FUNDAMENTALS OF MEDICAL BIOCEMISTRY.

Lecture #1. Introduction to Medical Biochemistry. Protein Misfolding. Enzymopathies

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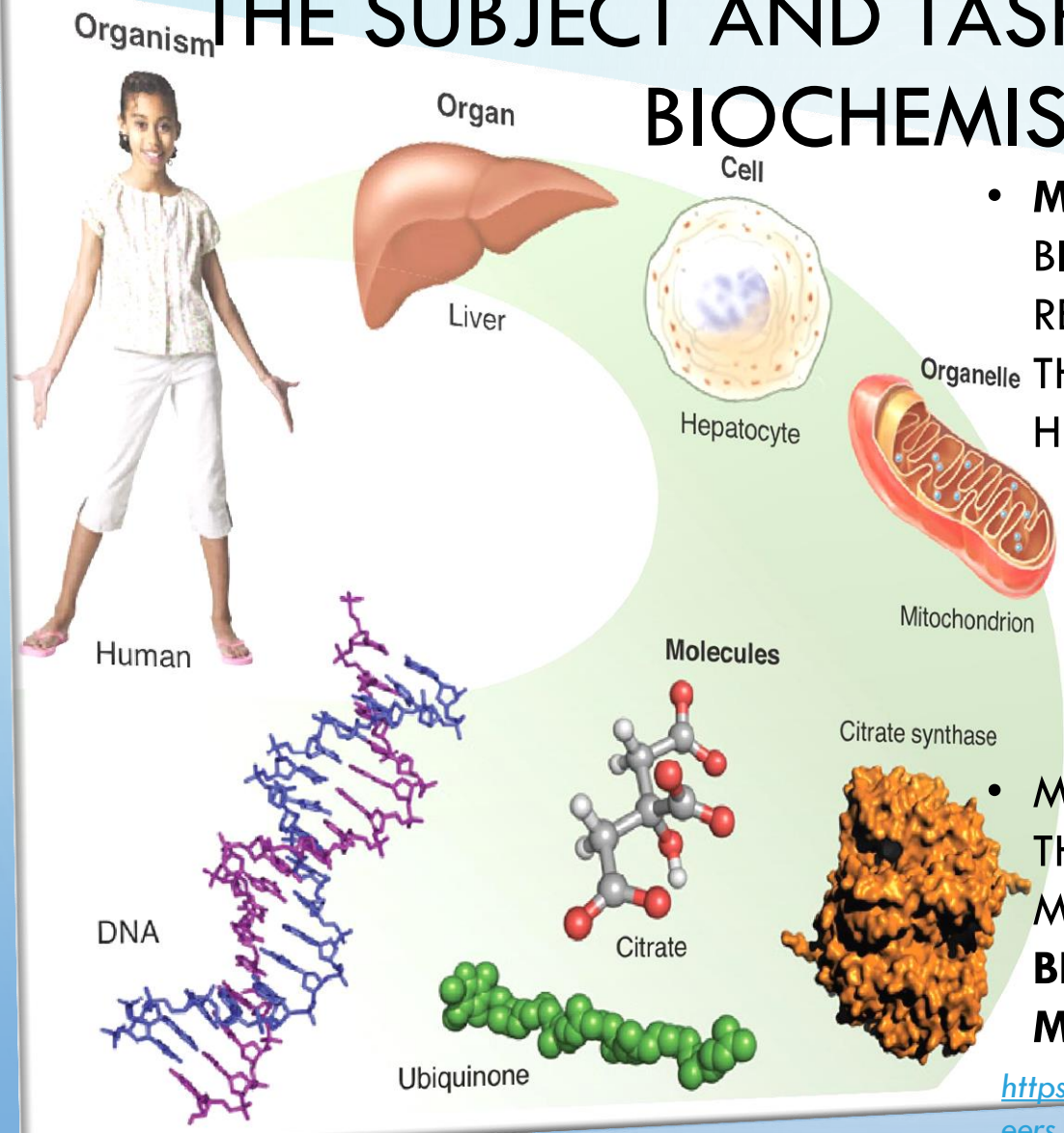
CONTENTS

- SUBJECT AND TASKS OF MEDICAL BIOCHEMISTRY.
- GENERAL CHARACTERISTICS OF THE PROTEIN BIOSYNTHESIS, PROCESSING, AND PROTEIN FOLDING.
- REPORT SPATIAL PROTEIN STRUCTURE AS A BASIS OF CONFORMATIONAL DISEASES.
- REPLACEMENT OF INDIVIDUAL AMINO ACIDS, AS A CAUSE OF SPATIAL STRUCTURE OF THE PROTEIN. SICKLE-CELL ANEMIA.
- AMYLOIDOSIS AND SERPINOPATHIES - DISEASES CAUSED BY CHANGES IN THE SPATIAL STRUCTURE OF THE PROTEIN AND ITS AGGREGATION.
- NEURODEGENERATIVE DISEASES OF A CHANGE IN THE SPATIAL STRUCTURE OF THE PROTEIN: HUNTINGTON'S CHOREA AND PARKINSON'S DISEASE.
- PRION PROTEIN. PRION DISEASES.
- PARKINSON'S DISEASE.

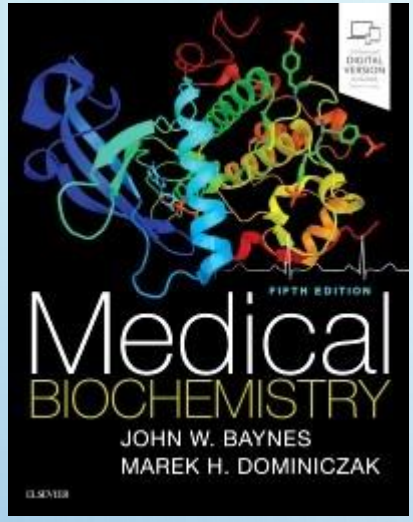
THE SUBJECT AND TASKS OF MEDICAL BIOCHEMISTRY



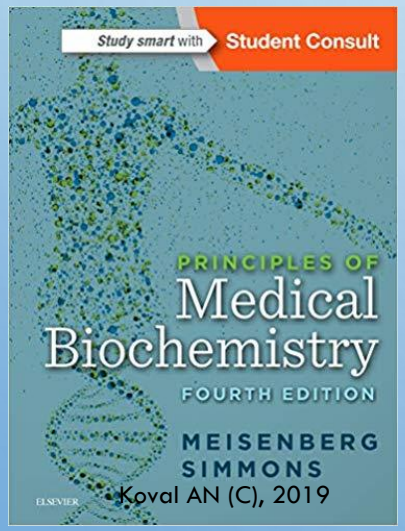
- **MEDICAL BIOCHEMISTRY –** BIOCHEMISTRY WITH PARTICULAR REFERENCE TO THE WAYS IN WHICH THIS RELATES TO MEDICINE AND HEALTH.
  - **MEDICAL BIOCHEMISTRY** IS A BRANCH OF MEDICINE THAT INCORPORATES BIOCHEMISTRY AND METABOLISM IN HUMAN AND DISEASE.
- MEDICAL BIOCHEMISTRY IS A FIELD THAT STUDIES DIFFERENT TYPES OF MOLECULES IN HOPES OF **BETTERING TECHNOLOGY AND MEDICINE**.

https://study.com/articles/Medical_Biochemistry_Careers_Job_Options_and_Requirements.html

SOURCES: TEXTBOOKS

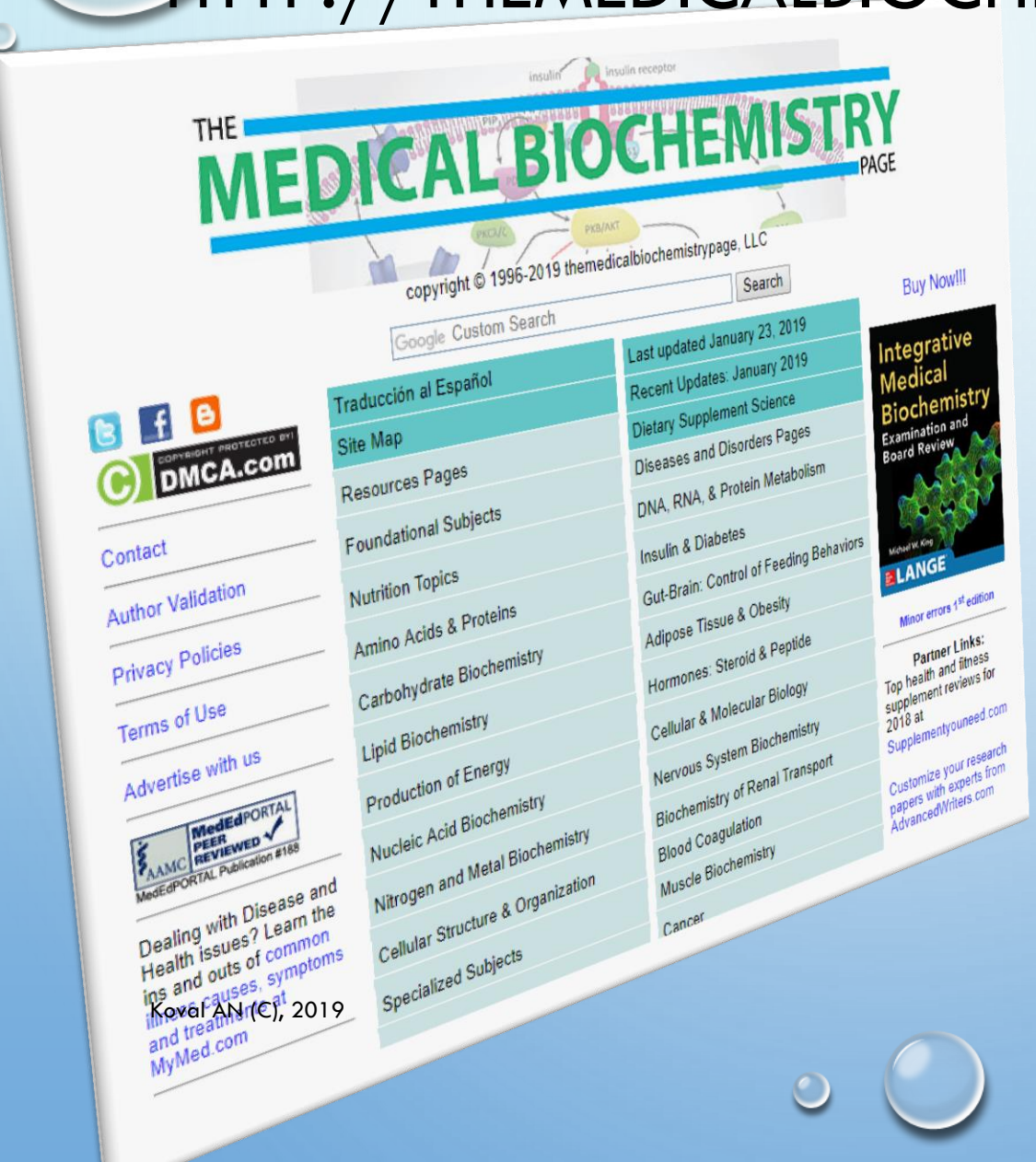


- MEDICAL BIOCHEMISTRY, 5TH EDITION, **AUTHORS:** JOHN BAYNES MAREK DOMINICZAK, 2019, 712 PAGES



- PRINCIPLES OF MEDICAL BIOCHEMISTRY, 4TH EDITION, AUTHORS: GERHARD MEISENBERG, WILLIAM H. SIMMONS, 2017, 657 PAGES

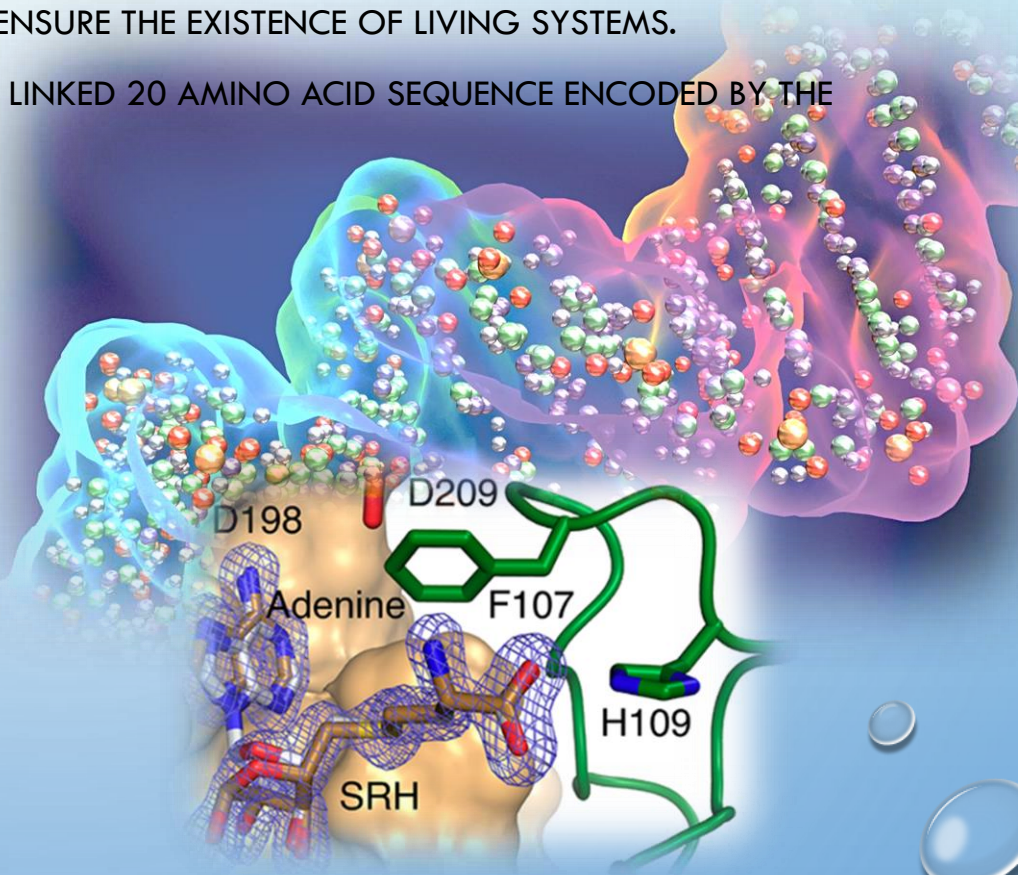
SOURCES: WEB-PAGE HTTP://THEMEDICALBIOCHEMISTRYPAGE.ORG



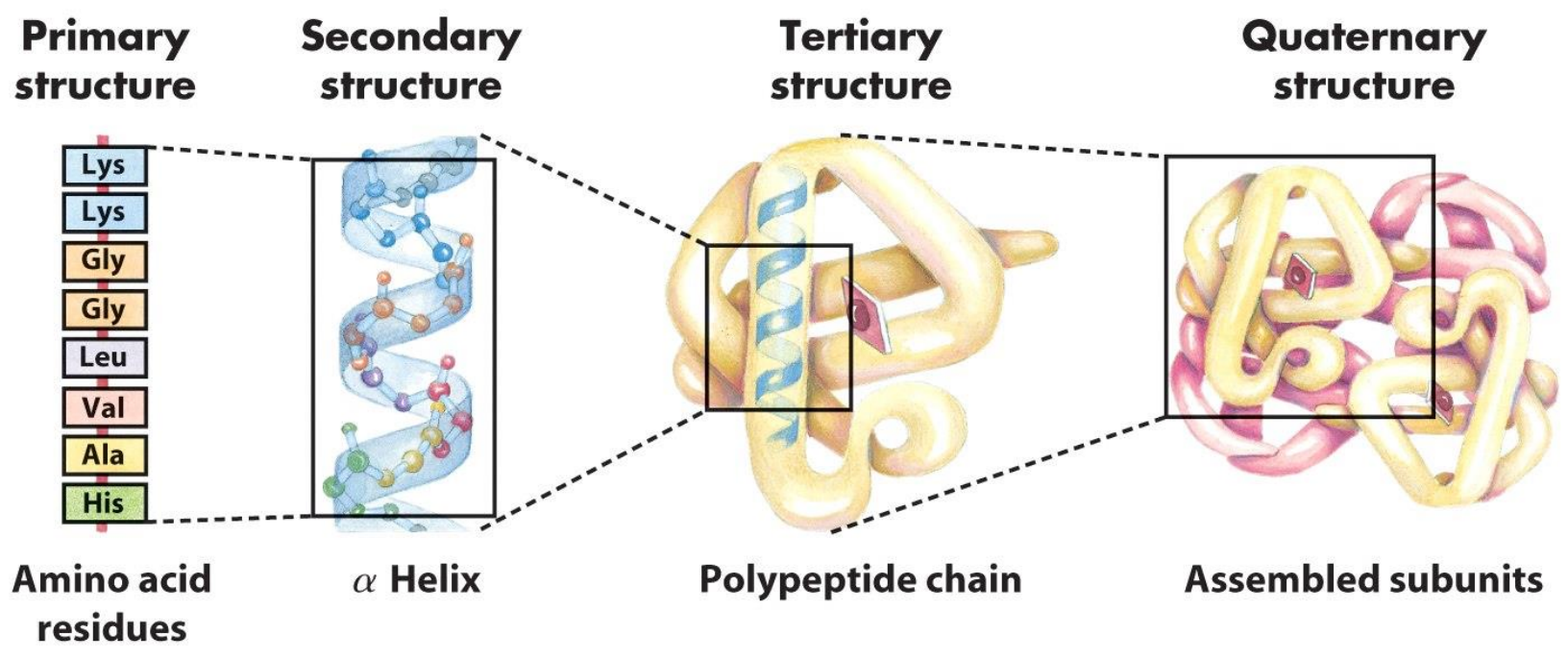
- EASY ACCESSIBLE SITE FOR MEDICAL STUDENTS.
- AUTHOR: MICHAEL W. KING
- CONSTANTLY UPDATED

GENERAL CHARACTERISTICS OF THE PROTEIN BIOSYNTHESIS, PROCESSING, AND PROTEIN FOLDING.

- PROTEINS PERFORM A VARIETY OF FUNCTIONS AND ENSURE THE EXISTENCE OF LIVING SYSTEMS.
- LINEAR CHAIN PROTEIN COMPOSED OF COVALENTLY LINKED 20 AMINO ACID SEQUENCE ENCODED BY THE GENETIC CODE.
- NUCLEOTIDE SEQUENCE DETERMINES THE ORDER OF AMINO ACIDS IN A PROTEIN, WITH ONE AMINO ACID CORRESPONDS TO THE DNA SEQUENCE OF THREE NUCLEOTIDES - CALLED A TRIPLET OR CODON. MOST AMINO ACIDS CAN BE CODED BY DIFFERENT TRIPLETS.
  - THAT IS, THE GENETIC CODE CAN BE REDUNDANT OR OTHERWISE DEGENERATE. THE GENETIC CODE ENCODING A DIFFERENT AMINO ACID HAVING A DIFFERENT DEGREE OF DEGENERACY (AMINO ACID ENCODED BY 1 TO 6 CODONS), IT DEPENDS ON THE FREQUENCY OF OCCURRENCE OF THE AMINO ACIDS IN PROTEINS.



PROTEIN'S LEVELS OF ORGANIZATION

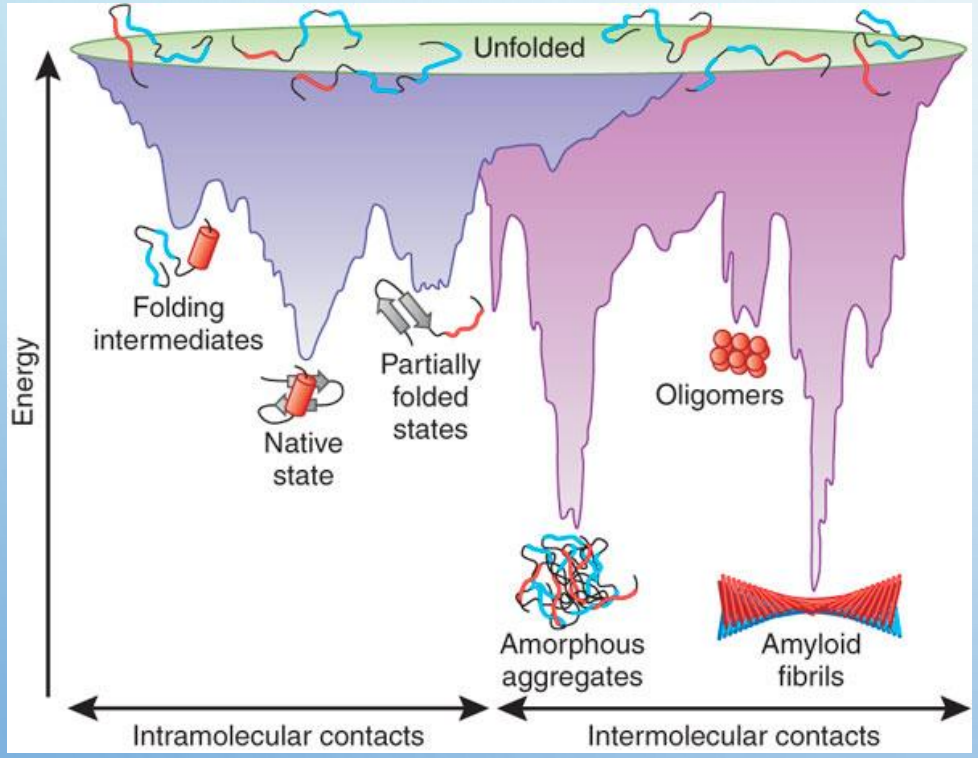


For the functioning of the protein molecules is important not only linear but also the spatial structure. For the formation of the latter, are linear chain protein molecules must emerge into unique for each type of protein three-dimensional structures.

PROTEIN LIFE CYCLE

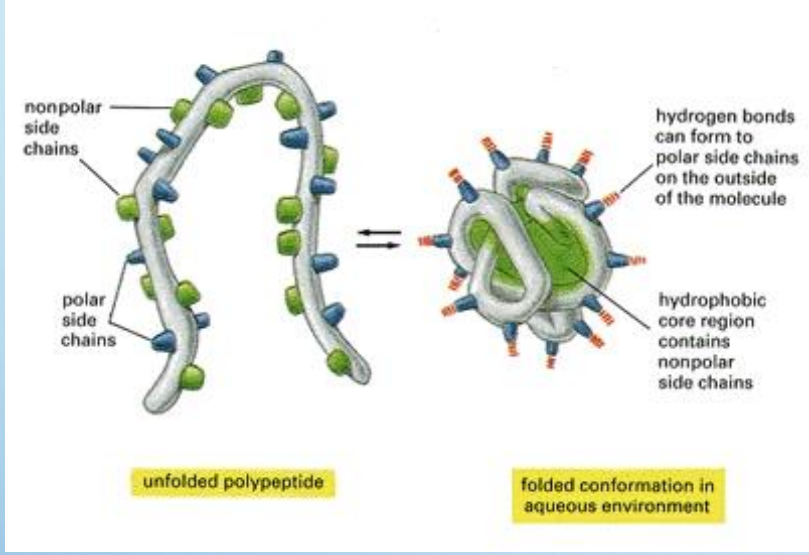
- CELLULAR COMPONENTS (PROTEINS, ORGANELLES) CAN BECOME DAMAGED.
- THE CELL REQUIRES MECHANISMS TO REMOVE THE DAMAGED MOLECULES TO ENSURE VIABILITY.
- THE PROCESSES OF PROTEINS AND ORGANELLES ARE DEGRADED, REMOVED AND RECYCLED ARE VITAL FOR CELLULAR SURVIVAL.
- HIGHLY SPECIFIC WAYS OF REGULATION.
- INCLUDE
  - PROTEIN MODIFICATION,
  - PROTEIN DEGRADATION AND AMINO ACID RECYCLING,
  - ORGANELLE TAGGING,
  - ENGULFMENT, AND
  - LYSOSOMAL DEGRADATION WITH COMPONENT PARTS BEING RECYCLED.

PROTEIN FOLDING

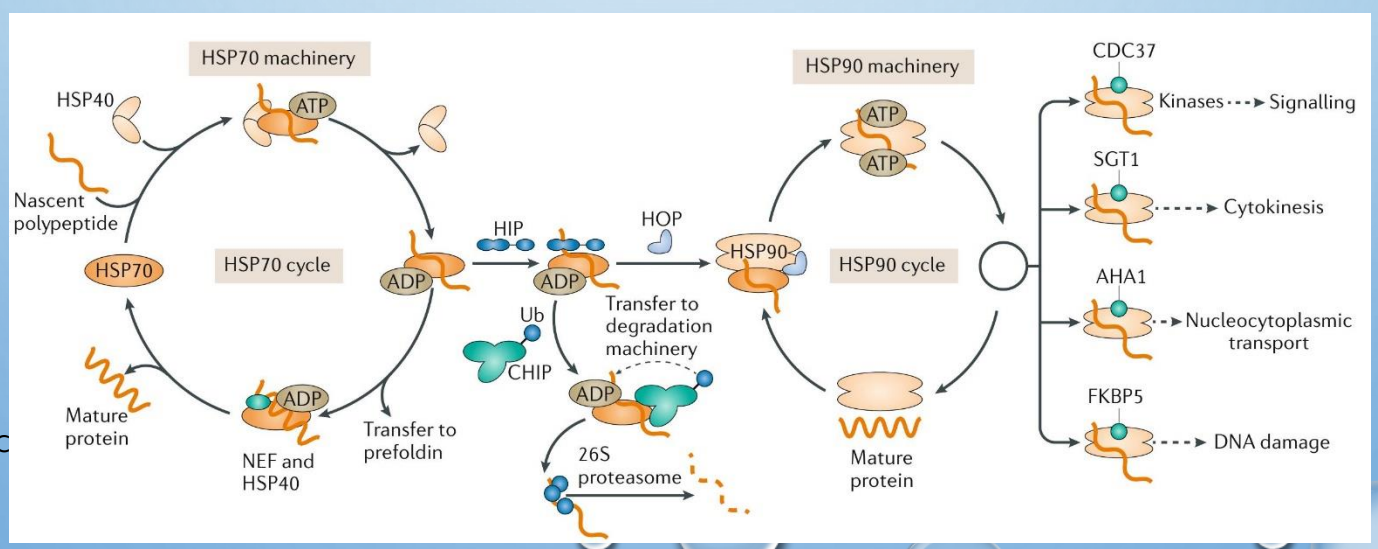


- THE PROCESS OF PROTEIN SYNTHESIS DOES NOT DIRECTLY RESULT IN THE GENERATION OF **FUNCTIONALLY AND STRUCTURALLY COMPLETE MACROMOLECULES**.
- MANY PROTEINS MUST UNDERGO ONE OR MORE FORMS OF MODIFICATION.
- THE FOLDING OF THE PROTEIN INTO A DEFINED THREE-DIMENSIONAL STRUCTURE.
- IN THE CELL NEWLY SYNTHESIZED PROTEINS ARE AT GREAT RISK OF ABERRANT FOLDING AND AGGREGATION => CAN LEAD TO THE FORMATION OF POTENTIALLY TOXIC SPECIES.

CHAPERONES



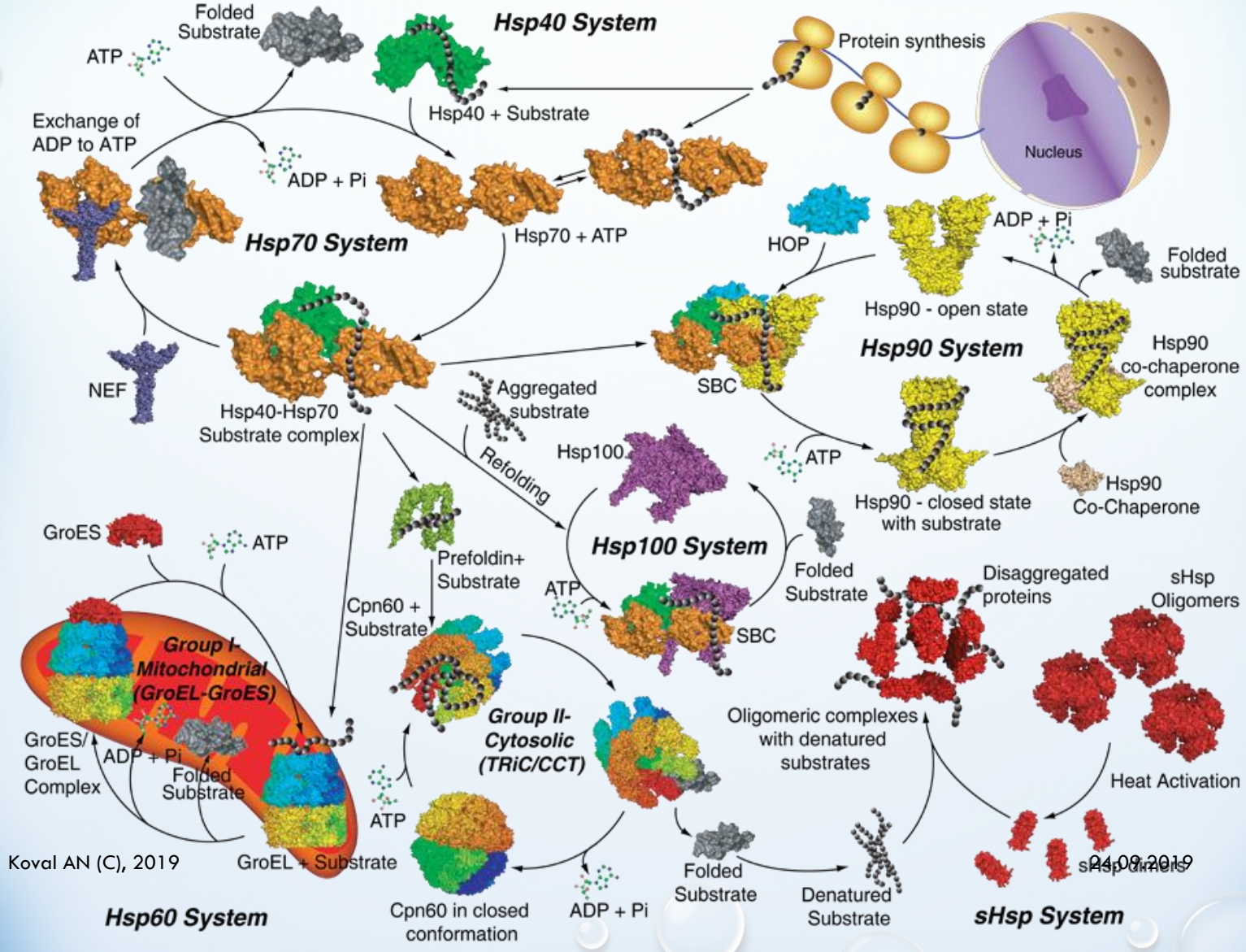
- TO REDUCE AND PREVENT THESE NEGATIVE OUTCOMES, CELLS HARBOR A COMPLEX NETWORK OF MOLECULAR CHAPERONES WHOSE FUNCTIONS ARE TO PROMOTE EFFICIENT FOLDING AND TO PREVENT PROTEIN AGGREGATION.
- THE STRUCTURE OF PROTEINS WITHIN THE CELL IS IN A HIGHLY DYNAMIC STATE AND, THEREFORE, CONSTANT MOLECULAR CHAPERONE SURVEILLANCE IS REQUIRED TO ENSURE PROTEIN HOMEOSTASIS



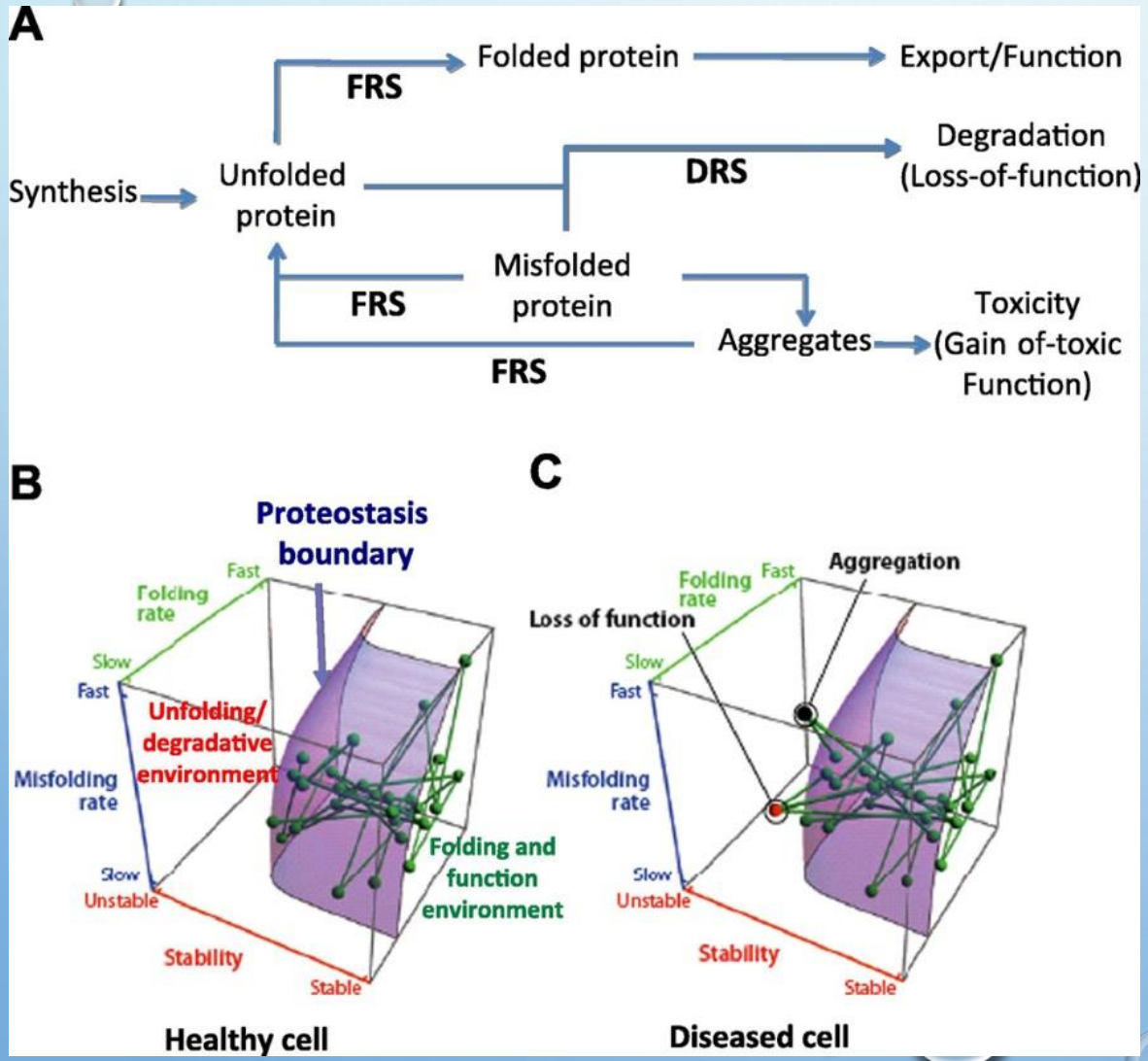
ALL CHAPERONES CAN BE DIVIDED INTO SIX MAJOR GROUPS:

1. HIGH MOLECULAR WEIGHT CHAPERONES, WITH A MOLECULAR WEIGHT OF FROM 100 TO 110 KDA;
2. CHAPERONES-90 - WITH A MOLECULAR WEIGHT OF FROM 83 TO 90 KDA;
3. CHAPERONES -70 - WITH A MOLECULAR WEIGHT OF 66 TO 78 KDA;
4. CHAPERONES -60 - WITH A MOLECULAR WEIGHT OF ABOUT 60 KDA;
5. CHAPERONES -40 - WITH A MOLECULAR WEIGHT OF ABOUT 40 KDA;
6. LOW MOLECULAR WEIGHT CHAPERONES ABOUT 15 TO 30 KDA.

PROTEIN FOLDING SYSTEM



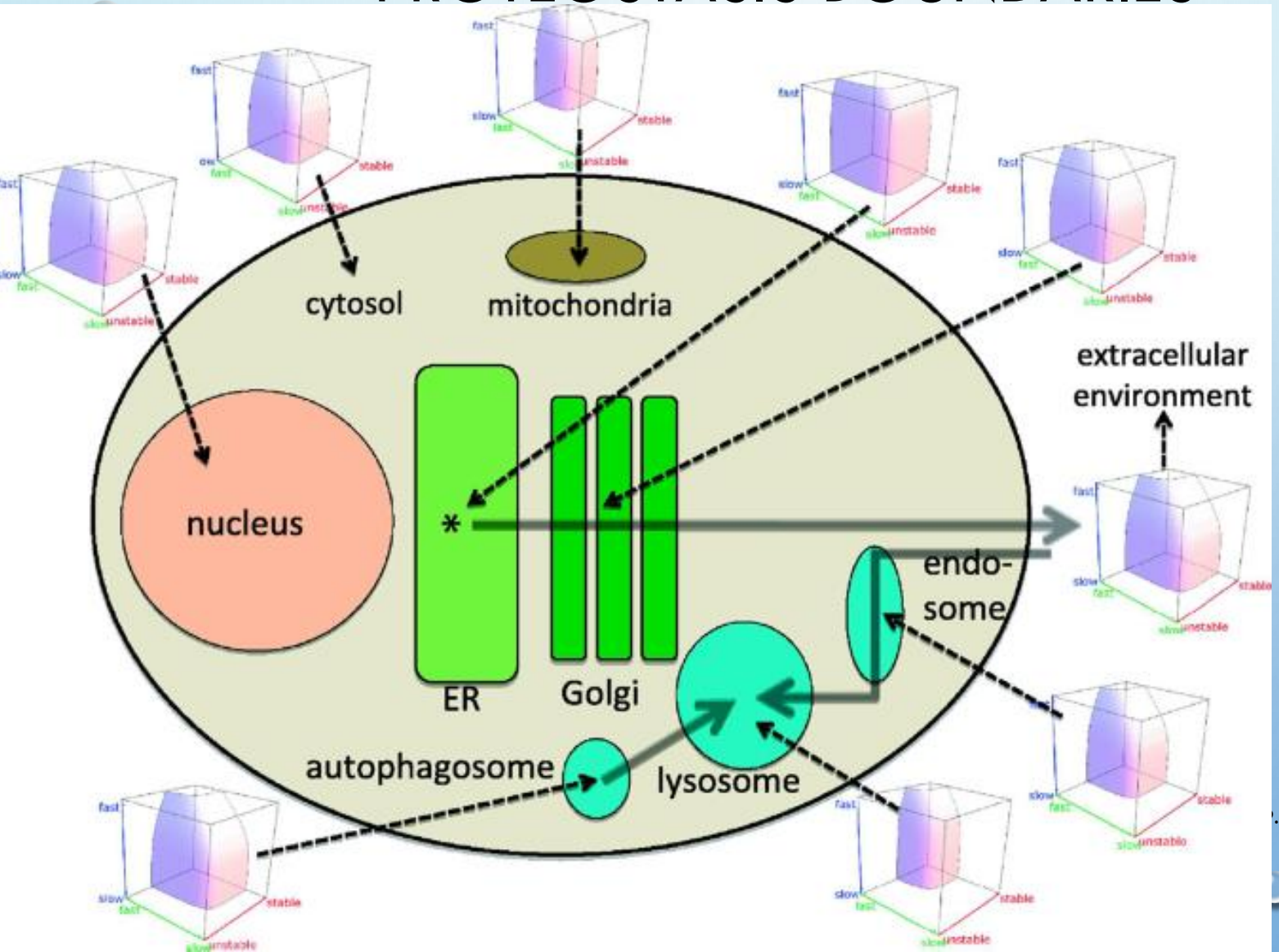
THE FOLDEX AND FOLDFX MODELS DEFINING THE PROTEOSTASIS BOUNDARY



(A) ILLUSTRATED ARE THE INTERACTIVE PATHWAYS THAT REQUIRE THE FRS TO EITHER COMPLETE THE FOLD FOR EXPORT FROM THE ER (FOLDEX MODEL) {WISEMAN, 2007 #616} OR FOR FUNCTION (FOLDFX MODEL) {POWERS, 2009 #613}, OR CONTRIBUTE TO MISFOLDING, AGGREGATION AND DEGRADATION THROUGH THE DRS. (B, C) ILLUSTRATED IS THE PROTEOSTASIS BOUNDARY (PB) (INDICATED BY THE ARROW) DEFINED BY KINETICS OF FOLDING (Z AXIS), KINETICS OF MISFOLDING (Y AXIS) AND THERMODYNAMICS (X AXIS) REFLECTING A TYPICAL CELLULAR COMPOSITION OF THE PN (SEE {WISEMAN, 2007 #190} FOR DETAILS). THE LOCATION OF A HYPOTHETICAL CELLULAR NETWORK FACILITATING CELL FUNCTION IS INDICATED BY THE GREEN NODES AND EDGES, WHICH, IN A HEALTHY CELL (**B**) IS PROTECTED BY THE PN AND THEREFORE BENEATH THE PB. IN DISEASE (**C**), A MUTATION CAN RESULT IN MISFOLDING (RED NODE AND EDGE) LEADING TO A LOSS-OF-FUNCTION DISEASE, OR AGGREGATION (BLACK NODE AND EDGE) THAT CAN LEAD TO A GAIN-OF-TOXIC FUNCTION DISEASE.

(B) SEE {WISEMAN, 2007 #190}{POWERS, 2009 #613} FOR A THOROUGH TREATMENT OF THE IMPACT OF MUTATION ON THE PN LEADING TO HUMAN DISEASES. PANELS B AND C ARE REPRODUCED WITH PERMISSION (ELSEVIER PRESS) IN A MODIFIED FORM.

COMPARTMENTALIZATION AND PROTEOSTASIS BOUNDARIES

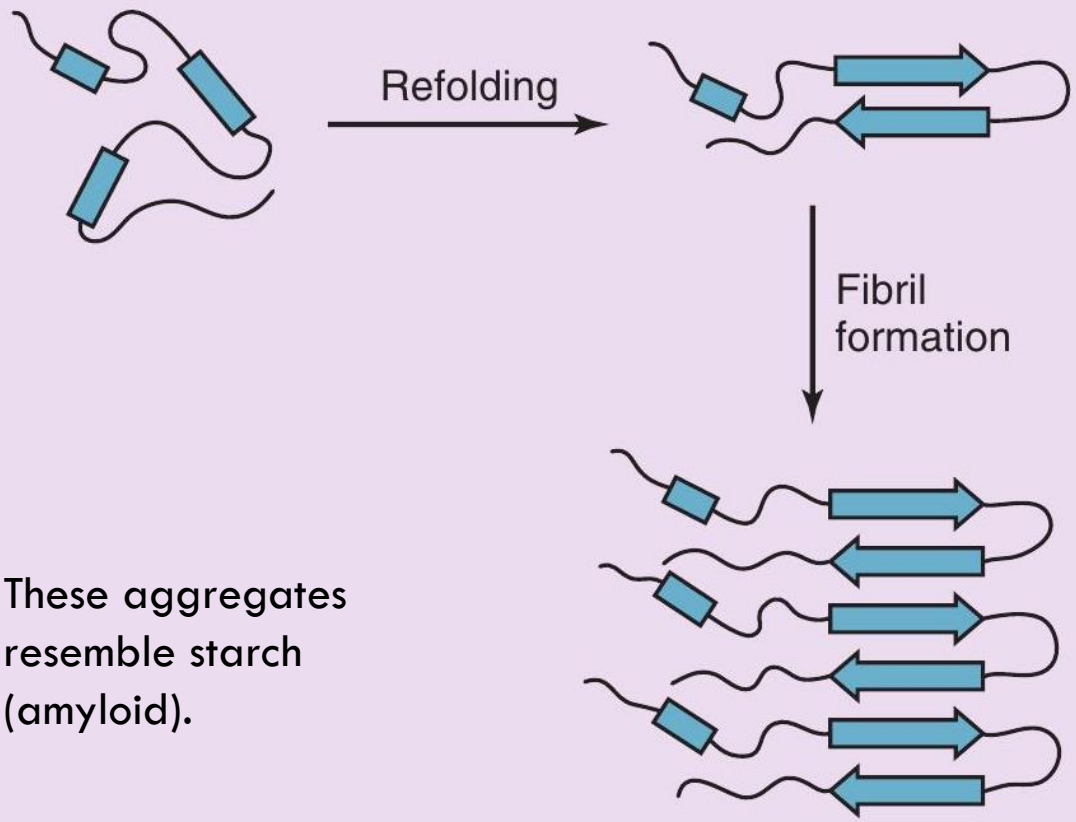


ILLUSTRATED IS A HYPOTHETICAL VIEW OF THE DIFFERING ORGANIZATIONS OF THE PB FOUND IN THE INDICATED COMPARTMENTS. THE DIFFERENCES IN THE SHAPE OF THE PBS REFLECT THE DIFFERENCES IN THE PN PRESENT IN EACH OF THESE COMPARTMENTS OR IN THE EXTRACELLULAR SPACE THAT PROMOTES FOLDING AND/OR MAINTENANCE OF THE FOLD.

AMYLOIDOSES

A globular protein that has a somewhat flexible higher-order structure in its normal state spontaneously refolds into a state with a high content of β-pleated sheet.

In some cases, stretches of α- helix rearrange into stretches of β-pleated sheet. Unlike the α-helix, which is strictly intramolecular, the β-pleated sheet can form extended structures that involve two or more polypeptides.



These aggregates resemble starch (amyloid).

AMYLOIDOSIS: SOME FORMS

Table 2.2 Some Forms of Amyloidosis

Type	Offending Protein	Sites of Deposition	Cause
Transthyretin amyloidosis	Transthyretin	Heart, kidneys, respiratory tract	Old age
AL amyloidosis	Immunoglobulin light chains	Systemic (excluding brain), sometimes local foci	Plasma cell dyscrasias (see Chapter 18)
AA amyloidosis	Serum amyloid A protein	Systemic (excluding brain)	Chronic inflammation
Dialysis-associated amyloidosis	β_2-Microglobulin	Bones, joints	Hemodialysis
Type 2 diabetes mellitus	Islet amyloid polypeptide	Pancreatic islets	Oversecretion?
Frontotemporal dementia	Tau protein	Brain	Age-related or inherited mutation
Parkinson disease	α-Synuclein	Substantia nigra	Age-related
Alzheimer disease	β-Amyloid precursor protein	Brain	Age-related, inherited mutation, or Down syndrome

AMYLOID IS NOT VERY TOXIC AND CAUSES NO IMMUNE RESPONSE, IT CAN DAMAGE THE ORGANS IN WHICH IT DEPOSITS

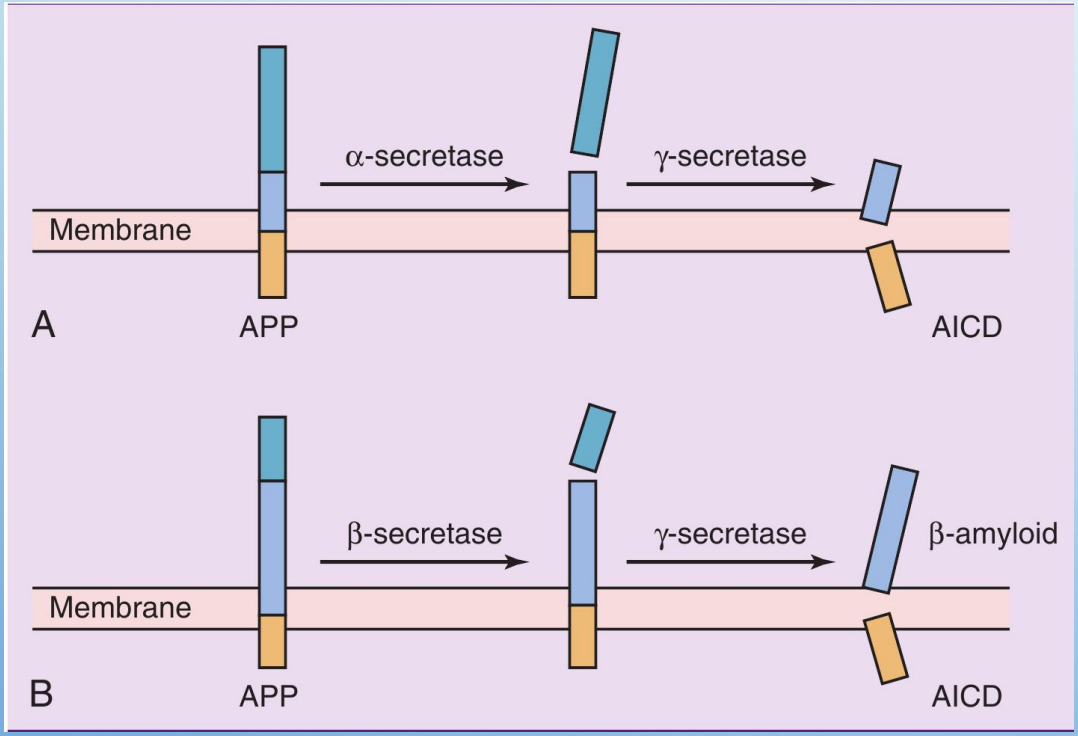
- **TAU PROTEIN**, WHICH STABILIZES THE MICROTUBULES IN THE AXONS OF NEURONS.
- ITS AFFINITY FOR MICROTUBULES IS REGULATED BY REVERSIBLE PHOSPHORYLATION AND DEPHOSPHORYLATION OF SERINE AND THREONINE SIDE CHAINS. IN SEVERAL NEURODEGENERATIVE DISEASES, INCLUDING **ALZHEIMER DISEASE** AND **FRONTOTEMPORAL DEMENTIA**, EXCESSIVELY PHOSPHORYLATED ("HYPERPHOSPHORYLATED") TAU PROTEIN FORMS FILAMENTOUS AGGREGATES IN THE AXONS, CAUSING THEIR EVENTUAL DEMISE.
- SOME PEOPLE ARE BORN WITH A STRUCTURALLY ABNORMAL TAU PROTEIN THAT IS MORE PRONE TO ABNORMAL PHOSPHORYLATION, DETACHES MORE EASILY FROM THE MICROTUBULES, OR IS MORE PRONE TO AGGREGATION AFTER IT HAS BEEN PHOSPHORYLATED AND HAS DETACHED FROM THE MICROTUBULES. MOST OF THESE PATIENTS DEVELOP AN INHERITED FORM OF FRONTOTEMPORAL DEMENTIA WITH PARKINSONISM.

ALZHEIMER DISEASE

B AMYLOID PROTEIN IS A MISFOLDED PROTEIN.

IT FORMS FIBROUS DEPOSITS OR PLAQUES IN THE BRAINS OF ALZHEIMER'S PATIENTS.

SYMPTOMS: MEMORY LOSS, DEMENTIA, IMPAIRMENT IN OTHER FORMS OF COGNITION AND BEHAVIOR



- NOT TRANSMISSIBLE BETWEEN INDIVIDUALS
- INTRACELLULAR AGGREGATES (FIBRILLAR TANGLES) OF PROTEIN CALLED **TAU**
- EXTRACELLULAR PLAQUES CONTAIN AGGREGATES OF B-**AMYLOID PEPTIDES (AB):**40-42-RESIDUE SEGMENTS DERIVED BY PROTEOLYTIC CLEAVAGE OF A MUCH LARGER PROTEIN (AMYLOID PRECURSOR PROTEIN, **APP) ATTACHED TO PLASMA** MEMBRANE OF NEURONS (FUNCTION UNKNOWN)

B-AMYLOID PRECURSOR PROTEIN (ABB)

- ALPHA-B IS FORMED BY THE PROTEOLYTIC CLEAVAGE OF B-AMYLOID PRECURSOR PROTEIN (APP), A MEMBRANE PROTEIN THAT TRAVERSES THE LIPID BILAYER OF THE PLASMA MEMBRANE BY MEANS OF AN A-HELIX.
  - AFTER AN INITIAL CLEAVAGE THAT IS CATALYZED BY THE PROTEASE **B-SECRETASE**, ANOTHER PROTEASE CALLED **Г-SECRETASE** CLEAVES THE REMAINING POLYPEPTIDE WITHIN THE LIPID BILAYER OF THE PLASMA MEMBRANE, CREATING AN INTRACELLULAR FRAGMENT AND THE EXTRACELLULAR AB.
- Г-SECRETASE CLEAVAGE IS IMPRECISE, AND EXTRACELLULAR POLYPEPTIDES OF 40 AND 42 AMINO ACIDS CAN BE FORMED.
- LESS THAN 10% OF THE PRODUCT IS AB-42, BUT THIS FORM IS FAR MORE AMYLOIDOGENIC THAN AB-40.
- IT FOLDS INTO A FORM THAT CONTAINS A PARALLEL B-PLEATED SHEET WITH TWO STRETCHES OF 10 TO 12 AMINO ACIDS EACH.
- THIS STRUCTURE POLYMERIZES INTO AMYLOID FIBRILS, FORMING THE SENILE PLAQUES.

ALPHA-SYNUCLEIN

- ANOTHER PROBLEM PROTEIN IS **A-SYNUCLEIN**, A SMALL (140 AMINO ACIDS), UNSTABLY FOLDED, MEMBRANE-ASSOCIATED INTRACELLULAR PROTEIN THAT CAN AGGREGATE INTO CYTOPLASMIC GRANULES CALLED **LEWY BODIES.**
- MOST PATIENTS WITH **PARKINSON DISEASE** HAVE LEWY BODIES IN THEIR AILING DOPAMINE NEURONS.
- PARKINSON DISEASE IS A MOTOR DISORDER MANIFESTED AS TREMOR, RIGOR, AND AKINESIA.
- IT IS THE SECOND MOST COMMON NEURODEGENERATIVE DISEASE AFTER ALZHEIMER DISEASE, AFFECTING 1% TO 3% OF PEOPLE OLDER THAN 65 YEARS.
- PEOPLE WHO ARE BORN WITH STRUCTURALLY ABNORMAL VARIANTS OF A-SYNUCLEIN OR WHO OVERPRODUCE STRUCTURALLY NORMAL A-SYNUCLEIN AS A RESULT OF GENE DUPLICATION OR TRIPLICATION CAN DEVELOP EARLY-ONSET FORMS OF PARKINSON DISEASE.
- WIDESPREAD DEPOSITS OF A-SYNUCLEIN IN THE BRAIN ARE FOUND IN SOME DEMENTED PATIENTS, AND SOME PARKINSON DISEASE PATIENTS BECOME DEMENTED WHEN NEURONS OTHER THAN THE DOPAMINE NEURONS OF THE SUBSTANTIA NIGRA BECOME INVOLVED IN THE DISEASE.

PARKINSON DISEASE

- **OTHER DISEASES INVOLVING ABNORMAL FOLDING/AGGREGATION OF *OTHER PROTEINS***
- **PARKINSON DISEASE**
- – PROTEIN THAT FORMS FIBRILS IS A-***SYNUCLEIN*.**
- – LESIONS ("LEWY BODIES") FORM IN CYTOSOL OF DOPAMINERGIC NEURONS IN SUBSTANTIA NEGRA OF BRAIN, ACCOMPANIED BY MUSCLE RIGIDITY AND RESTING TREMOR.

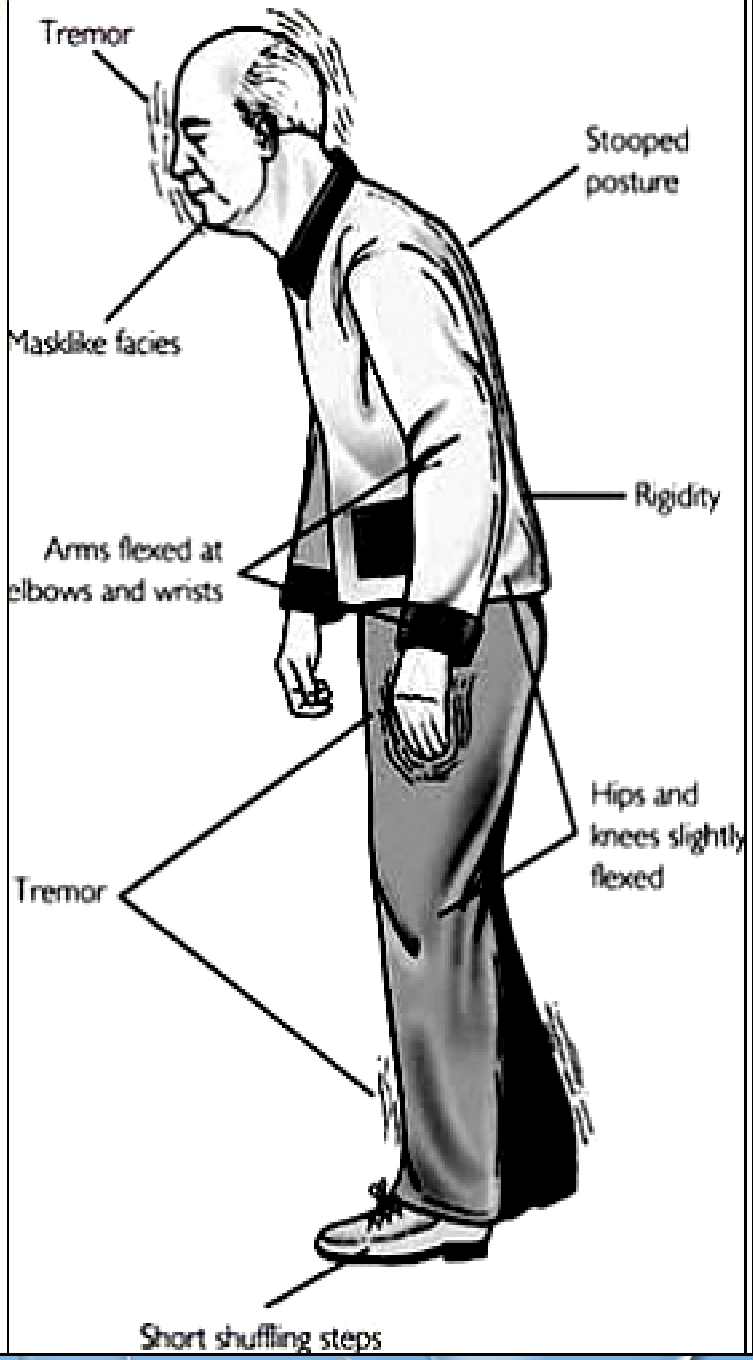
What is Parkinson's Disease?

Parkinson's disease (PD) is chronic and progressive movement disorder, meaning that symptoms continue and worsen over time. Nearly one million people in the US are living with Parkinson's disease. The cause is unknown, and although there is presently no cure, there are treatment options such as medication and surgery to manage its symptoms.

Parkinson's involves the malfunction and death of vital nerve cells in the brain, called neurons. Parkinson's primarily affects neurons in the an area of the brain called the substantia nigra. Some of these dying neurons produce dopamine, a chemical that sends messages to the part of the brain that controls movement and coordination. As PD progresses, the amount of dopamine produced in the brain decreases, leaving a person unable to control movement normally.

The specific group of symptoms that an individual experiences varies from person to person. Primary motor signs of Parkinson's disease include the following.

- **tremor** of the hands, arms, legs, jaw and face
- **bradykinesia** or slowness of movement
- **rigidity** or stiffness of the limbs and trunk
- **postural instability** or impaired balance and coordination



MISFOLDED PROTEIN CAN BE CONTAGIOUS

- AN UNUSUAL TYPE OF NEURODEGENERATION IS CAUSED BY AGGREGATES OF THE **PRION PROTEIN (PRP).** THE NORMAL CELLULAR PRION PROTEIN (**PRP^C**) IS AN ABUNDANT PROTEIN IN THE NERVOUS SYSTEM, WHERE IT IS TETHERED TO THE SURFACE OF NEURONS BY A COVALENTLY BOUND GLYCOSYLPHOSPHATIDYLINOSITOL ANCHOR THAT IS INSERTED INTO THE LIPID BILAYER OF THE PLASMA MEMBRANE. SMALLER AMOUNTS ARE PRESENT IN OTHER ORGANS, IN BLOOD, AND CEREBROSPINAL FLUID.

From sheep to cows to humans: Following a deadly brain disease

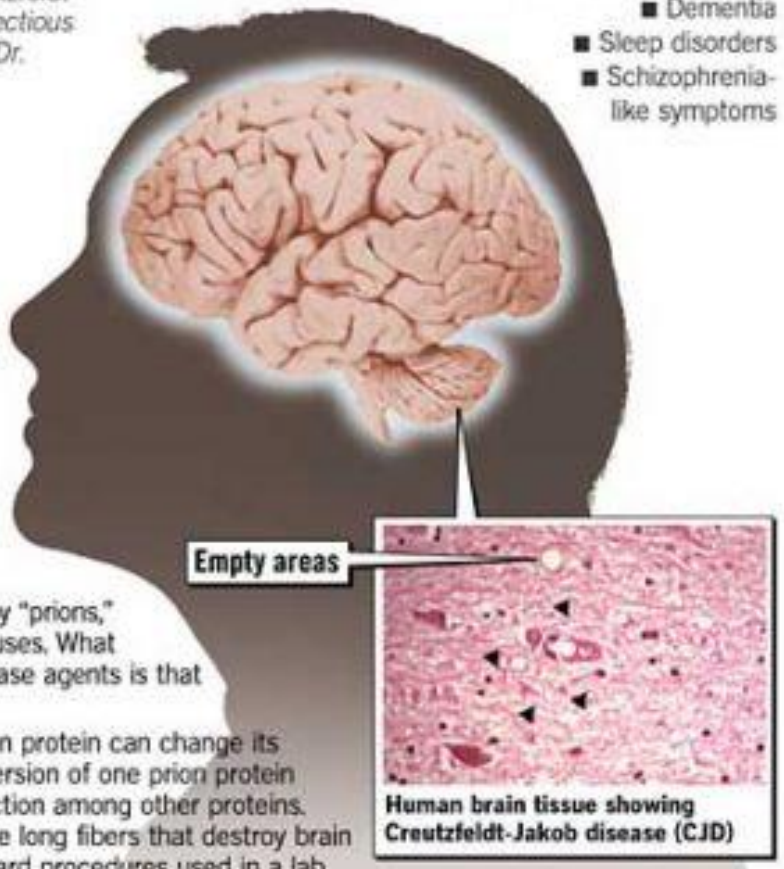
Scrapie in sheep. "Mad cow" disease in bovines. And a new variant of Creutzfeldt-Jakob disease in humans. All are believed caused by "prions," a type of infectious protein discovered by University of California at San Francisco neurologist Dr. Stanley Prusiner, who won the Nobel Prize in 1997 for his discovery.

■ **Scrapie** is a fatal brain disease affecting sheep and goats. First recognized in Europe more than 250 years ago, infected sheep will rub and "scrape" their skin raw and eventually die from brain degeneration. It was found in the United States in 1947.

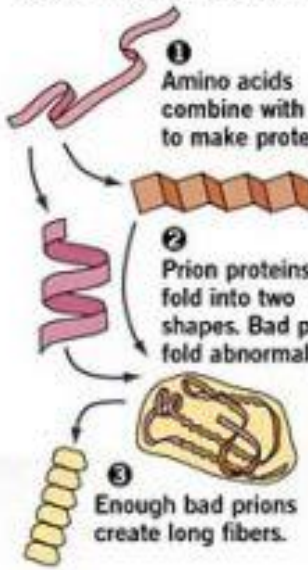
■ **Mad cow disease, or bovine spongiform encephalopathy (BSE),** first appeared in 1984 in a cow in Britain that was thought to have eaten feed that included offal from sheep that harbored scrapie. Since then, authorities have found more than 178,000 cases of BSE.

■ **Creutzfeldt-Jakob disease (CJD)** is the human equivalent of the fatal brain disease. It is a rare disease, typically occurring in one in a million older mature adults. A new variant, probably caused by eating infected beef, affects younger adults in the same way it atacks the brains of cattle. There have been about 100 deaths to date.

Symptoms of CJD
- Dementia
- Sleep disorders
- Schizophrenia-like symptoms



Human brain tissue showing Creutzfeldt-Jakob disease (CJD)



■ What causes the disease?

In all three species, the disease is caused by "prions," infectious proteins that are smaller than viruses. What makes prions unique among infectious disease agents is that they lack the genetic material.

A prion exists in two forms. The normal prion protein can change its shape to a disease-causing form. The conversion of one prion protein into a harmful form can trigger a chain reaction among other proteins. When enough bad proteins form, they create long fibers that destroy brain tissue. Prions are remakably durable. Standard procedures used in a lab, such as heat and chemicals, are not effective in neutralizing prions..

■ Promising treatment

Scientists in Prusiner's lab at UCSF have discovered two obscure drugs that show promise against prion-related diseases, at least in the lab. Both drugs are known to cross the "blood-brain barrier," a natural barrier that protects the brain from foreign chemicals and viruses. Two patients with CJD have begun trying the drug and a clinical trial is planned.

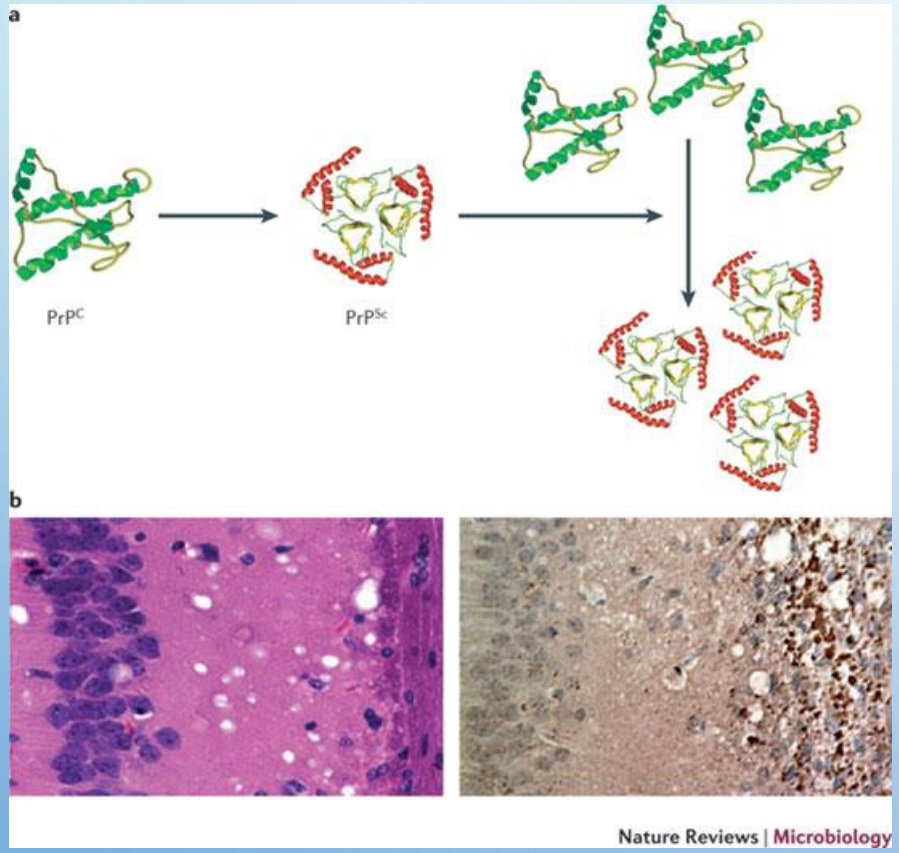
Sources: UCSF, World Health Organization, National Institute of Health Associated Press, Sperling Medical Foundation, Asian Wall Street Journal

JOHN BLANCHARD / The Chronicle

CREUTZFELDT-JAKOB DISEASE (CJD)

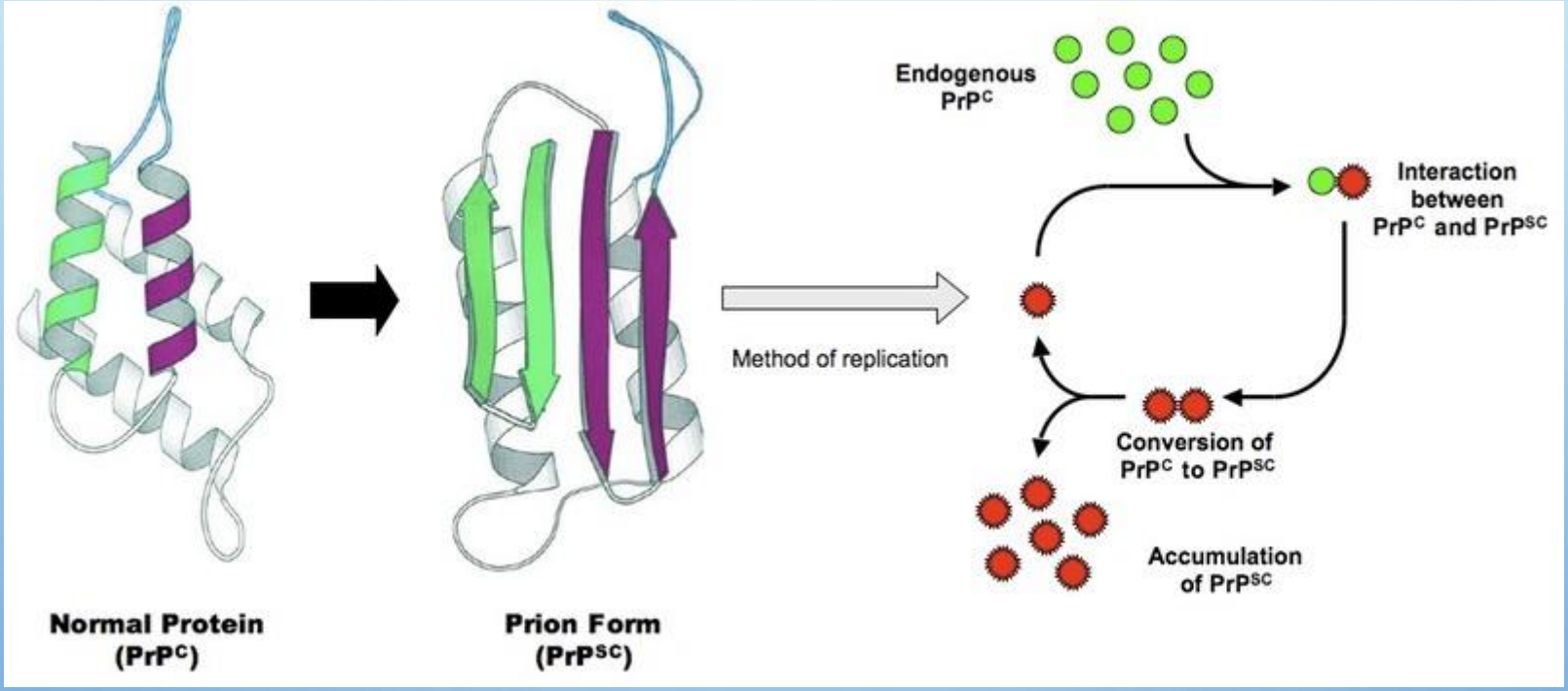
- **CREUTZFELDT-JAKOB DISEASE (CJD)** IS A RARE DISEASE (INCIDENCE ONE PER MILLION PER YEAR) OF MIDDLE-AGED AND OLD PEOPLE IN WHOM MENTAL DETERIORATION PROGRESSES TO DEATH WITHIN WEEKS OR MONTHS.
- AT AUTOPSY THE BRAIN IS FOUND TO BE RIDDLED WITH HOLES THAT MAKE IT LOOK LIKE SWISS CHEESE OR A SPONGE; THEREFORE, THIS TYPE OF DISEASE IS CHARACTERIZED AS A **SPONGIFORM ENCEPHALOPATHY.**

PRIONS AND CJD

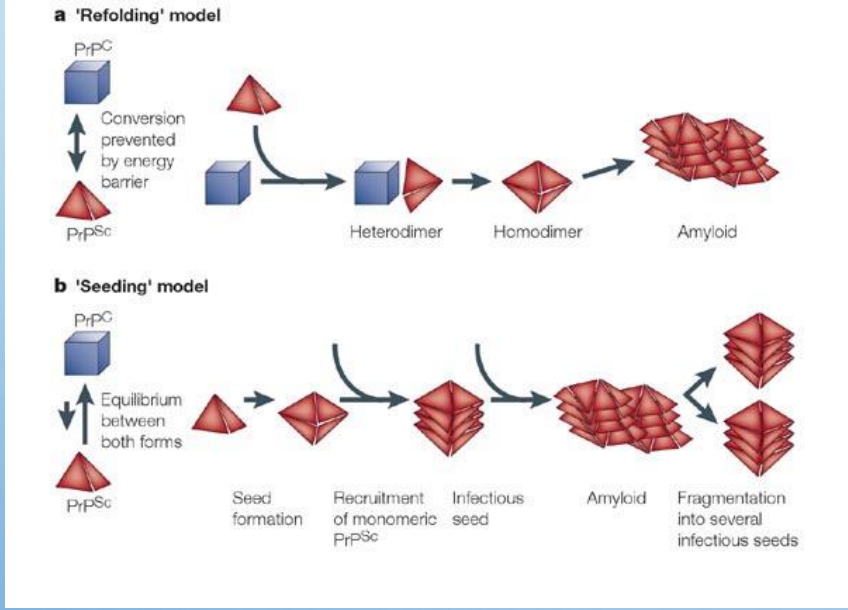


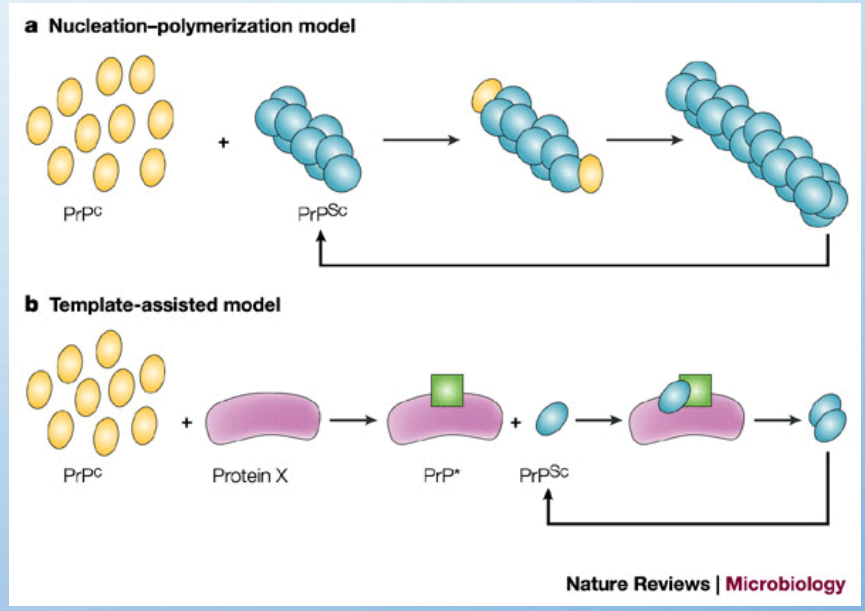
- *CJD DEVELOPS WHEN THE NORMAL PRP^{C} REFOLDS ITSELF INTO THE ABNORMAL PRP^{SC}* (SC STANDS FOR "SCRAPIE," THE CORRESPONDING DISEASE OF SHEEP).
- THIS CONFORMATIONAL TRANSITION APPEARS TO BE AN EXTREMELY RARE EVENT. HOWEVER, ONCE FORMED, PRP^{SC} CAN FORM TOXIC AGGREGATES WITH OTHER MOLECULES OF PRP^{SC}. MOST IMPORTANT IS THAT *PRP^{SC} INTERACTS WITH PRP^{C}, CAUSING IT TO REFOLD INTO PRP^{SC}. WHEN THIS HAPPENS ON THE SURFACE OF NEURONS THAT EXPRESS PRP, IT CAN KILL THE NEURONS.*
- THE PROCESS AMOUNTS TO A CHAIN REACTION IN WHICH A SMALL AMOUNT (PERHAPS A SINGLE MOLECULE) OF PRP^{SC} TRIGGERS AN AVALANCHE OF PROTEIN REFOLDING THAT LEADS TO A RAPIDLY PROGRESSIVE DISEASE.

PRP^C -> PRP^{SC}


Endogenous
PrP^C
Interaction
between
PrP^C and PrP^SC
Method of replication
Conversion of
PrP^C to PrP^SC
Accumulation
of PrP^SC
Normal Protein
(PrP^C)
Prion Form
(PrP^SC)

PRIONS' DYNAMICS

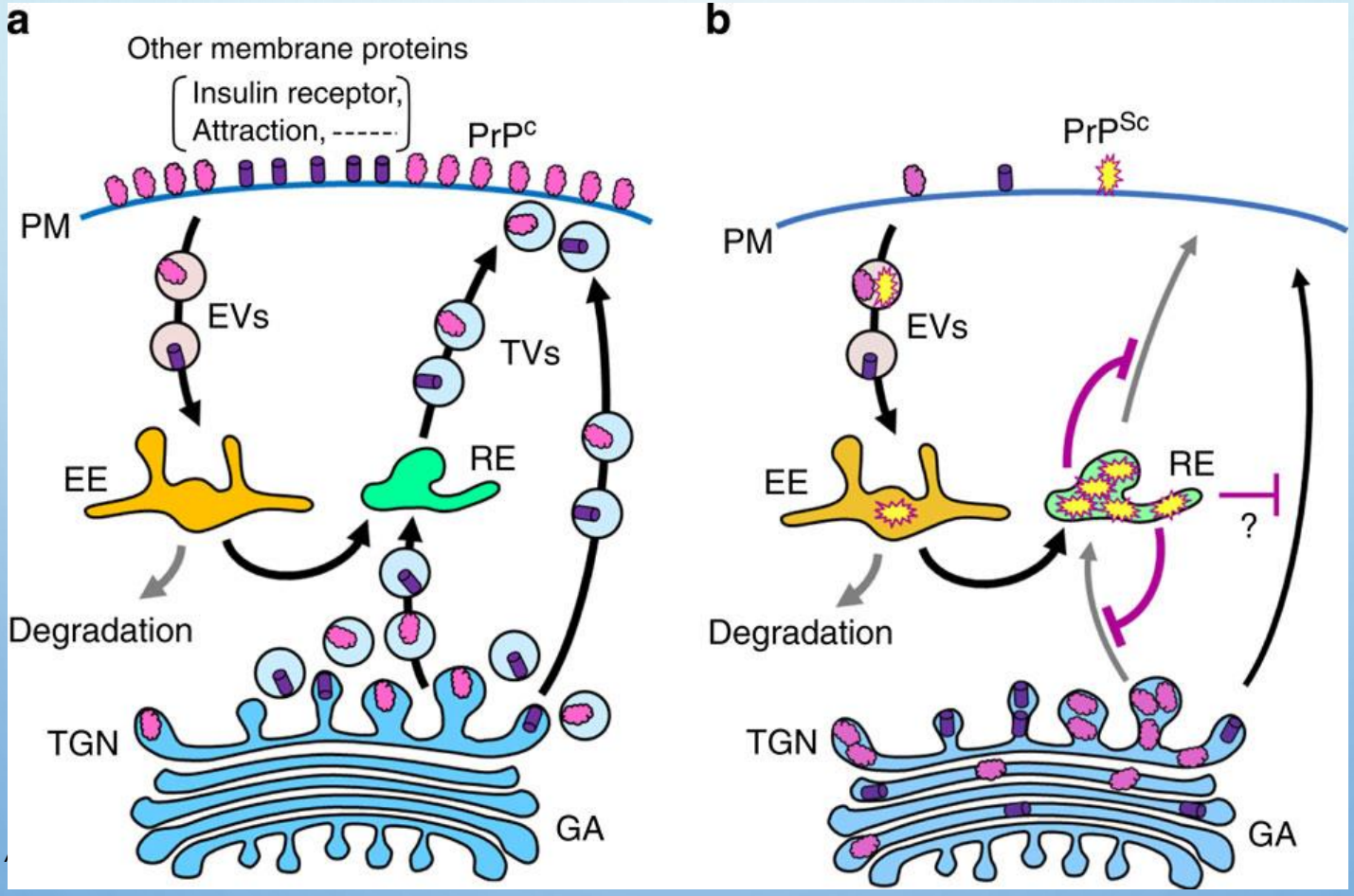




MAD COW DISEASE AND CJD

- DURING THE 1980S, WHEN CATTLE IN BRITAIN WERE FED INSUFFICIENTLY HEATED MEAT-AND-BONE MEAL PREPARED FROM SHEEP CARCASSES, MANY CATTLE DEVELOPED THE BOVINE EQUIVALENT OF CJD AND SCRAPIE. THIS DISEASE BECAME KNOWN AS *BOVINE SPONGIFORM ENCEPHALOPATHY* OR "MAD COW DISEASE." BETWEEN 1986 AND 2014, 177 PEOPLE IN BRITAIN AND 51 IN OTHER COUNTRIES DEVELOPED THE HUMAN EQUIVALENT, NAMED **VARIANT CREUTZFELDT-JAKOB DISEASE (VCJD)**, AFTER CONSUMING THE MEAT OF INFECTED CATTLE.
- **KURU** IS THE NATURALLY TRANSMISSIBLE SPONGIFORM ENCEPHALOPATHY OF HUMANS.

PRION PROTEIN RECYCLING IN NEURONS



ABNORMAL PROTEIN FOLDING IN CJD

- MOST CASES OF CJD ARE SPORADIC, BUT SOME ARE INHERITED AS AN AUTOSOMAL DOMINANT TRAIT. THE PATIENTS CARRY A SINGLE COPY OF A MUTANT GENE THAT ENCODES A STRUCTURALLY ABNORMAL PRP WITH A SINGLE AMINO ACID SUBSTITUTION. THIS STRUCTURAL ABNORMALITY INCREASES THE LIKELIHOOD THAT PRP REFOLDS ITSELF INTO THE AGGREGATION-PRONE FORM.
- THE MECHANISM OF CJD IMPLIES THAT THE DISEASE CAN BE TRANSMITTED FROM PERSON TO PERSON IF THE ABNORMALLY FOLDED PRION PROTEIN FROM A PATIENT ENTERS ANOTHER PERSON'S BODY. THIS OCCURS ONLY UNDER UNUSUAL CIRCUMSTANCES SUCH AS BLOOD TRANSFUSION OR TISSUE TRANSPLANTATION. PATHOLOGISTS KNOW TO BE EXTRA CAUTIOUS WHEN DISSECTING THE BRAIN OF A PATIENT WHO DIED OF CJD.

THANK YOU FOR ATTENTION!