

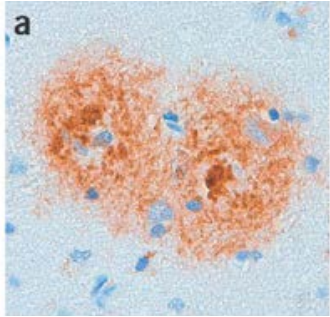
The Seeds of Neurodegenerative Disorders

ADC Meeting

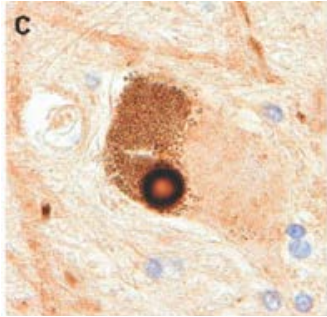
New Orleans 2012

Protein misfolding and aggregation is a common feature of neurodegeneration

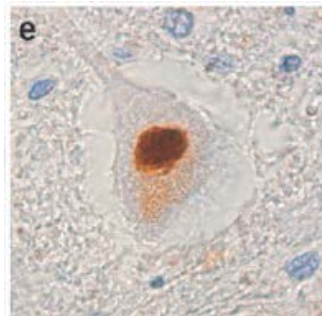
Alzheimer



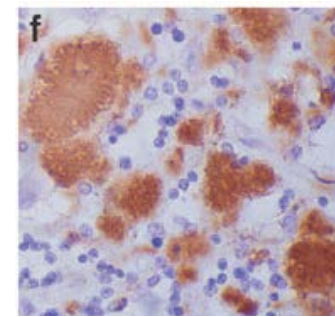
Parkinson



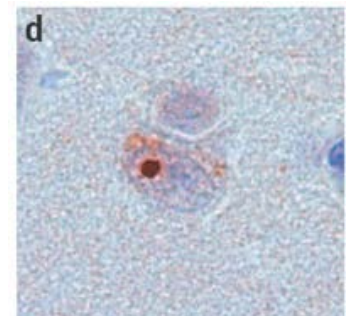
Amyotrophic lateral sclerosis



Creutzfeldt-Jakob



Huntington



Amyloid- β plaques

α -synuclein bodies

TDP-43 inclusions

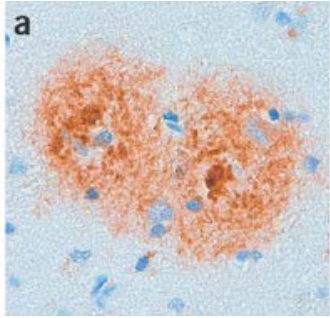
PrP^{Sc} plaques

Poly-Q inclusions

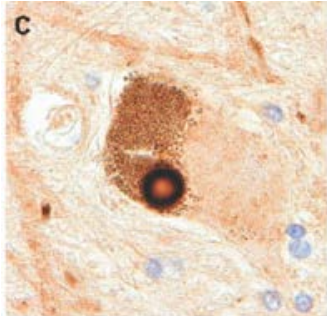
Modified from Forman et al, Nature Medicine, 2006

Protein misfolding and aggregation is a common feature of neurodegeneration

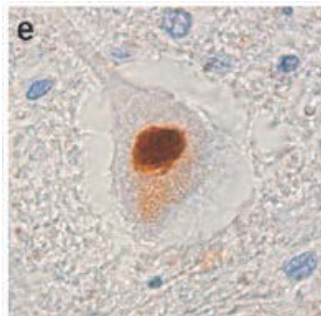
Alzheimer



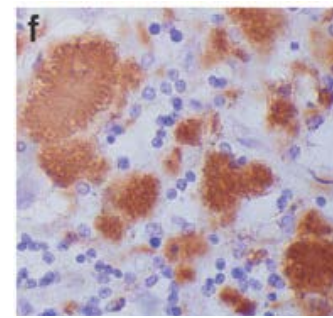
Parkinson



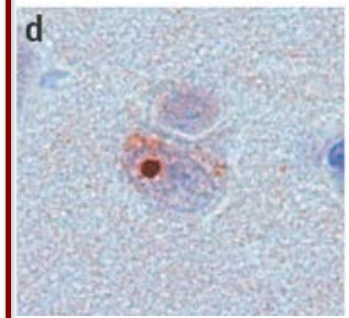
Amyotrophic lateral sclerosis



Creutzfeldt-Jakob



Huntington



Amyloid- β plaques **α -synuclein bodies**

TDP-43 inclusions

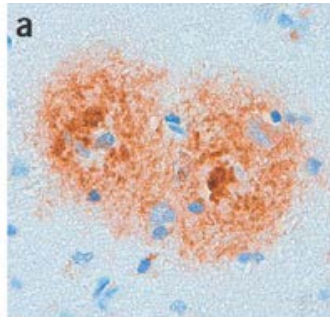
PrP^{Sc} plaques

Poly-Q inclusions

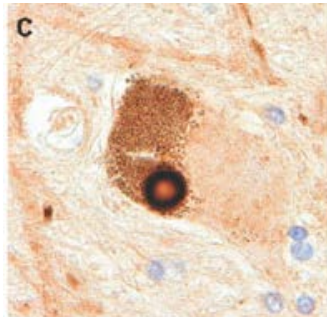
Modified from Forman et al, Nature Medicine, 2006

Protein misfolding and aggregation is a common feature of neurodegeneration

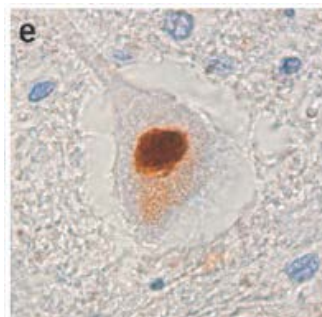
Alzheimer



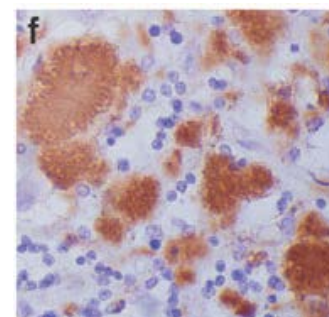
Parkinson



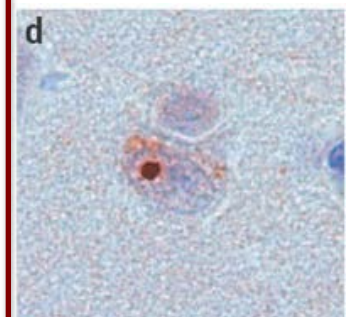
Amyotrophic lateral sclerosis



Creutzfeldt-Jakob



Huntington



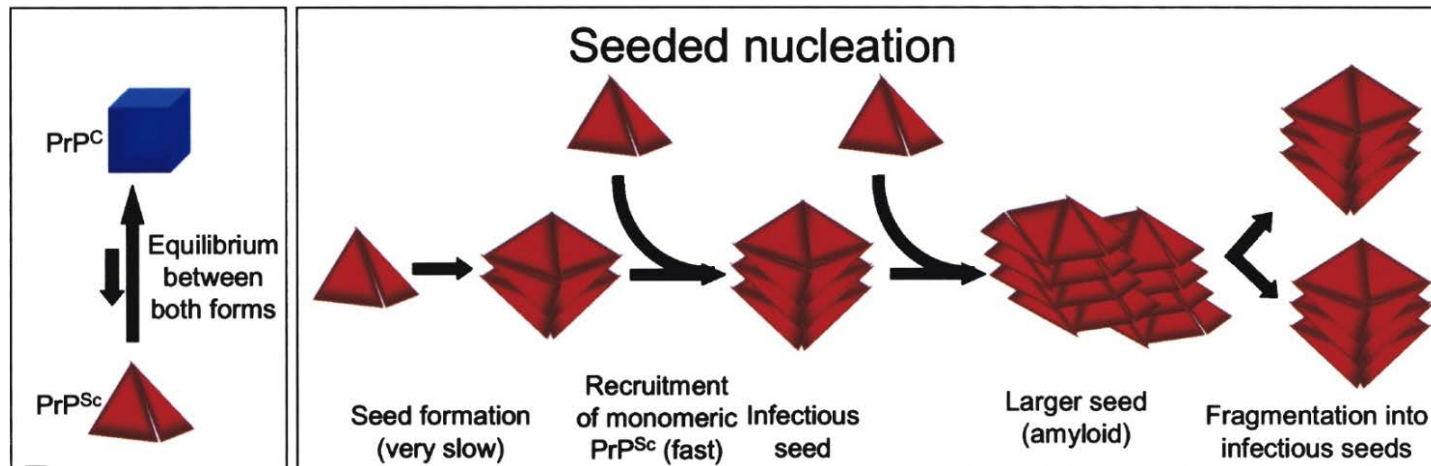
Amyloid- β plaques α -synuclein bodies

TDP-43 inclusions

PrP^{Sc} plaques

Poly-Q inclusions

Modified from Forman et al, Nature Medicine, 2006



Aguzzi and Polymenidou, Cell, 2004

Prion-like phenomena occur in several neurodegenerative diseases

| Aggregated Protein or Peptide | Main Associated Diseases in Humans | Acquired by Infection in Humans |
|-------------------------------|------------------------------------|---------------------------------|
| PrP ^{Sc} | variant or iatrogenic CJD, Kuru | yes |
| | sporadic CJD, GSS, FFI | no |
| Tau | FTLD, Alzheimer | no |
| α -synuclein | Parkinson | no |
| β -amyloid | Alzheimer | no |
| Poly-Q | Huntington | no |
| | spinocerebellar ataxias | no |
| SOD1 | ALS | no |
| TDP-43 | ALS, FTLD | no |
| FUS/TLS | ALS, FTLD | no |

Prion-like phenomena occur in several neurodegenerative diseases

| Aggregated Protein or Peptide | Main Associated Diseases in Humans | Acquired by Infection in Humans | Seeded Aggregation | | |
|-------------------------------|------------------------------------|---------------------------------|--------------------|-----------------|-----------------|
| | | | In Vitro | in Cell Culture | In Vivo in Mice |
| PrP ^{Sc} | variant or iatrogenic CJD, Kuru | yes | yes | yes | yes |
| | sporadic CJD, GSS, FFI | no | | | |
| Tau | FTLD, Alzheimer | no | yes | yes | yes |
| α -synuclein | Parkinson | no | yes | yes | yes |
| β -amyloid | Alzheimer | no | yes | yes | yes |
| Poly-Q | Huntington | no | yes | yes | n.d. |
| | spinocerebellar ataxias | no | | | |
| SOD1 | ALS | no | yes | yes | n.d. |
| TDP-43 | ALS, FTLD | no | yes | yes | n.d. |
| FUS/TLS | ALS, FTLD | no | n.d. | n.d. | n.d. |

Prion-like phenomena occur in several neurodegenerative diseases

| Aggregated Protein or Peptide | Main Associated Diseases in Humans | Acquired by Infection in Humans | Seeded Aggregation | | | Cell-to-Cell Spreading | |
|-------------------------------|------------------------------------|---------------------------------|--------------------|-----------------|-----------------|------------------------|-----------------|
| | | | In Vitro | in Cell Culture | In Vivo in Mice | in Cell Culture | In Vivo in Mice |
| PrP ^{Sc} | variant or iatrogenic CJD, Kuru | yes | yes | yes | yes | yes | yes |
| | sporadic CJD, GSS, FFI | no | | | | | |
| Tau | FTLD, Alzheimer | no | yes | yes | yes | yes | yes |
| α -synuclein | Parkinson | no | yes | yes | yes | yes | yes |
| β -amyloid | Alzheimer | no | yes | yes | yes | no | yes |
| Poly-Q | Huntington | no | yes | yes | n.d. | yes | n.d. |
| | spinocerebellar ataxias | no | | | | | |
| SOD1 | ALS | no | yes | yes | n.d. | yes | n.d. |
| TDP-43 | ALS, FTLD | no | yes | yes | n.d. | n.d. | n.d. |
| FUS/TLS | ALS, FTLD | no | n.d. | n.d. | n.d. | n.d. | n.d. |

Seeds of Neurodegenerative Disorders

- Lary Walker, Emory University
- Karen Duff, Columbia University
- Marc Diamond, Washington University
- Bradley Hyman, Mass General, HMS
- John Trojanowski, University of Pennsylvania