Prion Diseases – Historical Perspective

Discovery that Kuru was transmitted through ritualistic consumption of human brains

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D. Carleton Gajdusek

NIH intramural researcher

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Nobel Prize, 1976

Discovery of prion protein and its essential role in TSE disease

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Stanley Prusiner

University of California at San Francisco (NIH grantee)

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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

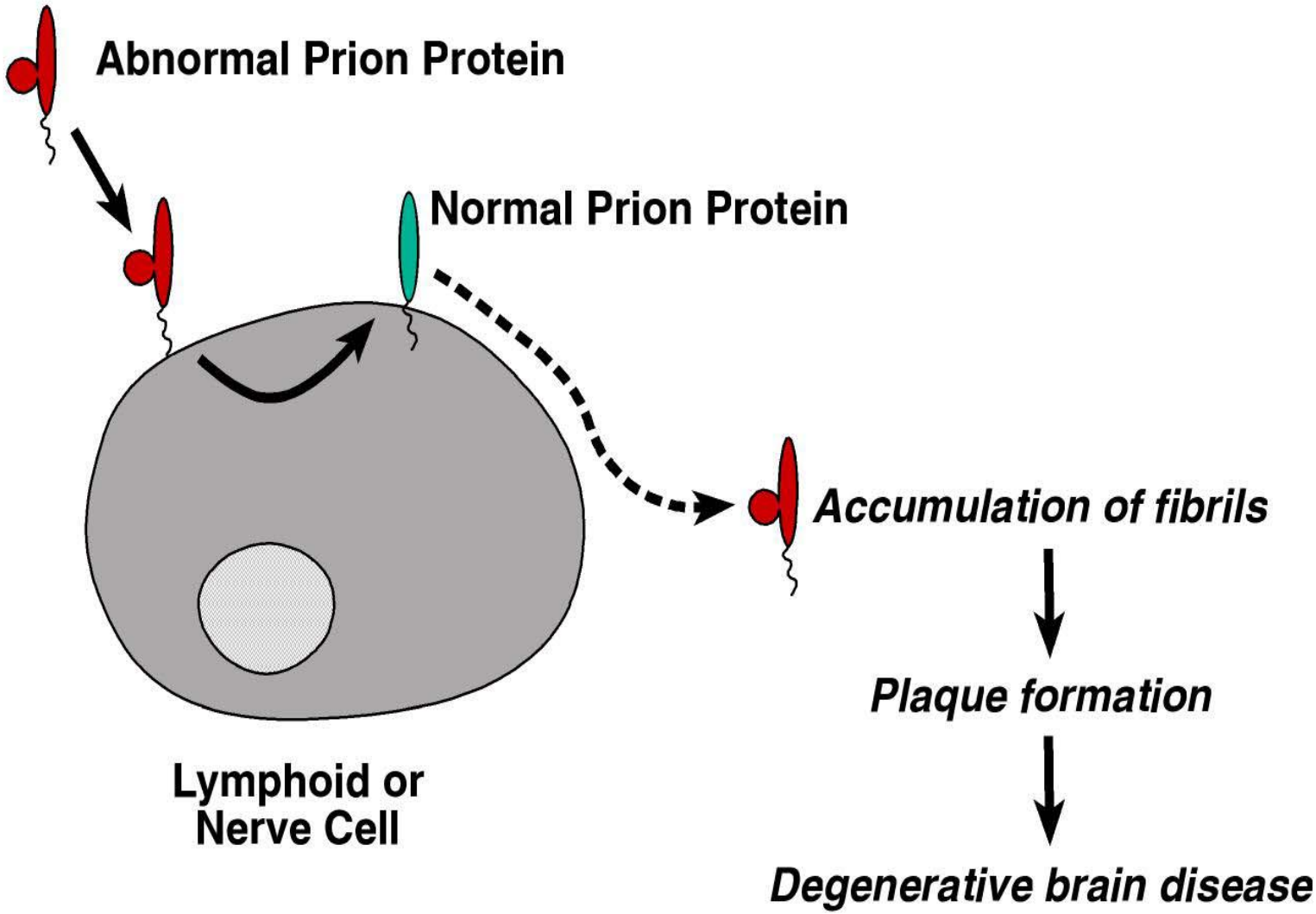
Transmissible Spongiform Encephalopathies (TSEs) in Animals

- 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; Gertsmann-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