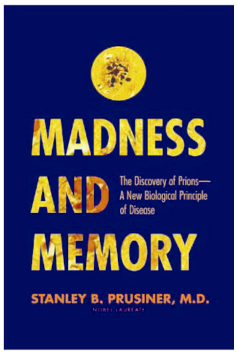

Madness and Memory: The Discovery of Prions – A New Biological Principle of Disease. Stanley B. Prusiner. Yale University Press, New Haven, USA. 2014. 344 pp. Price: US$ 30.

Prion diseases constitute a class of transmissible spongiform encephalopathies (TSEs) that correspond to fatal neurodegenerative disorders in both humans and animals and are manifested as infectious, genetic and sporadic diseases. A well-known candidate in this class is the mad cow disease or bovine spongiform encephalopathy that is infectious to humans. The human version of mad cow is known as Creutzfeldt–Jakob disease (CJD) that was first reported in the 1920s. The other widely characterized disease is scrapie in sheep and was initially reported in the 18th century in Europe. A common mechanistic thread has now been established between mad cow, scrapie and other TSEs in animals and CJD, kuru, fatal familial insomnia and Gerstmann–Sträussler–Scheinker syndrome in humans. A historical account on the TSEs reveals that in order to describe the unusual biological properties of the scrapie agent, the 'slow virus' hypothesis was just beginning to be accepted during the 1960s and 1970s. Stanley Prusiner serendipitously entered into the field in the 1970s, broke the status quo, revolutionized the understanding, solved the mystery and created an entirely new paradigm that challenged the tenets of modern biology. The identification and elucidation of molecular details of the causative (scrapie) agent of TSEs by Prusiner represent a fascinating saga in modern biomedical science that has been chronicled by him in this book.

This book is a first-person account providing a fascinating description of the development of the prion story that represents a disruptive and discontinuous quantum leap in modern biology. It starts with a preface, introduction and a brief narration of his childhood days. The chapter on 'The beginning of an odyssey' describes how he came upon the research problem in 1972 during his residency at UCSF, USA. One day, the hospital page operator summoned him to say that he was assigned a patient for evaluation of a rapidly progressive dementia, which was later diagnosed as CJD. This fortuitous call would later change his scientific career for the few decades to follow and would revolutionize the biological paradigm. He beautifully describes his harrowing journey through the scrapie field which was at that time populated with a torrent of conjectures concerning the composition of the scrapie form exhibiting unusual radiation resistance. In the midst of many plausible structural hypotheses, Prusiner decided to purify the scrapie agent and identify its molecular composition using an array of diligent and elegant approaches akin to chemists' approach that turned out to be a daunting task. He then recollects how his journey was impeded by an undisciplined approach from a different laboratory that claimed to have discovered DNA viroid as the infectious agent. Also, he had to wait for nearly three years to visit New Guinea and examine the kuru patients, which was absolutely critical for his investigation at that time. The narration of the surrounding events, academic politics behind him and many interesting scientific characters and peers, both supportive and unsupportive, during the entire course of his investigation is simply astonishing. He rightly says, 'there were times when little but my naïveté and exuberance sustained me'. He then describes his fascinating journey that led to the discovery of the novel protein and states as to how an astounding amyloid story unravelled in his laboratory. His tedious, painstaking and meticulous experiments that spanned two decades ruled out the slow viruses hypothesis and revealed that the disease causing scrapie agent is an aberrant (misfolded) form of an endogenous protein, which he termed as the prion protein, devoid of any genetic material such as nucleic acids. Naming the protein as the prion protein is a quite interesting story in itself. He constructed a two-dimensional matrix with 'i-n-f-e-c-t-i-o-u-s' along the *X*-axis and 'p-r-o-t-e-i-n' along the *Y*-axis and after considering many possibilities he finally came up with 'prion', with a pronunciation 'pree-on'. A line of investigations revealed that the misfolded isoform of the prion protein has an unusual (conformational) replication property by which it recruits the correctly folded native form and stimulates (deadly) conformational switch through aggregation and culminates into ordered amyloid aggregates. This autocatalytic chain reaction converts the (benign) good form ('Dr Jekyll') into the (infectious) bad form ('Mr Hyde') through binding, misfolding and corrupting events that can account for its infectivity. For this groundbreaking discovery, in 1997, Prusiner was awarded the Nobel Prize for Physiology or Medicine. Similar prion-like mechanism is now believed to underlie a number of debilitating protein-folding disorders such as Alzheimer's and Parkinson's diseases that are characterized by amyloid deposits that ravage and riddle the brain. Interestingly, more recent studies have shown that the prion-like amyloid mechanisms could serve as functional 'information transfer' means, for instance long-term memory, in many organisms.

This book narrates many interesting stories that depict the genesis of an extraordinary phenomenon in modern biological sciences and the ultimate triumph of an invincible spirit. This memoir captures Prusiner's extraordinary passion, emotions, drawn-out and strenuous battle for tenure/grants/laboratory space and his perseverance against formidable skepticism and hostile reactions. In his book he rightly says, 'I feared that neither science historians nor journalists could construct an accurate narrative of my investigations.' This enthralling book is written for non-specialists with little or no formal background in biology. This book is a must read, not just for specialists, but for every practitioner of science. This story will act as a powerful stimulus to the younger generation of scientists, especially students, postdocs and assistant professors who are willing to take up challenging research problems in their scientific career.

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