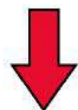
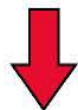


Prion Diseases – Historical Perspective

Discovery that Kuru was transmitted through ritualistic consumption of human brains

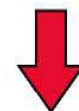


**D. Carleton Gajdusek
NIH intramural
researcher**



Nobel Prize, 1976

Discovery of prion protein and its essential role in TSE disease



**Stanley Prusiner
University of California
at San Francisco
(NIH grantee)**



Nobel Prize, 1997

Transmissible Spongiform Encephalopathies (TSEs) or Prion Diseases

- **Rare and fatal neurodegenerative diseases of humans and other animals**
- **Called “spongiform” because of the pathological appearance of degenerative holes in the brain resembling the holes in a sponge together with the appearance of fibrils made up of abnormal prion proteins**
- **Symptoms of dementia and ataxia**
- **Rapidly progressive**
- **No treatment**

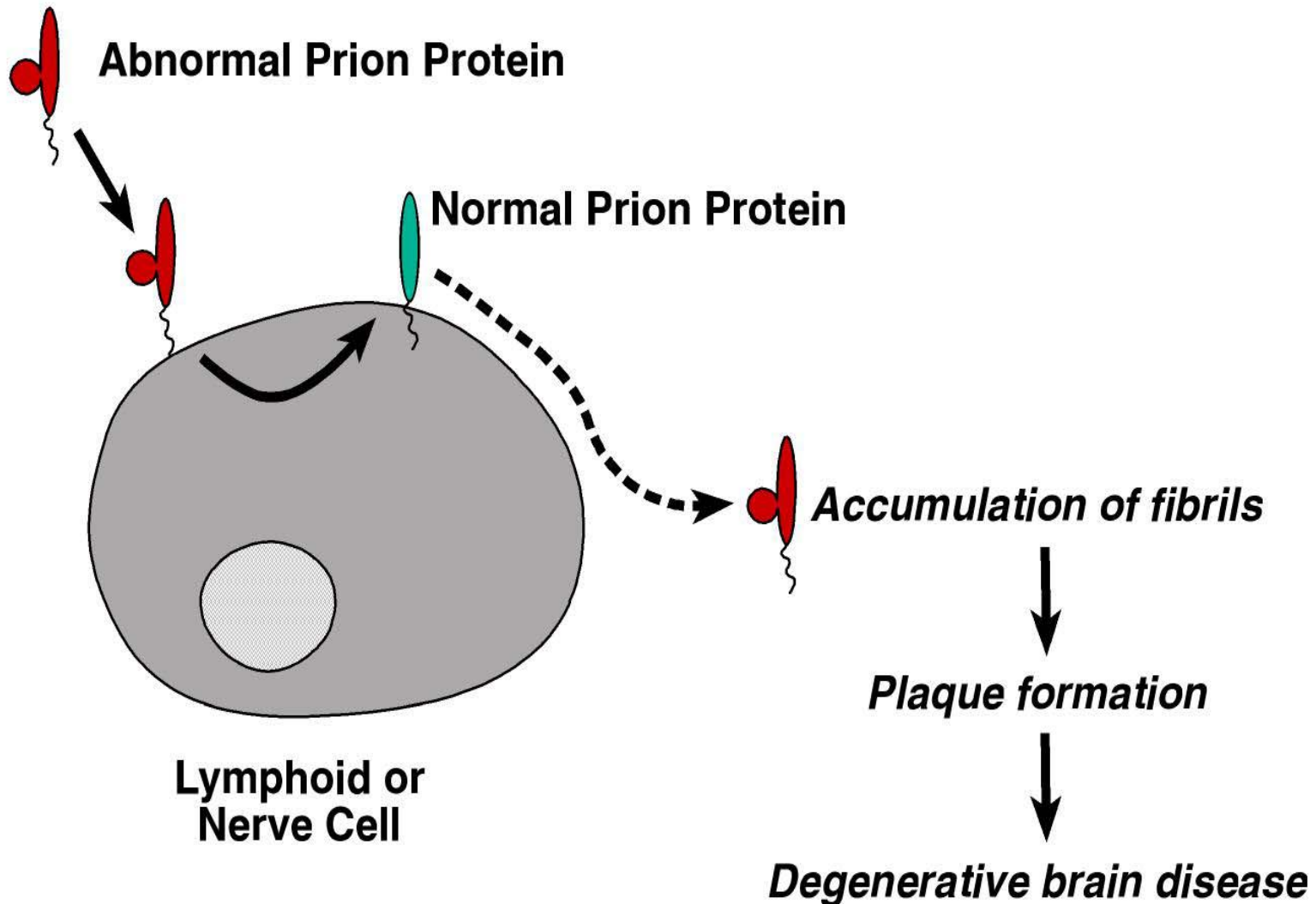
Transmissible Spongiform Encephalopathies (TSEs) in Animals

- **Scrapie – sheep**
- **Bovine spongiform encephalopathy (BSE)**
- **Chronic wasting disease (CWD) – deer and elk**
- **Transmissible mink encephalopathy (TME)**
- **Species barriers and experimental animals – chimpanzees, mice, hamsters, etc.**

Human Transmissible Spongiform Encephalopathies (TSE)

- **Sporadic Creutzfeldt-Jacob Disease (CJD)**
 - Incidence – 1:1,000,000
 - No Prion Protein (PrP) mutation
 - No known exposure to infectious agent
- **Familial TSEs**
 - Familial CJD; Gertsman-Straussler-Scheinker Syndrome; Fatal Familial Insomnia
 - Associated with PrP mutations
 - No known exposure to infectious agent
- **Infectious TSEs**
 - Variant CJD – associated with bovine spongiform encephalopathy (BSE)
 - Kuru
 - Iatrogenic (transmitted via contaminated growth hormone, corneal transplants, neurosurgical instruments)
 - Known exposure to infectious agent

Abnormal Prion Protein Formation in a TSE-Infected Cell



NIH-Supported Research on Transmissible Spongiform Encephalopathies (TSEs)

FY 2004 (est.) = \$33.2M

- **Discovery of prion protein**
- **Development of antibody test for detection of abnormal prion protein in TSE brain**
- **Identification of essential role of prion protein in TSE susceptibility and cross-species transmission**
- **Development of TSE-infected cell cultures**
- **Use of infected cultures for drug discovery**

Future NIH Research Agenda on Transmissible Spongiform Encephalopathies (TSEs)

- **Pathogenesis** – mechanisms of transmission of prion disease (species barriers)
- **Diagnostics** – in animals and humans prior to onset of disease
- **Therapeutics** – drug screening and targeted drug development
- **Prevention** - vaccines