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Review article

Mechanisms and pathology of protein misfolding and aggregation

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Supplementary information

Mechanisms and pathology of protein misfolding and aggregation

Nikolaos Louros[1,2], *Joost Schymkowitz*[1,2,#] *and Frederic Rousseau*[1,2,#]

[1] Switch Laboratory, VIB-KU Leuven Center for Brain & Disease Research, Herestraat 49, 3000 Leuven, Belgium

[2] Department of Cellular and Molecular Medicine, KU Leuven, Herestraat 49, box 802, 3000 Leuven, Belgium

e-mail(s): Joost.schymkowitz@kuleuven.be, Frederic.rousseau@kuleuven.be

corresponding authors

Includes Supplementary Table 1

Table 1. Representative amyloid-associated pathologies or functions and the proteins and aggregation-prone regions (APRs) related to their formation.

Protein	Structural properties	Experimental APRs	Pathology/Function
Pathological Amyloid			**Pathology**
Apolipoprotein A I	Globular, all-α	14-22, 53-58, 69-72, 227-232[1,2]	ApoAI Amyloidosis
Apolipoprotein A II	Globular, all-α		ApoAII Amyloidosis
Apolipoprotein A IV	Globular, all-α		ApoAIV Amyloidosis
Apolipoprotein C II	Globular, all-α	19-37, 57-64[3]	ApoCII Amyloidosis
Apolipoprotein C III	Globular, all-α		ApoCIII Amyloidosis
Transthyretin	Globular, all-β	12-17, 25-33, 37-52, 65-73, 80-85, 91-96, 105-112, 119-124[2,4]	Transthyretin amyloidosis (ATTR)
β2-microglobulin	Globular, Ig-like fold	54-59[5], 60-66[6]	Dialysis-related amyloidosis, Hereditary visceral amyloidosis
Aβ peptide (Aβ)	IDP	16-21[2,7,8], 29-34[2,8], 35-42[2,7,8]	Alzheimer's Disease (AD), Cerebral Amyloid Angiopathy (CAA)
α-Synuclein (αS)	IDP	35-41, 47-56, 63-79, 86-91[2,8]	Multiple system atrophy (MSA), Parkinon's Disease (PD)
Tau	IDP	275-280[9,10], 305-311[9,10], 326-331[9], 337-342[11], 350-362[9]	Alzheimer's Disease (AD), Pick's Disease (PiD), Chronic Traumatic Encephalopathy (CTE), Corticobasal Degeneration (CBD), Argyrophilic grain disease (AGD), Progressive supranuclear palsy (PSP)
Prion protein (PrP)	IDP	170-175[2,8]	Creutzfeldt-Jakob disease (CJD), Gerstmann-Sträussler-Scheinker disease (GSS)
Transmembrane 106B (TMEM106B)	Transmembrane		Frontotemporal lobar degeneration diseases (FTLD)
Islet amyloid polypeptide (IAPP)	IDP	8-18[12], 22-27[8]	Type-II Diabetes (T2D)
Insulin	all-α	36-41 (β-chain)[8], 57-87 (C-chain)[13]	Iatrogenic Amyloidosis
Medin	IDP	7-25[14], 31-43[15]	Cerebral Amyloid Angiopathy (CAA), Aortic amyloid
Proteins S100A8/A9	All-α, EF hand-like fold	8-19, 70-80 (predicted)[16]	Prostate cancer
TDP-43	Globular (NTD, RNA recognition motifs RRM1, RRM2), Disordered C-terminal domain	300-306, 321-326, 328-333, 333-343, 370-375, 396-402[17]	Frontotemporal lobar degeneration diseases (FTLD), Amyotrophic Lateral Sclerosis (ALS)
Huntingtin	All-α, (disordered poly Q)	poly Q expansions[18]	Huntington's Disease (HD)
Ataxin-7	Globular, core histone-like	poly Q expansions[19]	Spinocerebellar ataxia-7 (SCA7)
C9orf72	Globular (longin, DENN folds)	Dipeptide expansion repeats (GA), (GR), (PA), (PR), (GP)[20]	Frontotemporal lobar degeneration diseases (FTLD), Amyotrophic Lateral Sclerosis (ALS)
Serum amyloid A (SAA)	Globular, All-α, SAA-like four-helix bundle		Secondary amyloidosis (AA)
Immunoglobulin light chain	Globular, Ig-like fold	variable[21]	Light chain or Primary Amyloidosis (AL)
Functional Amyloid			**Function**
Merozoite surface protein 2 (MSP2)	IDP	1-25[22]	P. falciparum coating
Sup35	IDP	7-13[23], 103-113[24]	Yeast prion
Zona pellucida proteins	Globular, Ig-like fold	variable[25-27]	Mammalian oocyte coats
RIPK1/RIPK3		532-549 (RIPK1), 448-462 (RIPK3)[28]	Necrosome complex
PMEL		405-413[29]	Melanin synthesis
hnRNPDL-2		226-276[30]	Reversible fibrillation, Nucleic acid binding
HET-s	β-solenoid		Heterokaryon incompatibility
Major/Minor curli subunits (CsgA / CsgB)	β-solenoid	45-50, 47-52, 129-134, 137-142 (CsgA)[2,31] / 46-52, 67-72, 89-93, 112-117, 135-139, 144-148 (CsgB)[32]	Biofilm formation
Synaptic translation regulator Orb2			Long-term memory

β-endorphin			Endogenous opioid neuropeptide
Phenol soluble modulins (PSM-α)	cross-α / cross-β	1-22[33]	Biofilm formation

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