

STANLEY PRUSINER

NOBEL LAUREATE IN NEUROSCIENCE

Saad Shaqat

Aga Khan University

There is so much in the story of Stan Prusiner and his discovery of prions that inspires and illuminates. In the face of overwhelming opposition from peers, he set out on a long and lonely walk against the winds of biological dogma. His guiding light was the discipline of rigorous scientific method and the unassailable logic of scientific reasoning.

Prusiner's interest in "slow virus" infections was triggered by a clinical encounter during his neurology residency at University of California at San Francisco (UCSF). Once during an on-call night in the summer of 1972, he admitted a patient with progressive memory loss and myoclonus. She was diagnosed with Creutzfeldt-Jakob disease (CJD) and Prusiner's professors told him this was a mysterious condition presumably caused by a "slow virus" infection. 'The amazing properties of the presumed causative agent captivated my imagination and I began to think that defining the molecular structure of this elusive agent might be a wonderful research project,' Prusiner later wrote.

His first hurdle was a research plan, and the second was funding. Scrapie, a "slow virus" infection well described in sheep, provided a natural animal model for experiments. It was, however, considered a dull topic for investigation and research grants were hard to secure. But Prusiner toughed it out and began studies to characterize the properties of the putative infectious agent.

The hypothesis was that scrapie is caused by a viral particle, but a series of unexpected results began appearing. According to Prusiner's data, the infectious material contained protein but no nucleic acid, which flew in the face of established paradigms. These puzzling research conclusions coincided with a very difficult time in Prusiner's career when his research support from the Howard Hughes Medical Institute was not renewed, and he was turned down for promotion to tenure at UCSF, where he had stayed on as faculty. 'It was the unwavering, enthusiastic support of a few of my closest colleagues that carried me through this very trying and difficult period,' wrote Prusiner about this time of ordeal.



Stanley Prusiner

Fortunately, the tenure decision was reversed and funding came through from an alternative source. After a few years of painstaking experimentation, Prusiner felt he had thoroughly confirmed his findings. "Identification of a protein that purifies with the scrapie prion" by Bolton, McKinley and Prusiner appeared in *Science* in December 1982, and provoked a firestorm.

The remainder of Prusiner's career has been devoted to verifying this revolutionary discovery and overcoming the misplaced hostility and resistance of the scientific community. The battle has been sweetly won. Prions are now universally accepted as transmissible proteins causing diseases such as CJD, bovine spongiform encephalopathy, fatal familial insomnia and, of course, scrapie. In 1997, the Nobel Committee honored Dr. Prusiner with the Nobel Prize in Physiology or Medicine for "his discovery of prions - a new biological principle of infection."