

Нейродегенерация без границ

Клубок протеинопатий

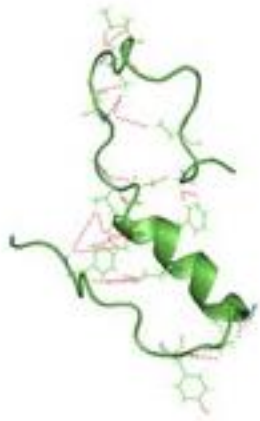


Зоопарк нейродегенераций

Disease Group	Protein	Disease Type	Form	Phenotype
AD	Tau, A β	AD	SP/GEN	DEM
Tauopathy (FTLD-Tau *)	Tau	PiD	SP	FTD
		GGT	SP	FTD
		CBD	SP	MD/FTD
		PSP	SP	MD/FTD
		AGD	SP	DEM
		NFT-dementia/PART FTDP-17T	SP GEN	DEM FTD/MD
TDP-43 proteinopathy	TDP-43	FTLD-TDP (type A–D)	SP/GEN	FTD
		MND-TDP	SP/GEN	MD
		FTLD-MND-TDP	SP/GEN	FTD-MD
FUS (FET)-proteinopathy FTLD/MND-FUS (FET)	FUS/FET	aFTLD-U, NIFID, BIBD	SP	FTD/MD
		MND-FUS	GEN	MD
α -Synucleinopathy	α -Synuclein	PD	SP/GEN	MD
		DLB	SP/GEN	DEM/MD
		MSA	SP	MD
Prion disease	PrP	sCJD, VPSPr, sFI	SP	DEM/MD
		iCJD	ACQ	DEM/MD
		vCJD	ACQ	DEM/MD
		Kuru	ACQ	DEM/MD
		gCJD, GSS, FFI, PrP-CAA	GEN	DEM/MD
TRD **	Huntingtin	HD	GEN	MD
	Ataxin 1, 2, 3, 7, CACNA1A, TBP	SCA 1, 2, 3, 6, 7, 17	GEN	MD
	FMRP	FXTAS	GEN	MD
	ARP	SBMA	GEN	MD
	Atrophin-1	DRPLA	GEN	MD
Other forms	Ferritin	Hereditary ferritinopathy	GEN	DEM/MD
	Neuroserpin	Neuroserpinopathy	GEN	DEM
	ABri, ADan, gelsolin, cystatin, transthyretin, A β	Hereditary amyloidoses/CAA	GEN	DEM
	Only UPS	FTLD-UPS	GEN	FTD
	Not determined	FTLD-ni	SP	FTD
	Tau, α -Synuclein	NBIA	GEN	DEM/MD
	Tau, a-Synuclein, TDP-43	Various genetic and sporadic diseases (“secondary” proteinopathy forms)	SP/GEN	DEM/MD

Проблемные белки

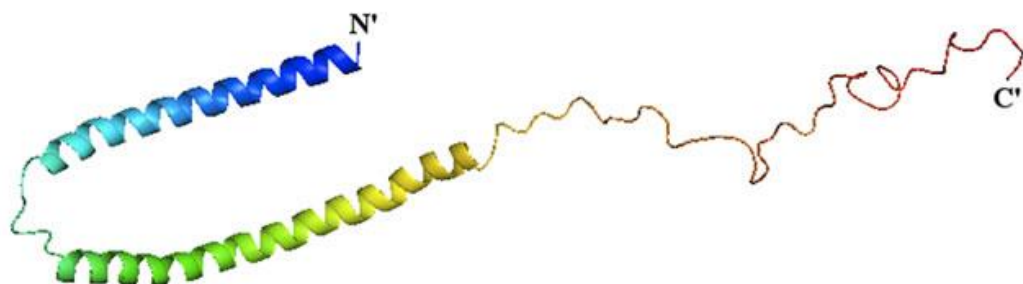
β -амилоидный
пептид



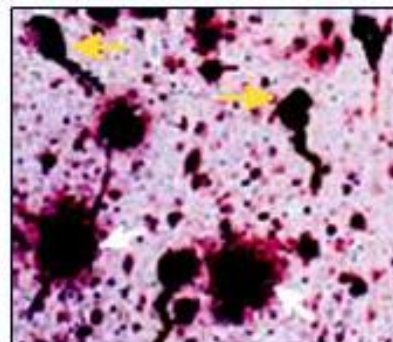
TDP-43



α -синуклеин

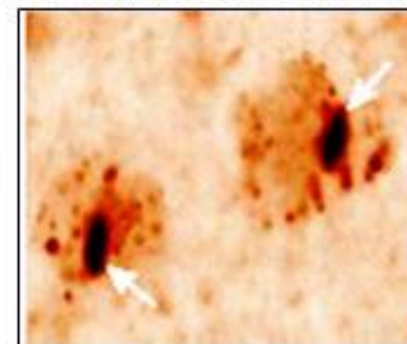


Alzheimer's



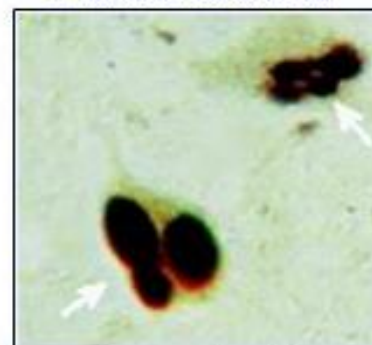
Plaques and tangles

PolyQ diseases



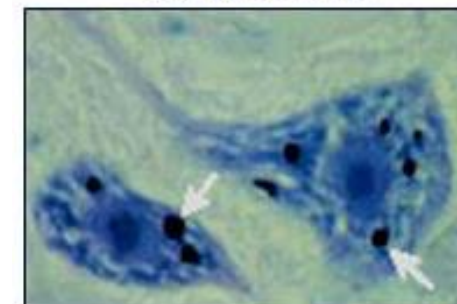
Intranuclear inclusions

Parkinson's



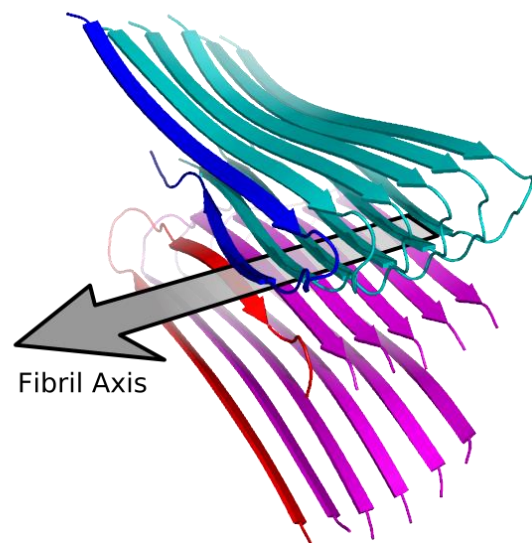
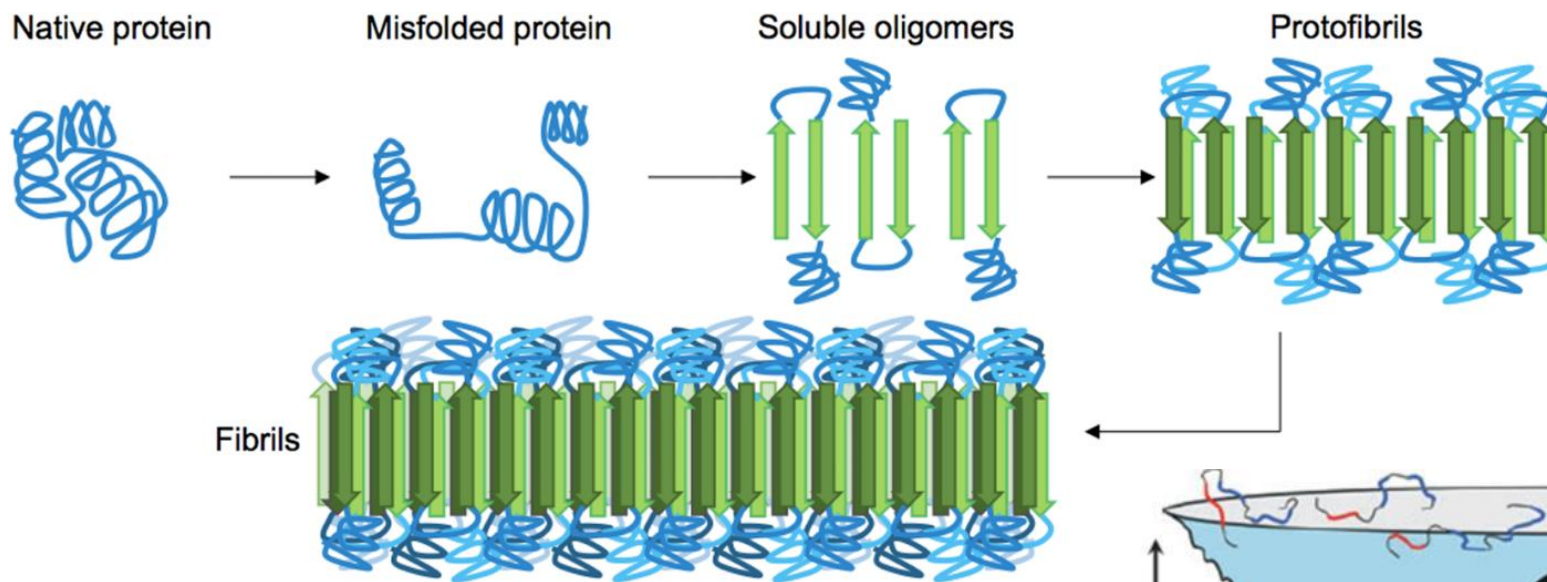
Lewy bodies

**Amyotrophic lateral
sclerosis**

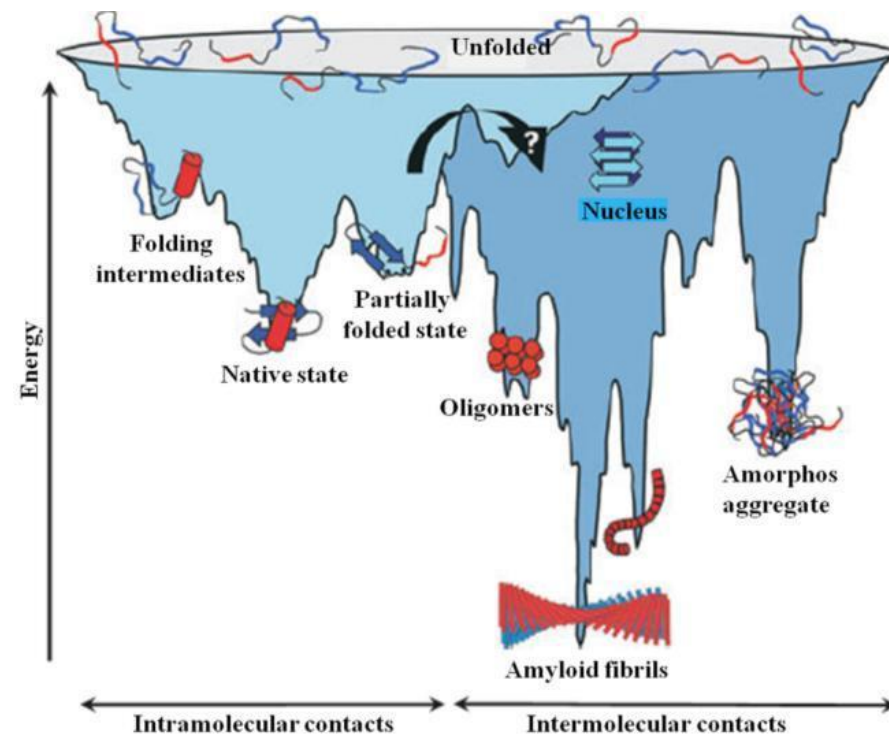


Aggregates

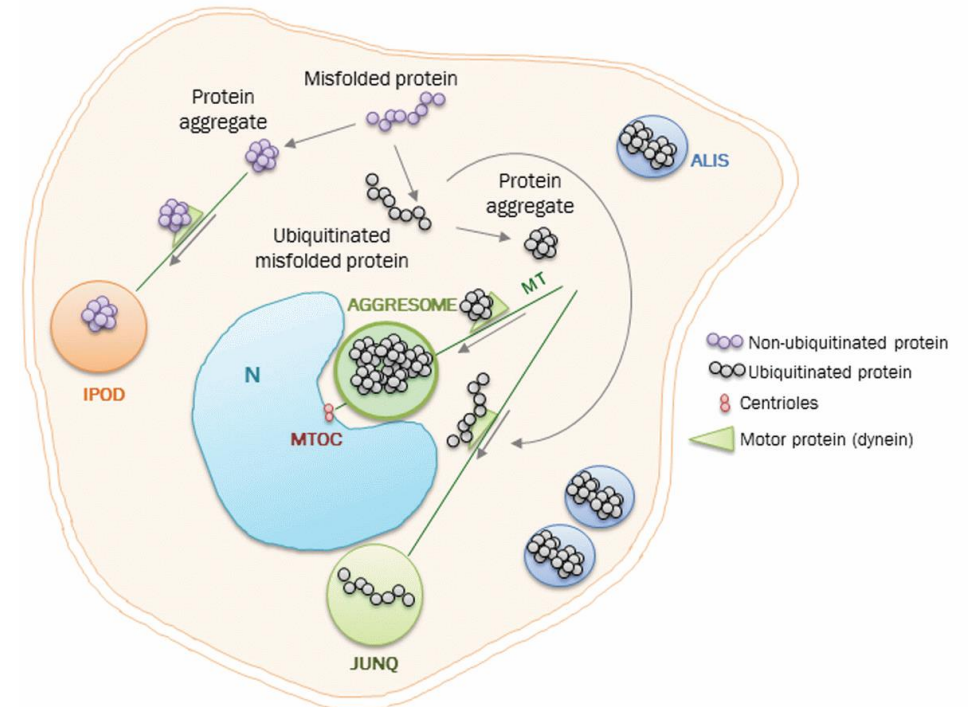
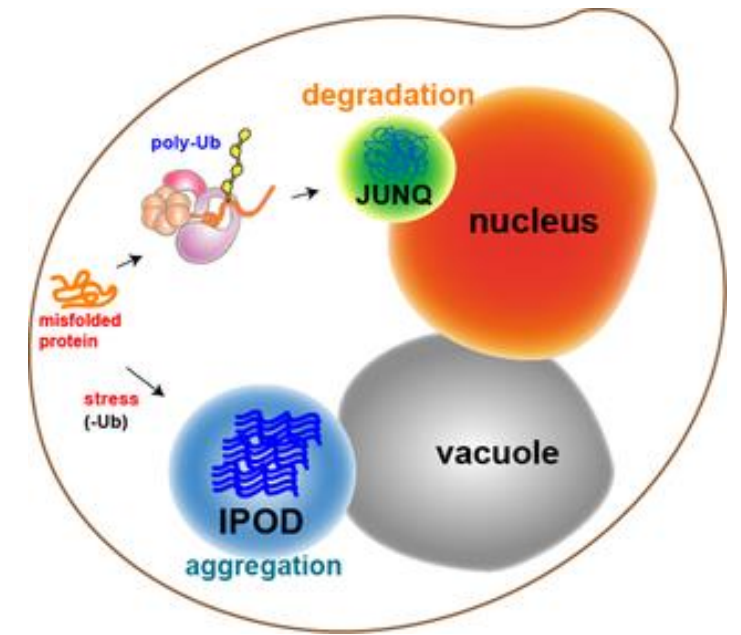
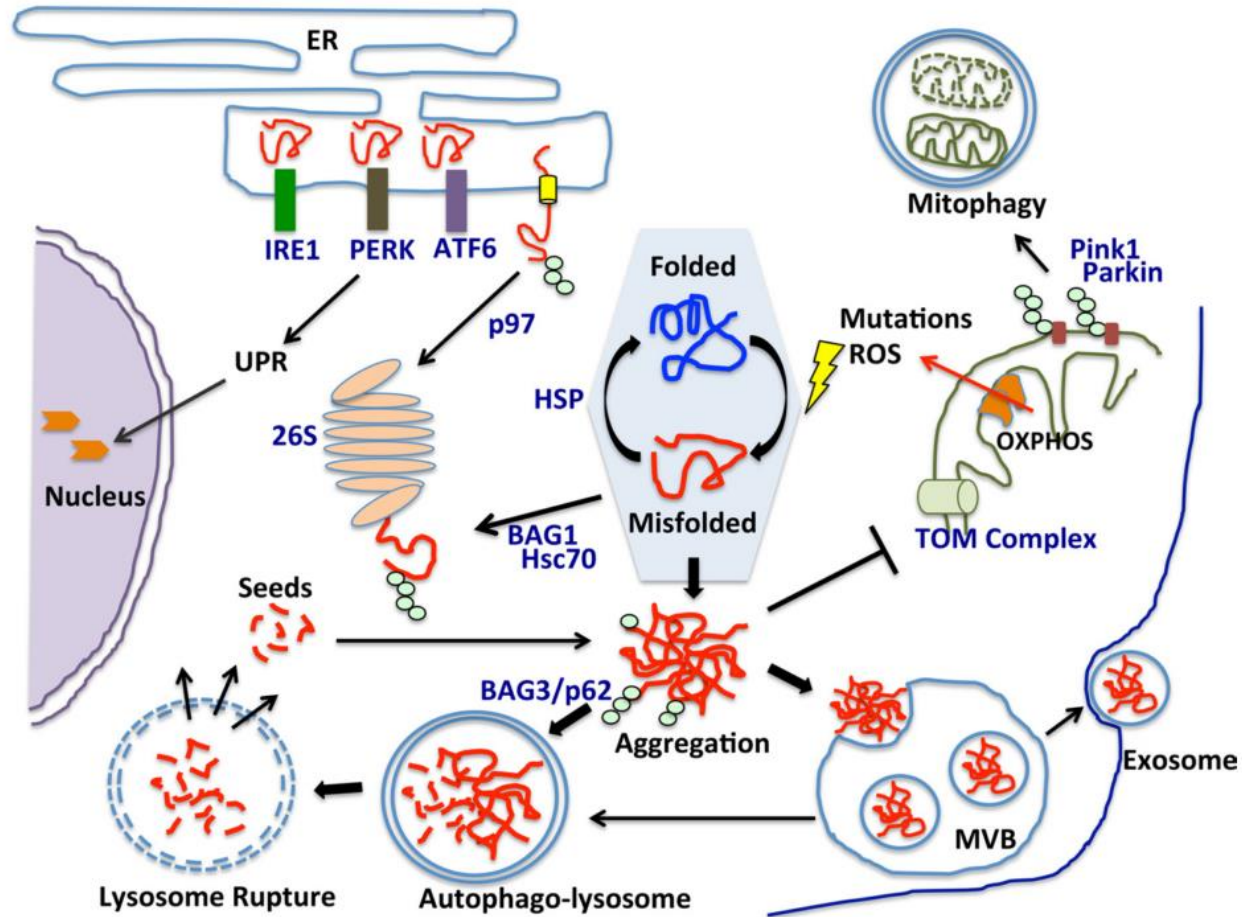
Биофизика мисфолдинга

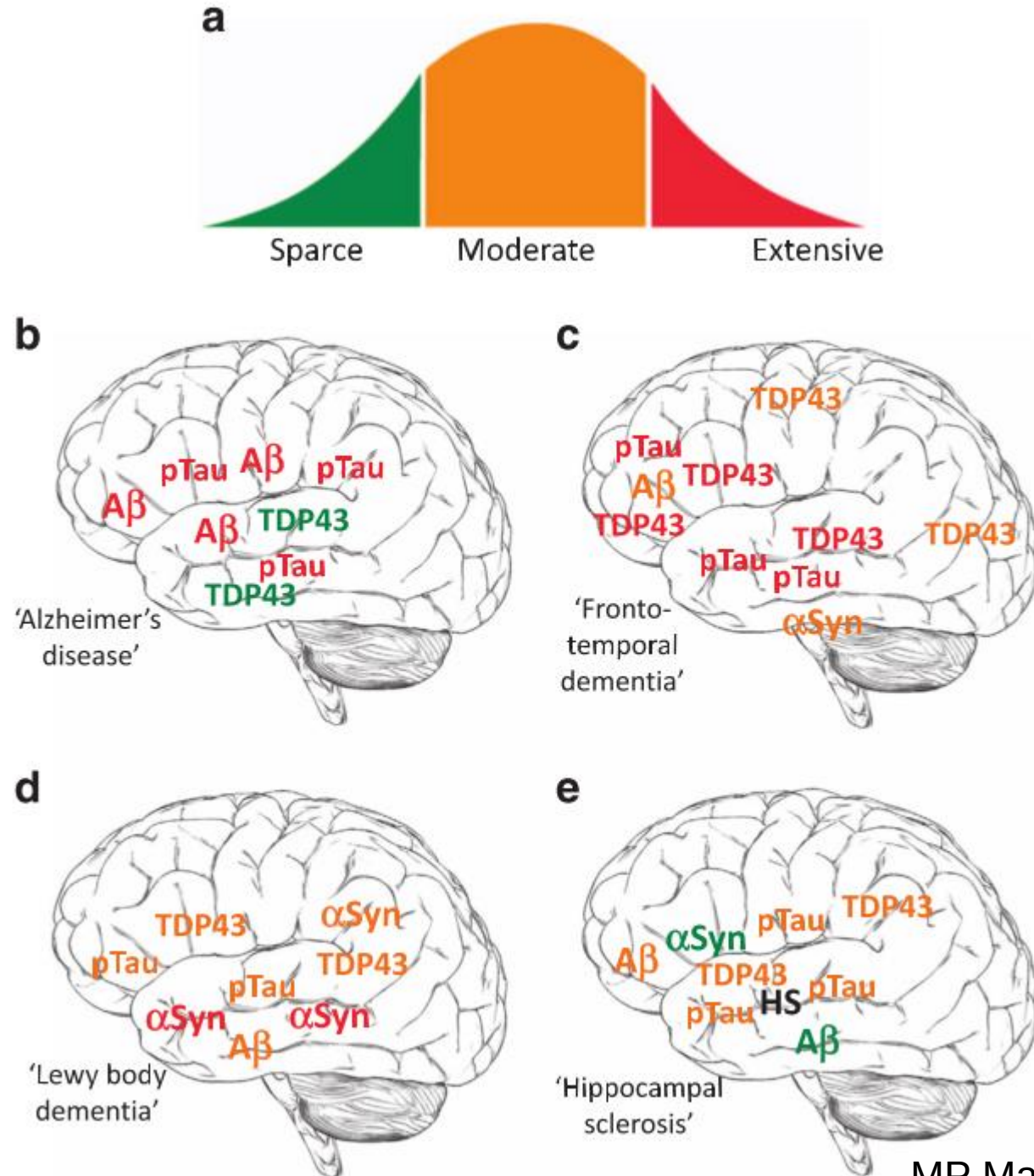
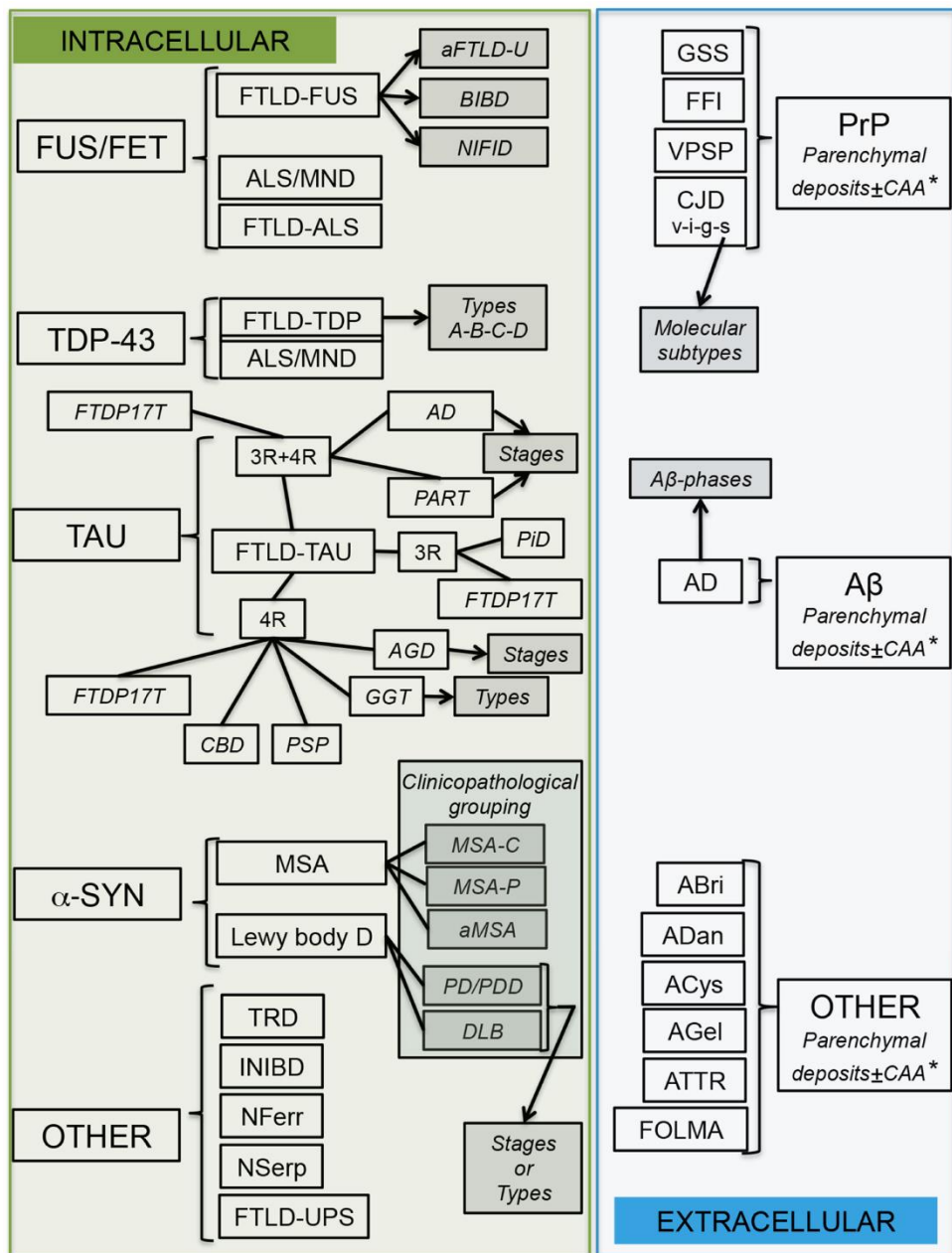


Образование
гидрофобных
cross-beta sheets –
основа необратимой
агрегации белков

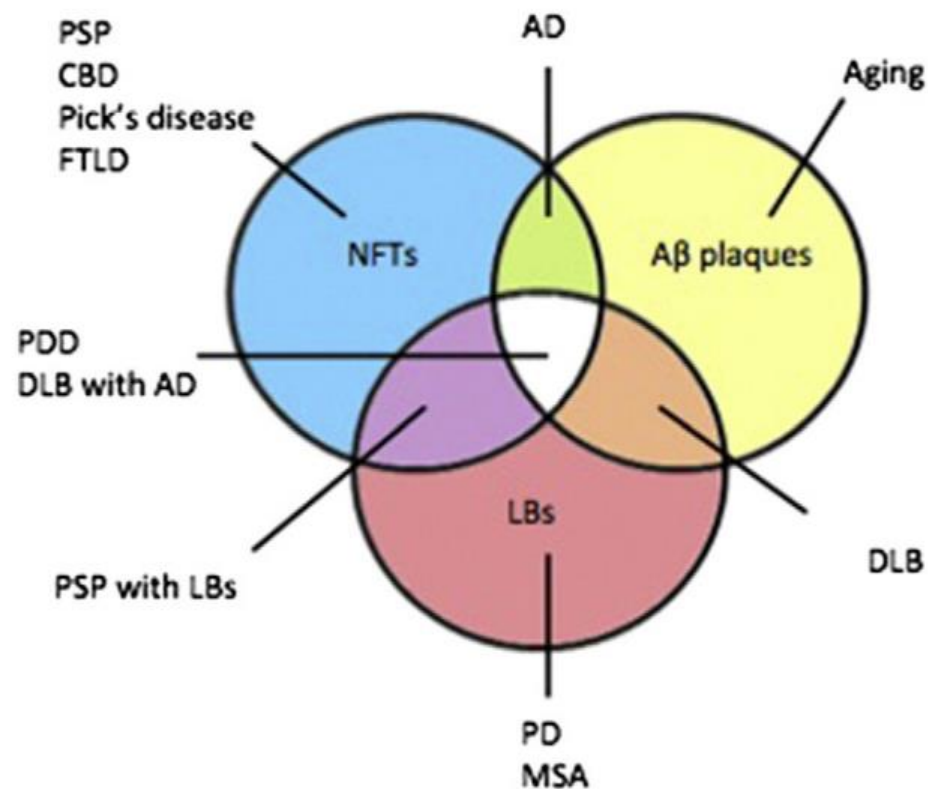


Защитная роль включений

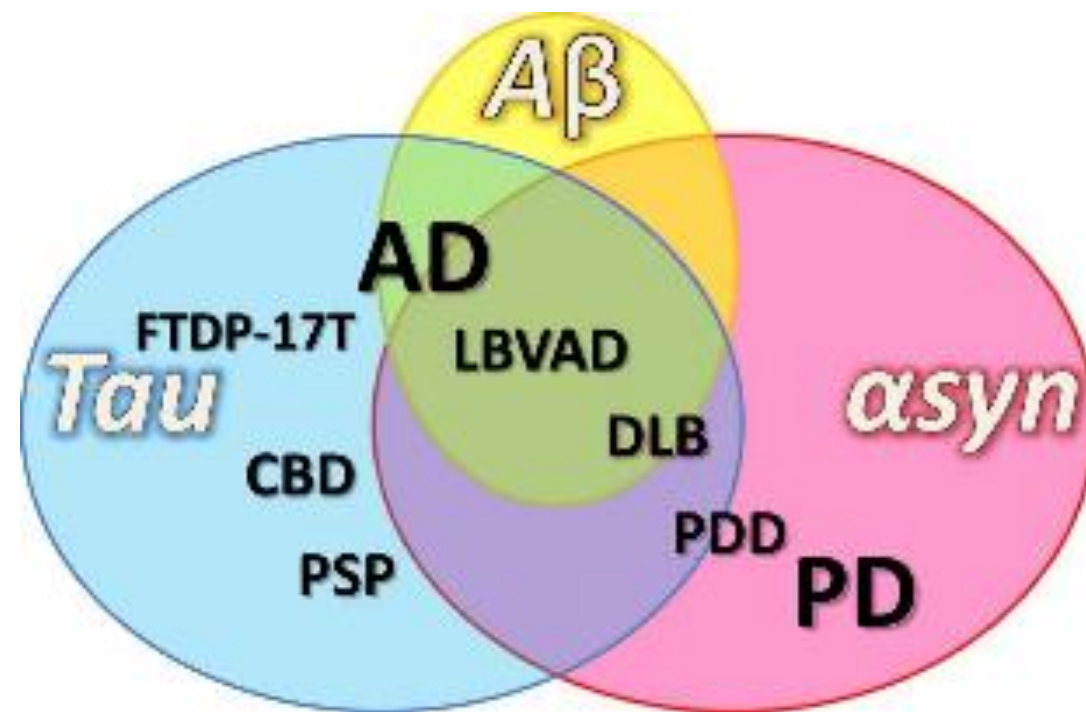




«Фазовое пространство» нейродегенераций

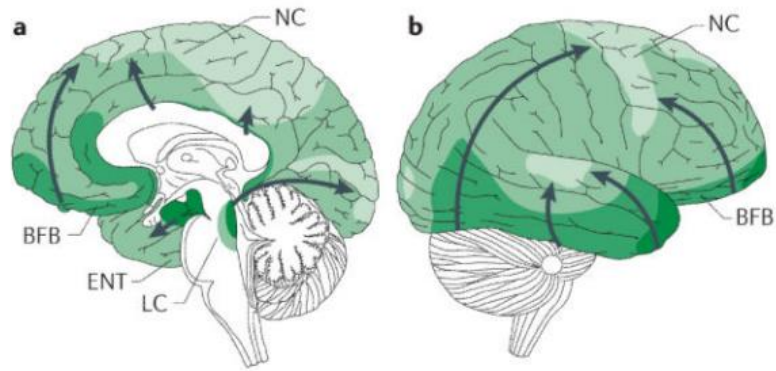


C Swart - 2014

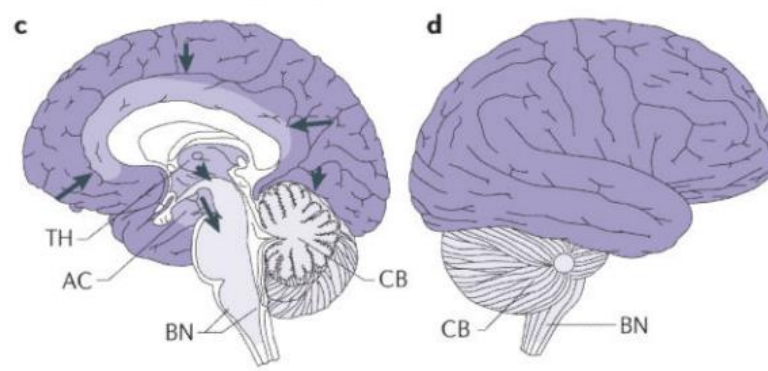


S Moussaud - 2014

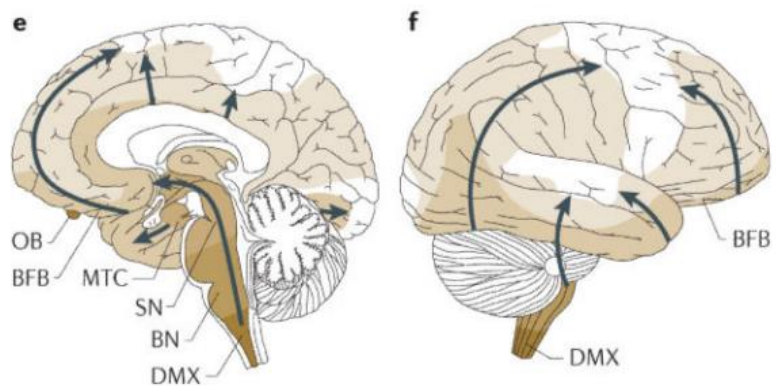
Alzheimer disease: tau



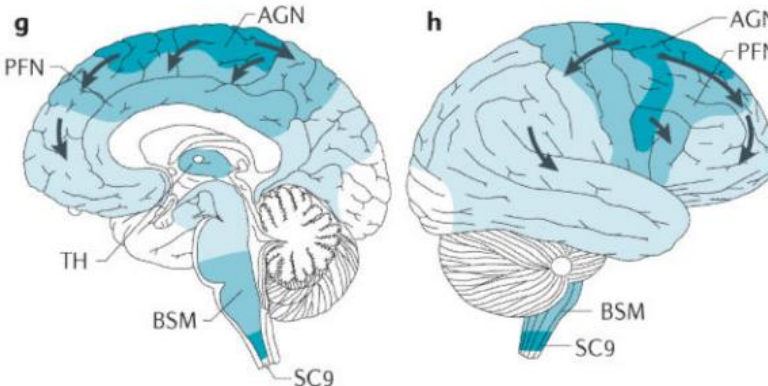
Alzheimer disease: amyloid- β



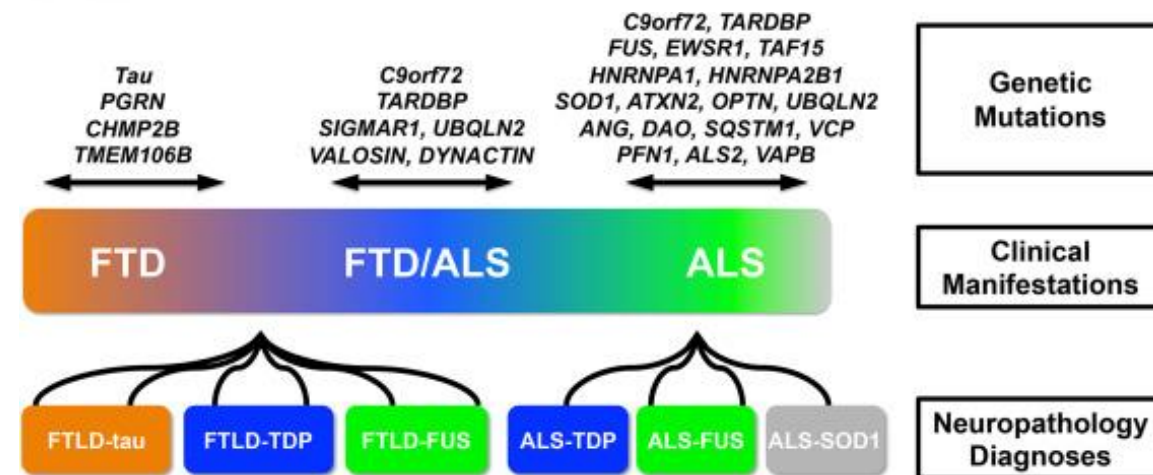
Parkinson disease: α -synuclein



Amyotrophic lateral sclerosis: TDP43

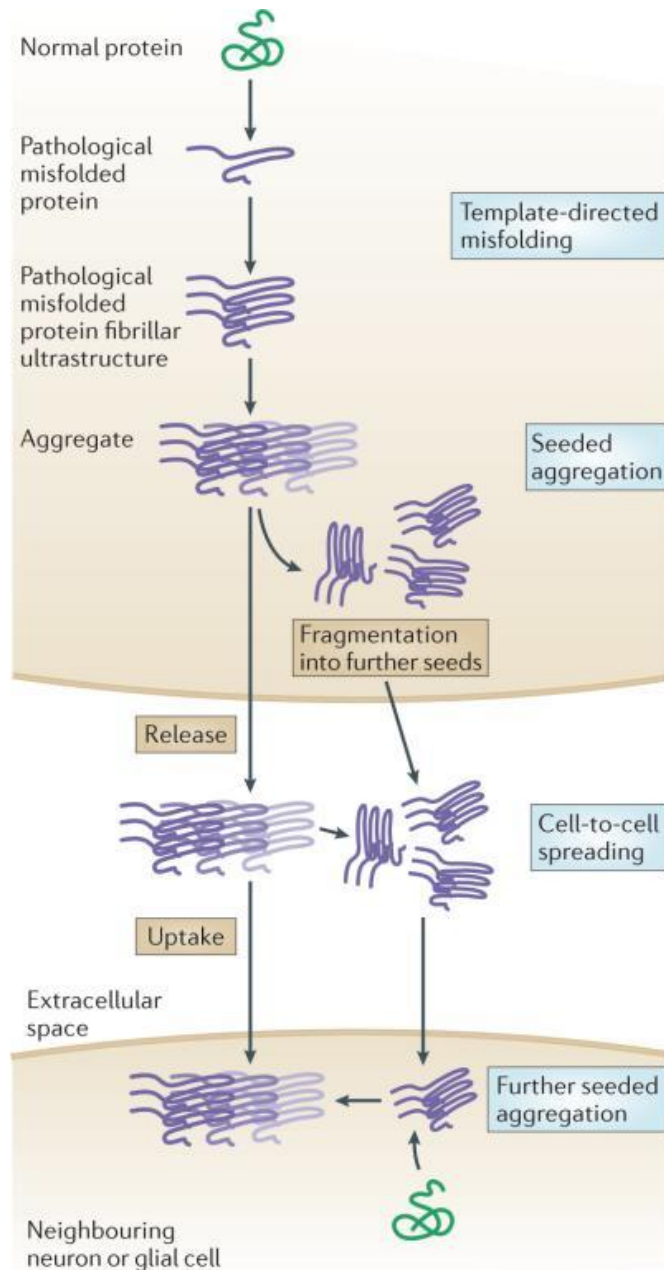


J Brettschneider - 2015



S Lee - 2017

Прионно-подобное распространение патологии



nature
REVIEWS **NEUROSCIENCE**

Access provided by Institute of Cytology and Genetics of SB RAS



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Review Article

Spreading of pathology in neurodegenerative diseases: a focus on human studies

Johannes Brettschneider, Kelly Del Tredici, Virginia M.-Y. Lee & John Q. Trojanowski

nature
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Opinion

A critical appraisal of the pathogenic protein spread hypothesis of neurodegeneration

Dominic M. Walsh & Dennis J. Selkoe

AGING



Impaired bioenergetics
Impaired calcium Handling
Oxidative damage
Impaired autophagy
Inflammation



PROTEIN AGGREGATION/TOXICITY
A β
Tau
TDP-43
 α -Synuclein



Impaired adaptive
stress responses
Reduced neurotrophic
support



Synapse dysfunction
Synapse degeneration
Neuronal death



DEMENTIA

