Neurology and Neurotherapeutics and Physiology, University of Texas Southwestern Medical Center (Dallas, TX, USA). "His diversity of interests and remarkable creativity continuously for 50 years establishes him at the very forefront of neurogeneticists."

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*Lancet Neurol* 2018

Published Online  
February 5, 2018  
[http://dx.doi.org/10.1016/S1474-4422\(18\)30004-8](http://dx.doi.org/10.1016/S1474-4422(18)30004-8)

For the study linking Charcot-Marie-Tooth disease to chromosome 1 see *Am J Hum Genet* 1982; 34: 388–94

For the study proposing *PSEN2* as a candidate gene for familial Alzheimer's disease see *Science* 1995; 269: 973–77