BATTEN DISEASE
An Overview

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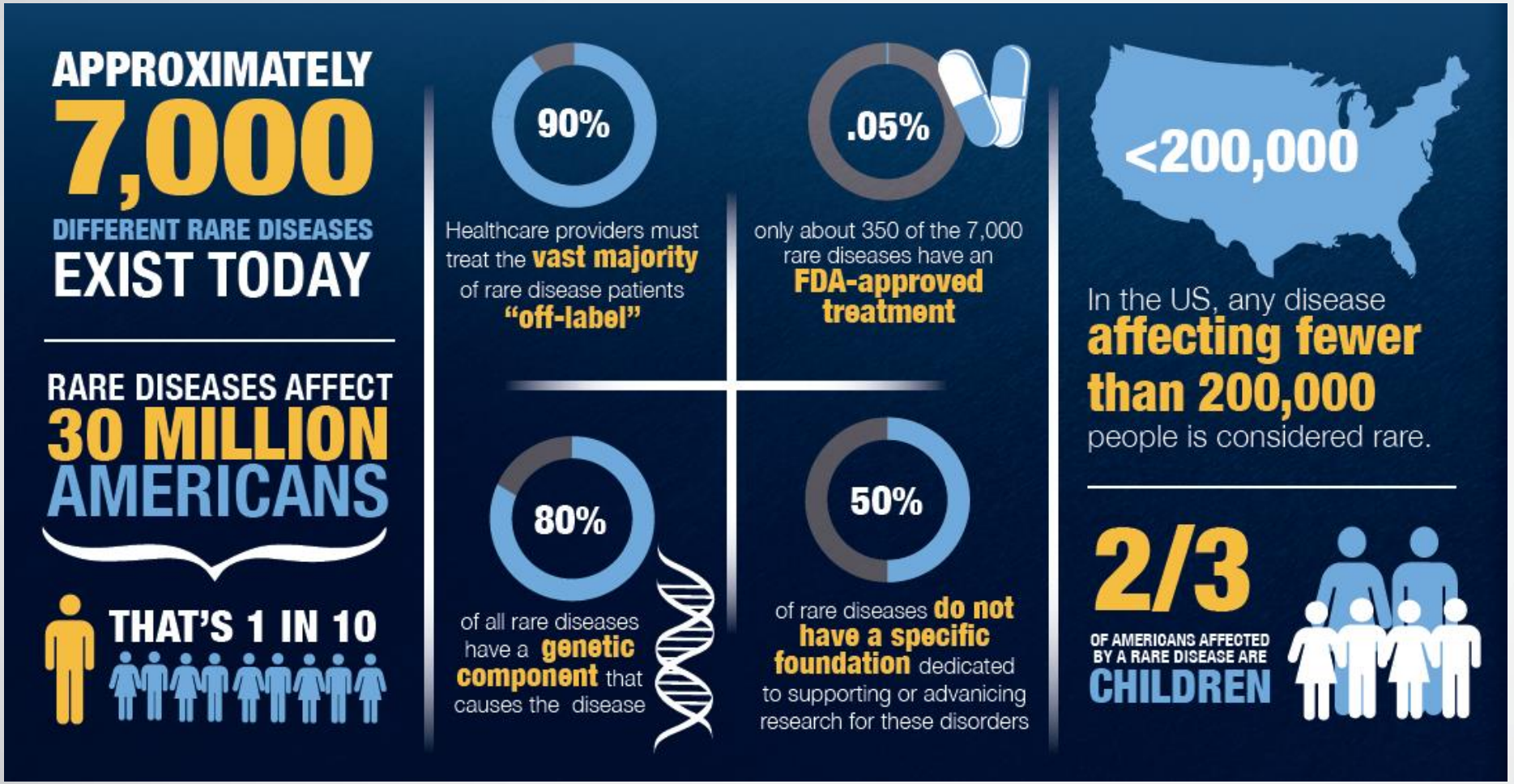
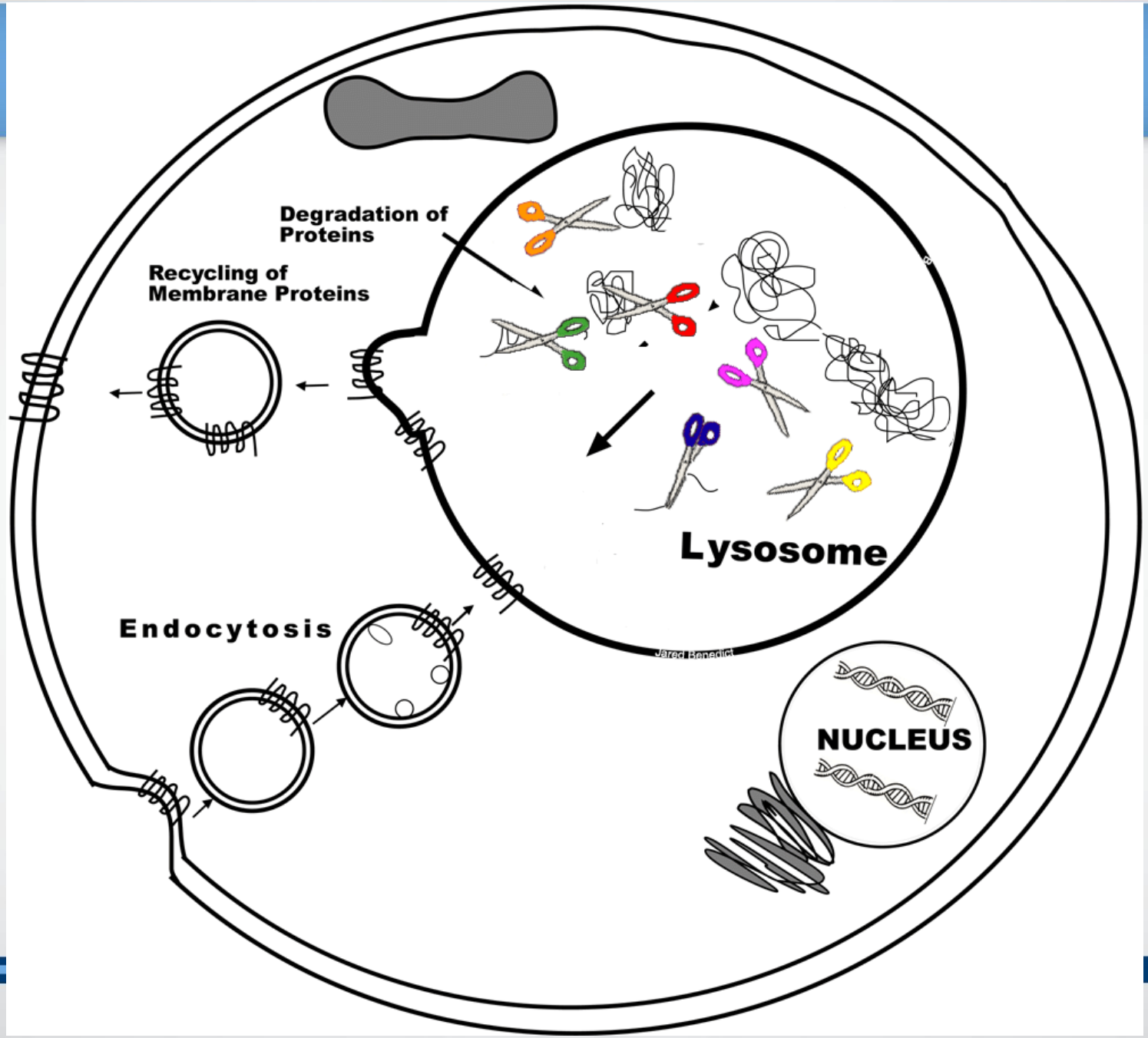
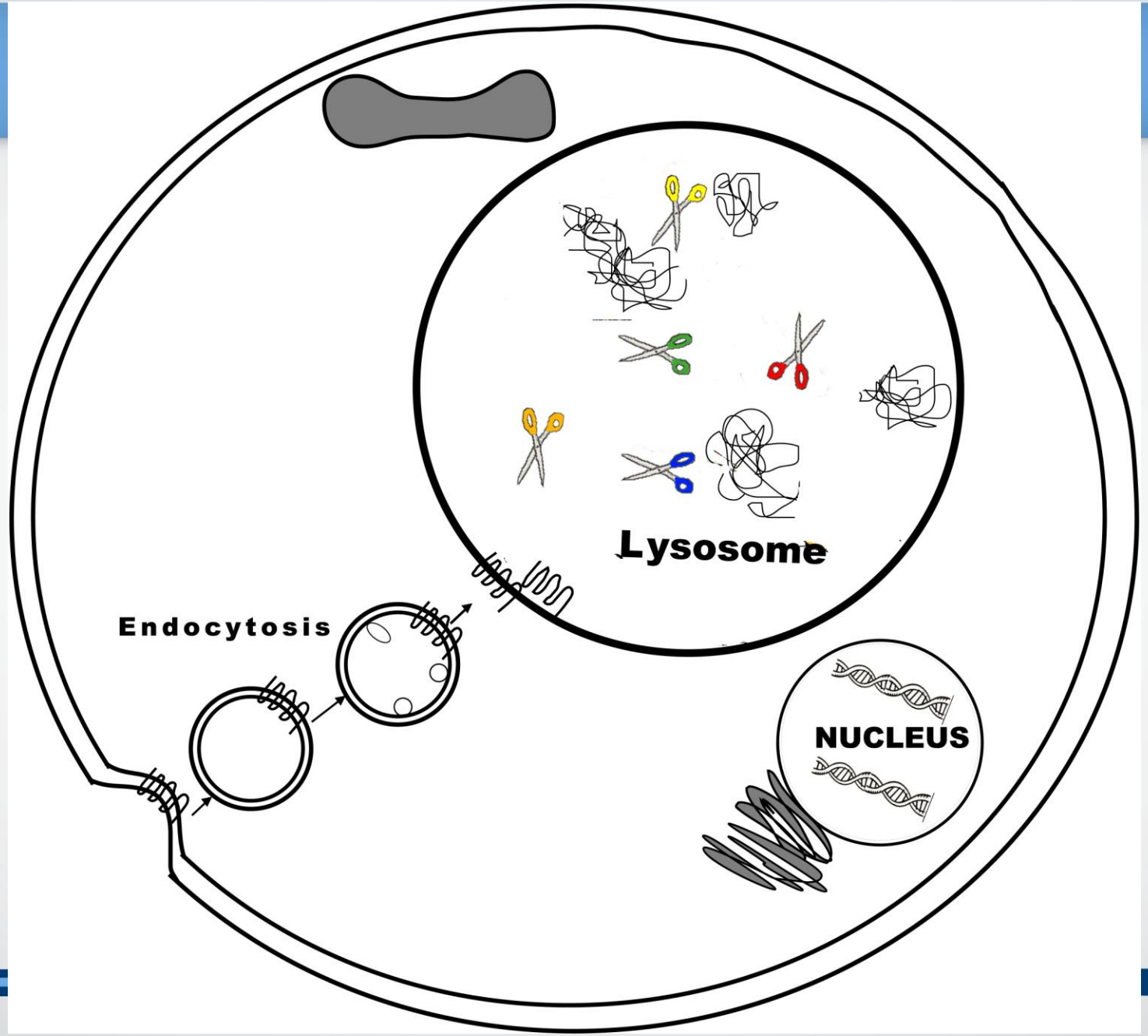
SANFORD HEALTH

Studying Rare Diseases at Sanford



Acquired nephrogenic diabetes insipidus
Acute Lymphoblastic Leukemia
Acute Myeloid Leukemia
Alagille Syndrome
Alopecia Areata
Arrhythmogenic right ventricular dysplasia
Ataxia telangiectasia
Atherosclerosis
ATRT
Atypical Werner syndrome
Autism
Autosomal recessive deafness 76, DFBN76
Bronchopulmonary dysplasia
Busche-Ollendorff syndrome
Cadmium poisoning
Cardiomyopathy dilated, type 1A
Cerebral palsy
Cervical cancer
Charcot-Marie-Tooth Disorder axonal, type 2B1
Choroid plexus carcinomas
Chronic traumatic encephalopathy (CTE)
CLN1-Batten Disease
CLN2-Batten Disease
CLN3-Batten Disease
CLN6-Batten Disease
Congenital hydrocephalus
Cystic kidney diseases
Developmental programming of cardiovascular disease, metabolic syndrome, diabetes, neurological dev
Distal renal tubular acidosis
Dystonia
Emery-Dreifuss muscular dystrophy, dominant and recessive
Epilepsy, progressive myoclonic 9
Familial partial lipodystrophy, Dunnigan
Fetal alcohol spectrum disorders
Fetal and neonatal nutrition
Genital warts
Glioma
Graft versus host disease
Greenberg Dysplasia
Hajdu-Cheney syndrome
Head and neck squamous cell carcinoma
Head trauma
Heart Hand syndrome, Slovenian type
Hutchinson-Gilford progeria syndrome
Hydrocephalus
Leukodystrophy, demyelinating Adult onset, autosomal dominant
Limb-girdle muscular dystrophy type 1B
Lipidomics and metabolic and mitochondrial dysfunction in aging and disease
Malouf syndrome
Mandibuloacral dysplasia with type A or type B lipodystrophy
Medulloblastoma
Neurofibromatosis type 1
Nestor-Guillermo progeria syndrome
Niemann-Pick Type C1
Osteoma
Osteopoikilosis
Osteoporosis
Osteosarcoma
Osteosclerosis
Pancreatic Endocrine Cancers
Pelger-Huet Anomaly
Primary ciliary dyskinesia
Respiratory distress syndrome
Respiratory papillomatosis
Restrictive dermopathy
Restrictive dermpopathy/tight skin contracture syndrome
Reynolds syndrome
Sjorgen's Syndrome
Smith Lemli Opitz syndrome
Spinocerebellar Ataxia
Stroke
Susceptibility to acquired partial lipodystrophy
Torsion dystonia 1, AD, DYT1
Type 1 diabetes


Degradation of Proteins
Recycling of Membrane Proteins
Lysosome
Endocytosis
NUCLEUS


Lysosome
Endocytosis
NUCLEUS

BATTEN DISEASE

Batten Disease (Neuronal Ceroid Lipofuscinoses) is a **family of diseases** with **>10 variants** caused by mutations in **14 different genes**

COLLECTIVELY MOST COMMON NEURODEGENERATIVE PEDIATRIC DISORDER

OVERALL INCIDENCE IS: **1: 100,000 LIVE BIRTHS WORLDWIDE**

INCURABLE DISEASE THAT RESULTS IN **PREMATURE DEATH**

Variants have **overlapping** clinical and pathological **symptoms**

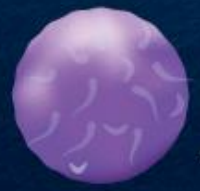
- Retinopathy leading to blindness
- Motor abnormalities
- Seizure
- Synaptic degeneration, cortical atrophy, neuronal loss, and glial activation
- Dementia
- Sleep disorders
- Premature death

FINDING A CURE

Natural Therapies

Stem Cell Therapy

Enzyme Replacement Therapy



Lysosome Modulators

Neuronal Ceroid Lipofuscinoses

Gene Therapy

Anti-inflammatory Compounds

Small Molecule Therapies

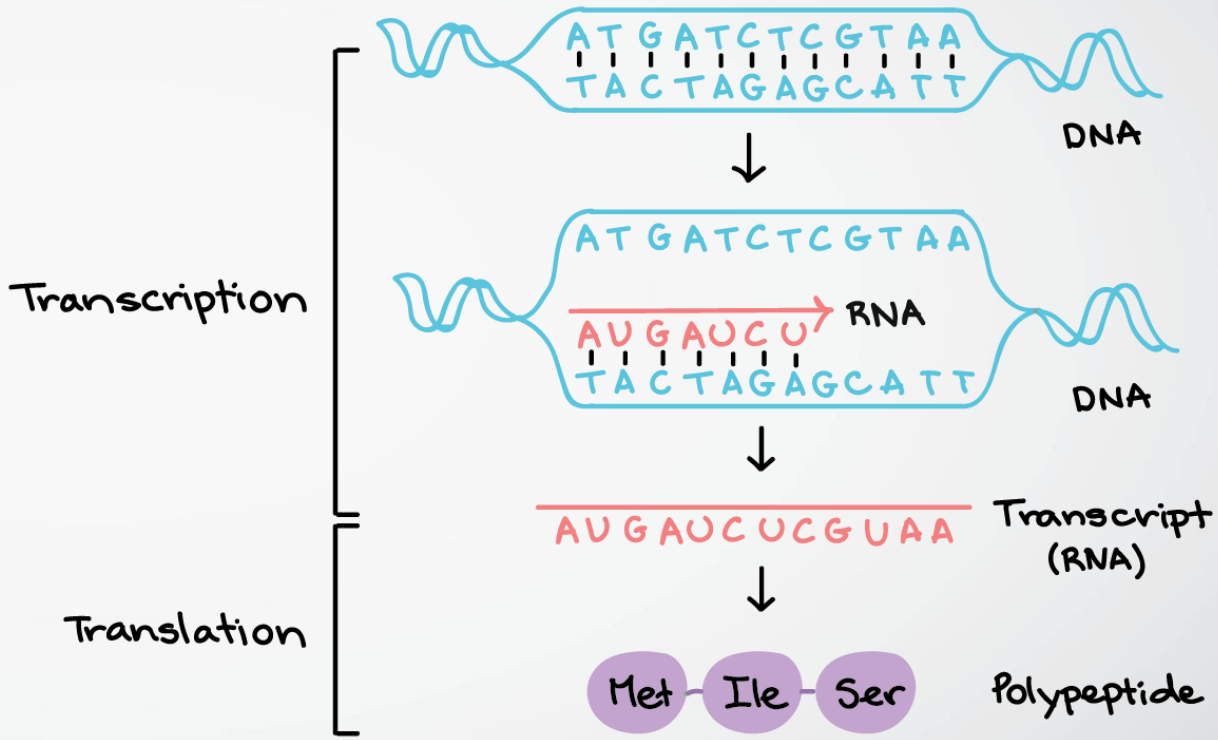
RNA/DNA Modulation Therapies

Biology Class Review

TRANSCRIPTION & TRANSLATION

- Science speak for:

  How our body makes proteins to carry out everyday functions



https://www.khanacademy.org/science/biology/gene-expression-central-dogma/transcription-of-dna-into-rna/a/overview-of-transcription

CLN1	• Infantile NCL • Defective Protein: Palmitoyl Protein Thioesterase 1 (PPT1)	These changes result in abnormal storage of proteins and lipids in neurons and other cells and impaired cellular function
CLN2	• Late Infantile NCL • Defective Protein: Tripetidyl Peptidase 1	These changes result in abnormal storage of protein and lipids in neurons and other cells and impaired cellular function
CLN3	• Juvenile NCL • Defective Protein: CLN3	These changes result in a CLN3 protein that can no longer perform it's biological function properly, leading to nerve cells that do not function properly
CLN4	• Adult Onset NCL • Defective Protein: Cystein proteinα (CSPα)	These changes result in a CSPα that can no longer perform its biological function thought to help with nerve cell communication

CLN5

- Variant Late-Infantile NCL
- Defective Protein: CLN5

The function of CLN5 is not understood well at this time, but is thought to play a role in the process by which lysosomes break down needed protein

CLN6

- Variant Late-Infantile NCL
- Defective Protein: CLN6

The function of CLN6 is not understood well at this time, but it is thought to play a role in helping cells get ride of materials they no longer need

CLN7

- Variant Late-Infantile NCL
- Defective Protein: MFSD8

These changes result in the dysfunction of the MFSD8 protein that is involved with the transportation of substances across cell membranes

CLN8

- EPMR/Late Infantile Onset NCL
- Defective Protein: CLN8

These changes result in a dysfunctional CLN8 protein that is embedded in internal cell membranes

CLN10

- Congenital, Neonatal, and Late Infantile NCL
- Defective Protein: Cathepsin D

These changes result in a change to the Cathepsin D protein, a lysosomal enzyme that breaks apart other proteins in the lysosome

CLN11

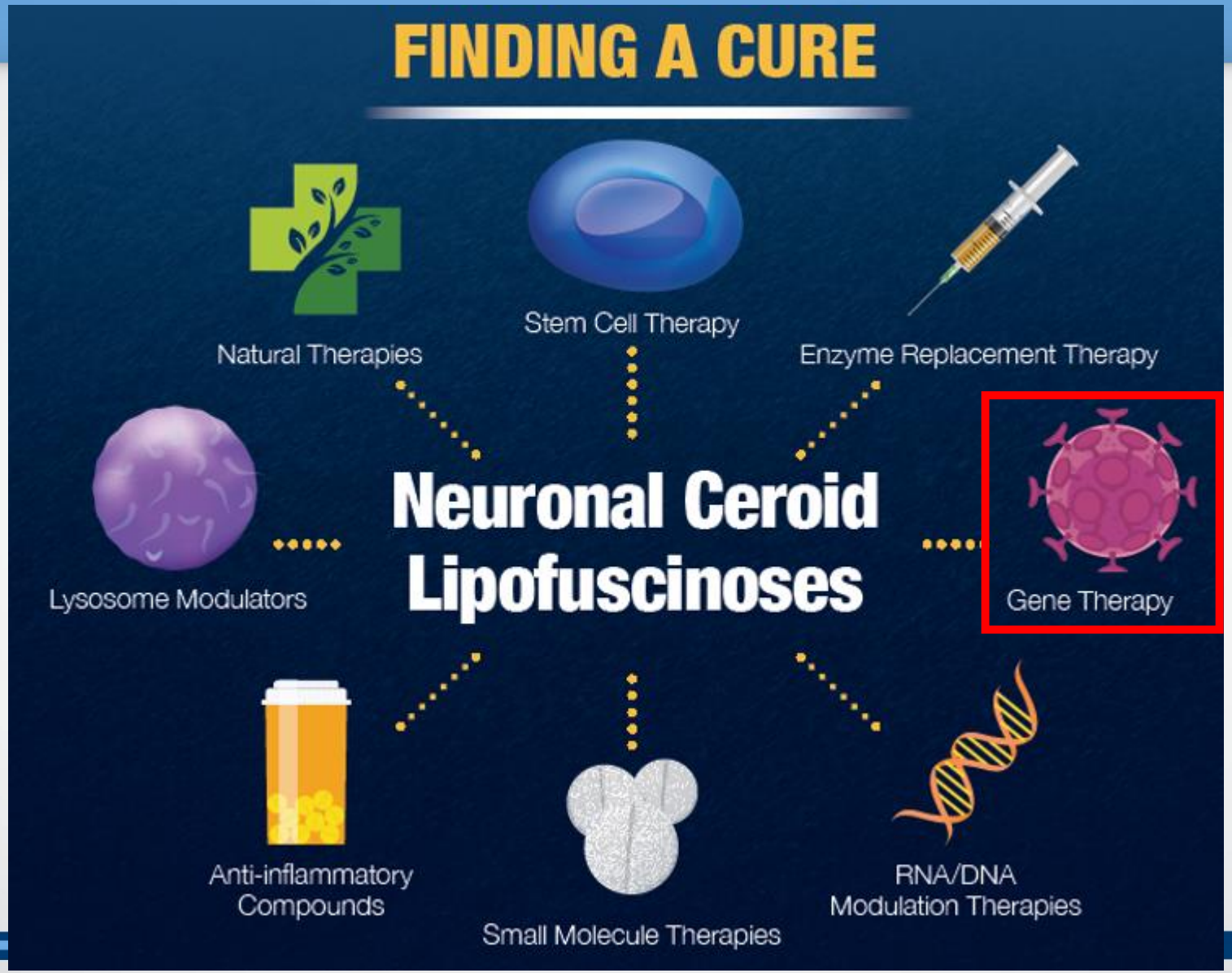
- Adult Onset NCL
- Defective Protein: Progranulin

These changes result in a change to the Progranulin protein, whose function is poorly understood

CLN12

- Juvenile NCL, Kufor-Rakeb Syndrome
- Defective Protein: P-Type ATPase

These changes result in a change to the CLN12 protein, P-Type ATPase, whose function is poorly understood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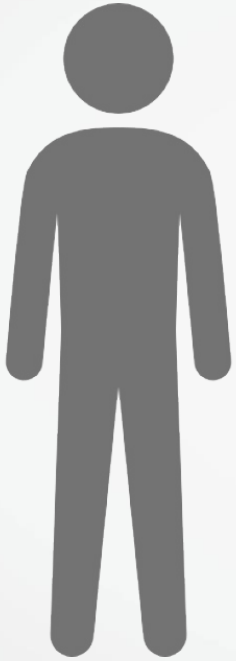
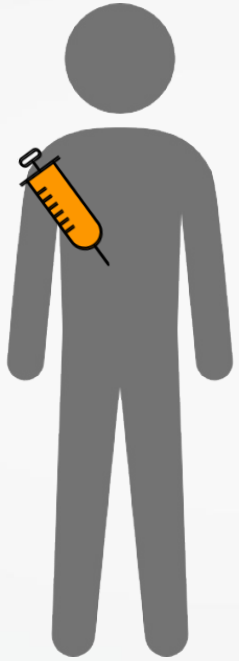
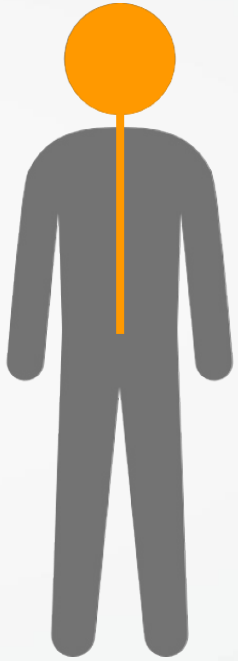
Gene Therapy - Intrathecal



Affected Individual

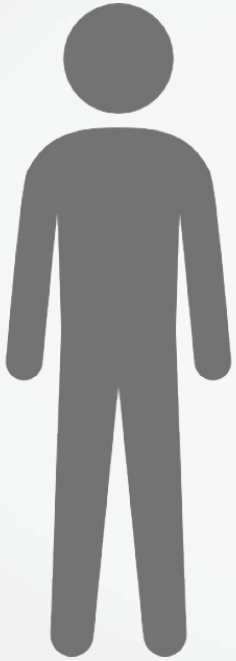


Gene Therapy Delivered Intrathecally

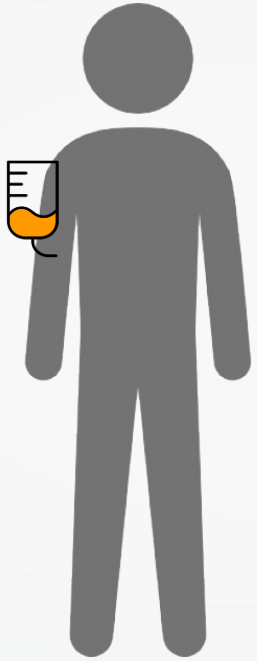


Gene Therapy Spreads throughout central nervous system

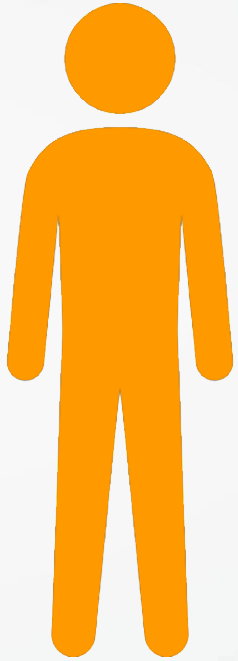
Gene Therapy - Intravenous



Affected Individual

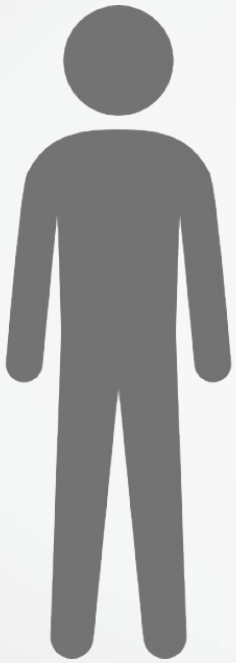


Gene Therapy Delivered Intravenously



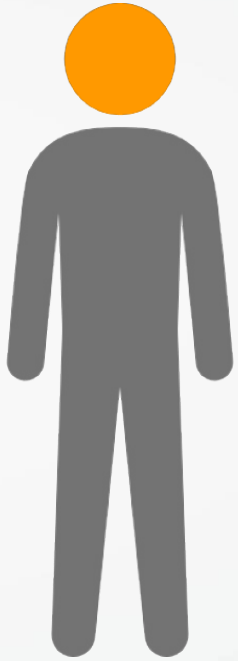
Gene Therapy Spreads throughout body

Gene Therapy - Intracranial



Affected Individual

Gene Therapy Delivered Intracranially



Gene Therapy Spreads throughout the brain

Gene Therapy

CLN6

CLN3

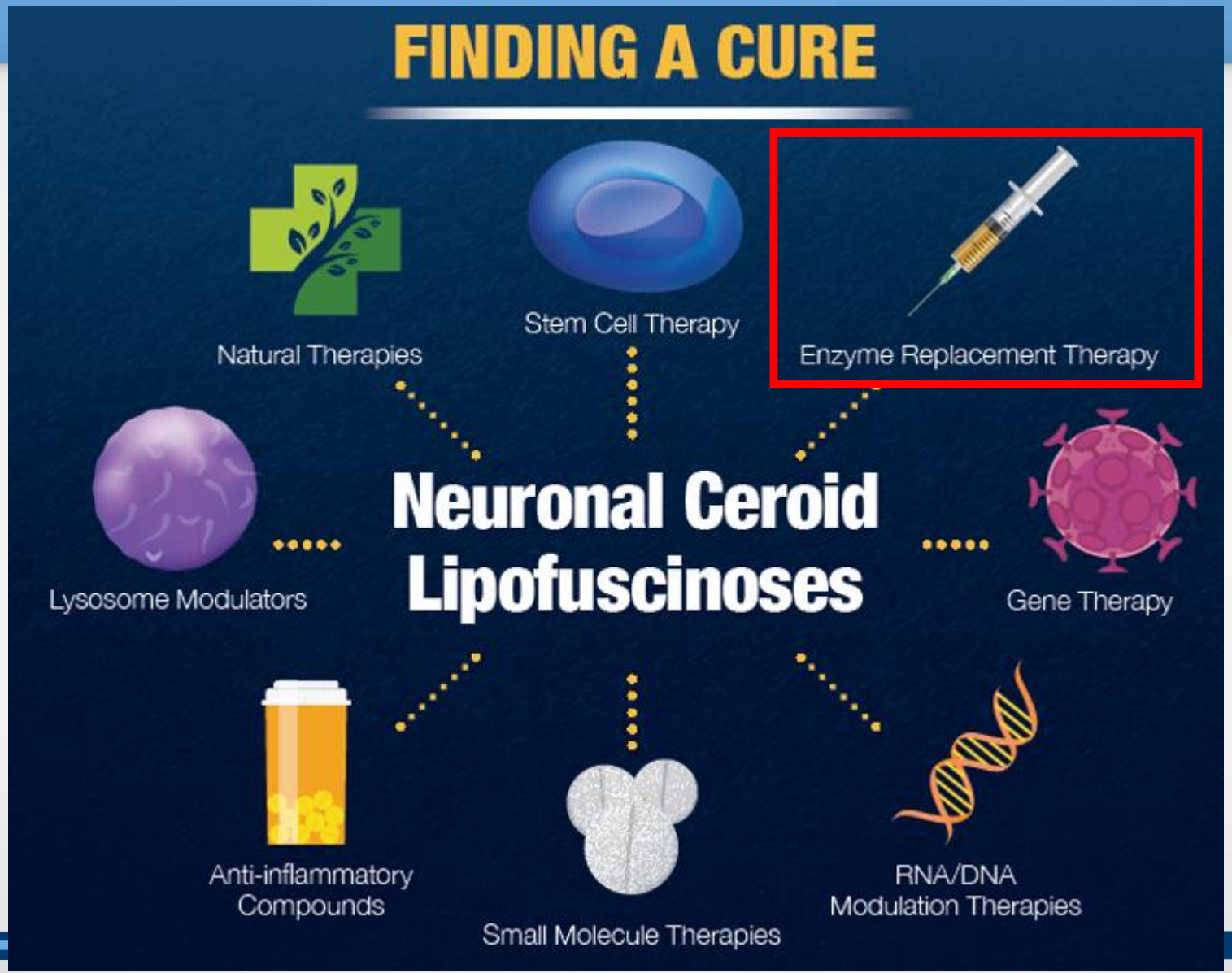
Under Development

REGENXBIO

Abeona THERAPEUTICS

Spark THERAPEUTICS

Amicus Therapeutics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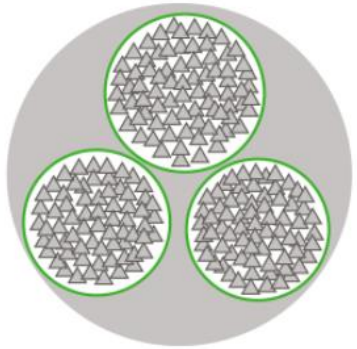
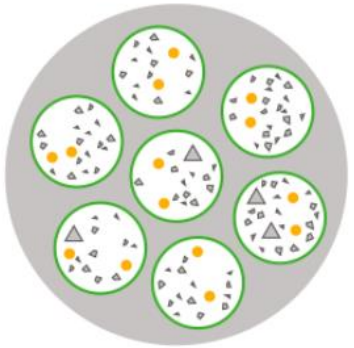
Enzyme Replacement Therapy



The TPP1 enzyme is missing or not working properly in children with CLN2 disease. This leads to a buildup of storage materials in their lysosomes, associated with cell damage in the brain.[1-3]

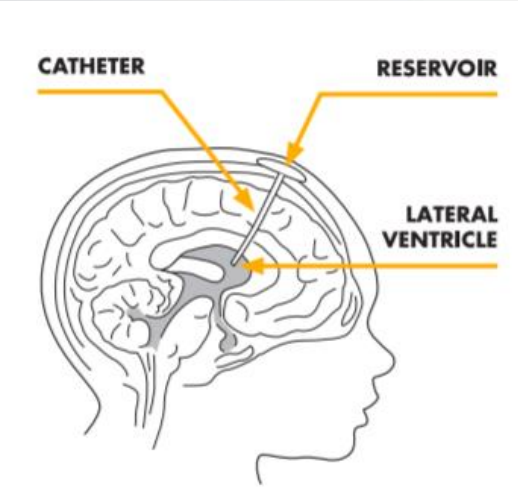


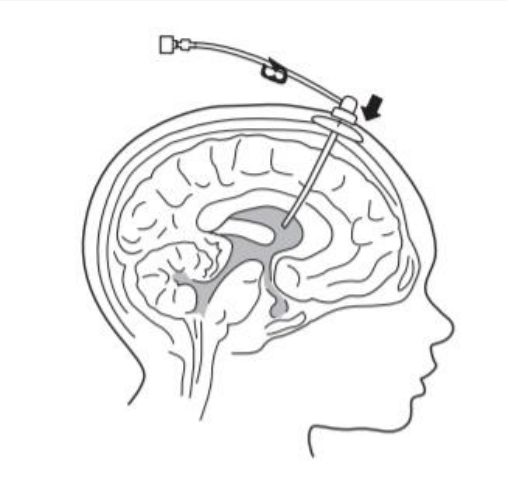
When Brineura is delivered to a child with CLN2 disease, it helps replace the missing TPP1 enzyme.[4]

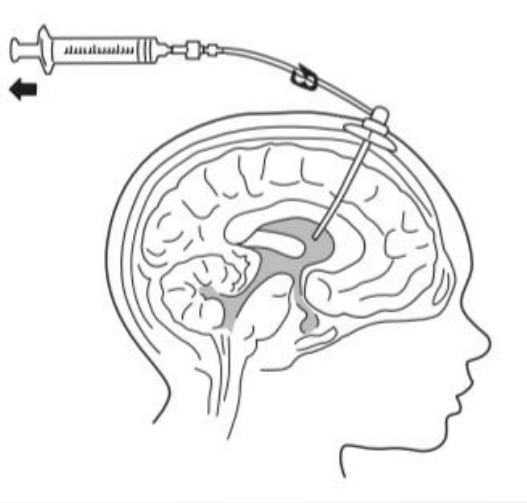
Lysosomes Storage material TPP1 enzyme

https://www.brineura.com/about/

Enzyme Replacement Therapy







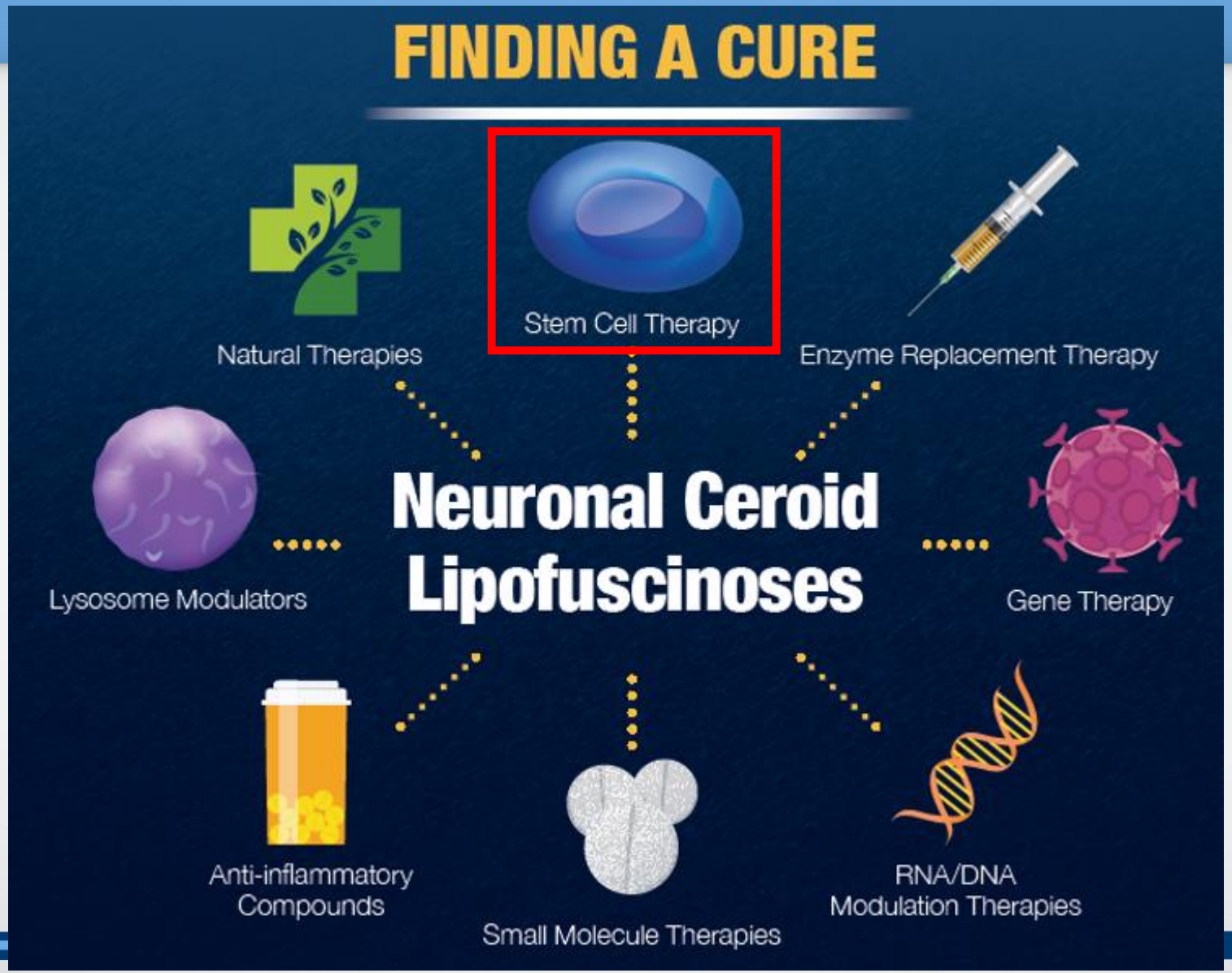
FDA approved, Brineura, for CLN2- Batten Disease is introduced to patients every 2 weeks through a port inserted in their skull.

https://www.brineura.com/wp-content/themes/jupiter-child/assets/pdfs/resources/Brineura-Dosing-and-Administration-Guide.pdf

Enzyme Replacement Therapy

BIOMARIN®

COLLABORATIONS PHARMACEUTICALS, INC.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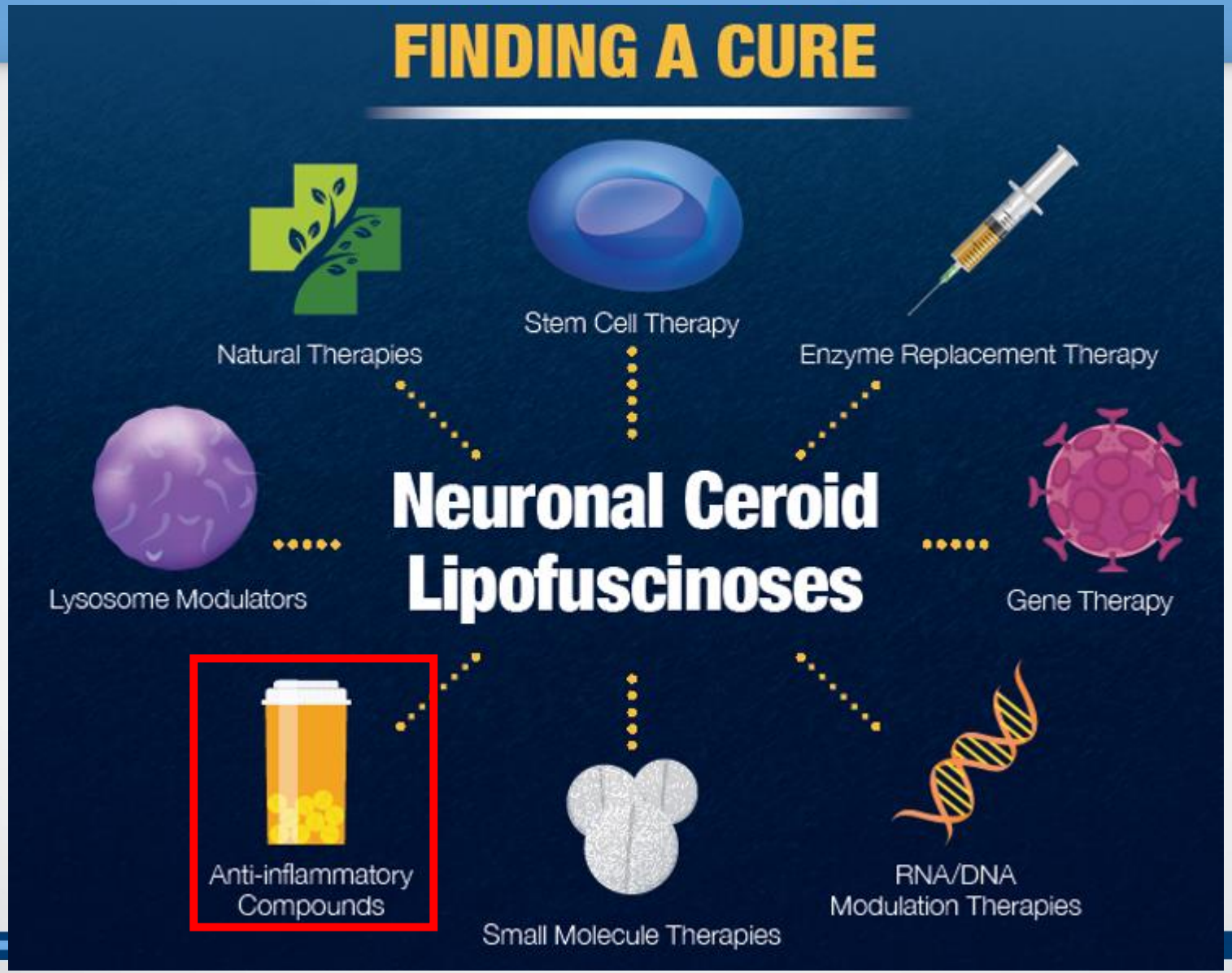
Stem Cells

Completed

Stem Cells Incorporated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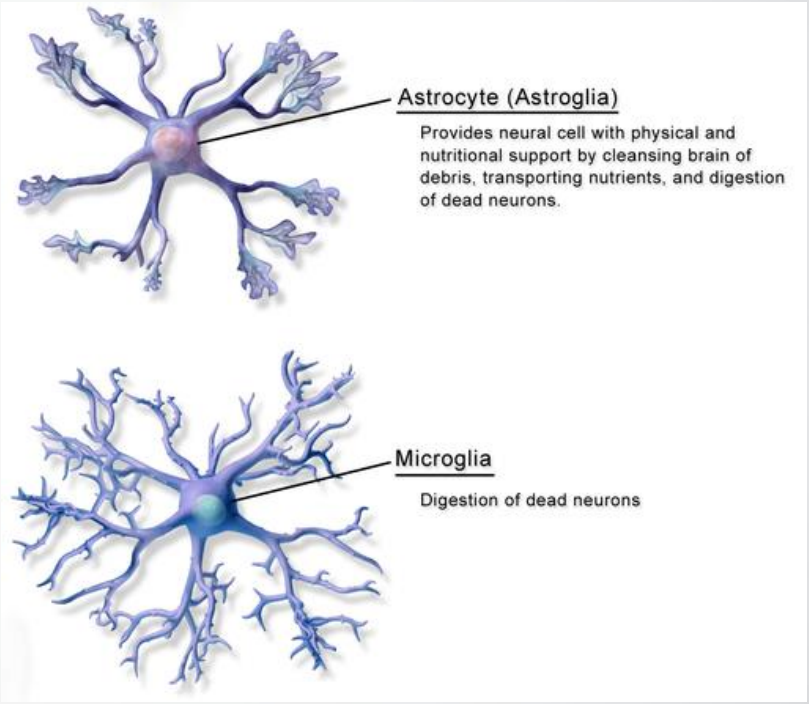
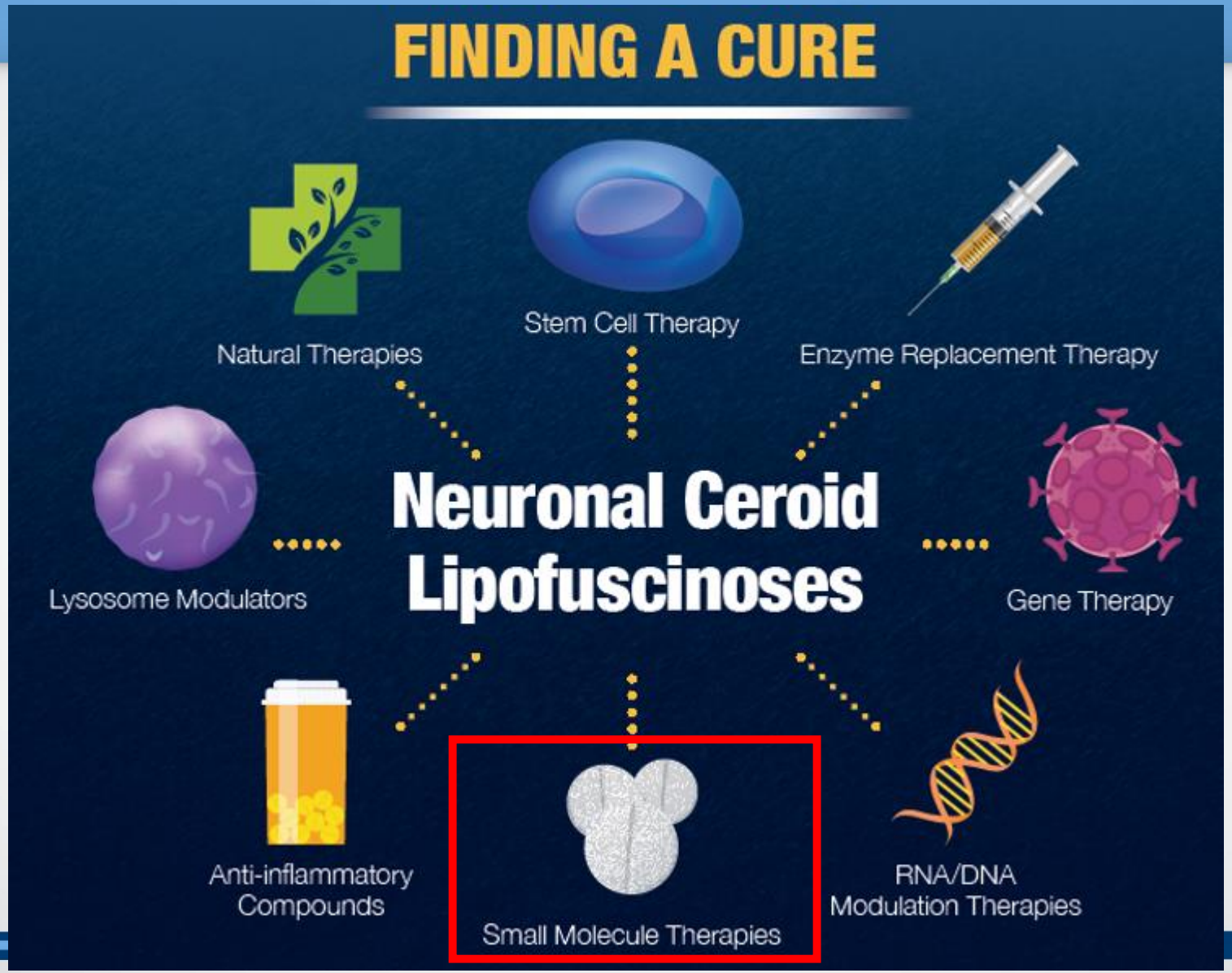
Anti-inflammatory Compounds

You keep hearing about astrocytes and microglial inflammation of the brain

- Compounds that are anti-inflammatory
- Mycophenolate

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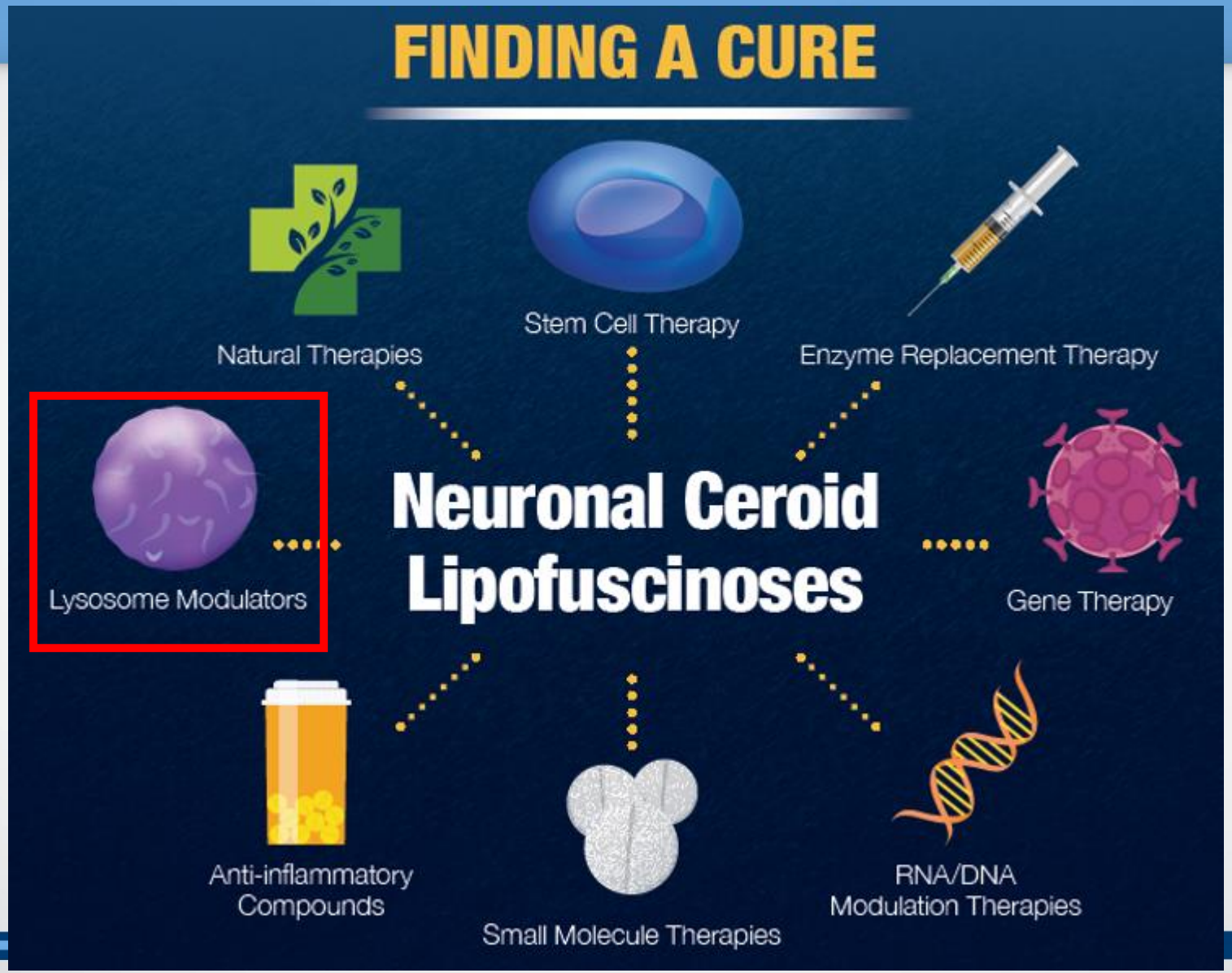
Small Molecule Therapies

Existing Drugs or

New Drugs?

- Modulate activity of CLN-products
- Clear storage material

Small Molecule Therapies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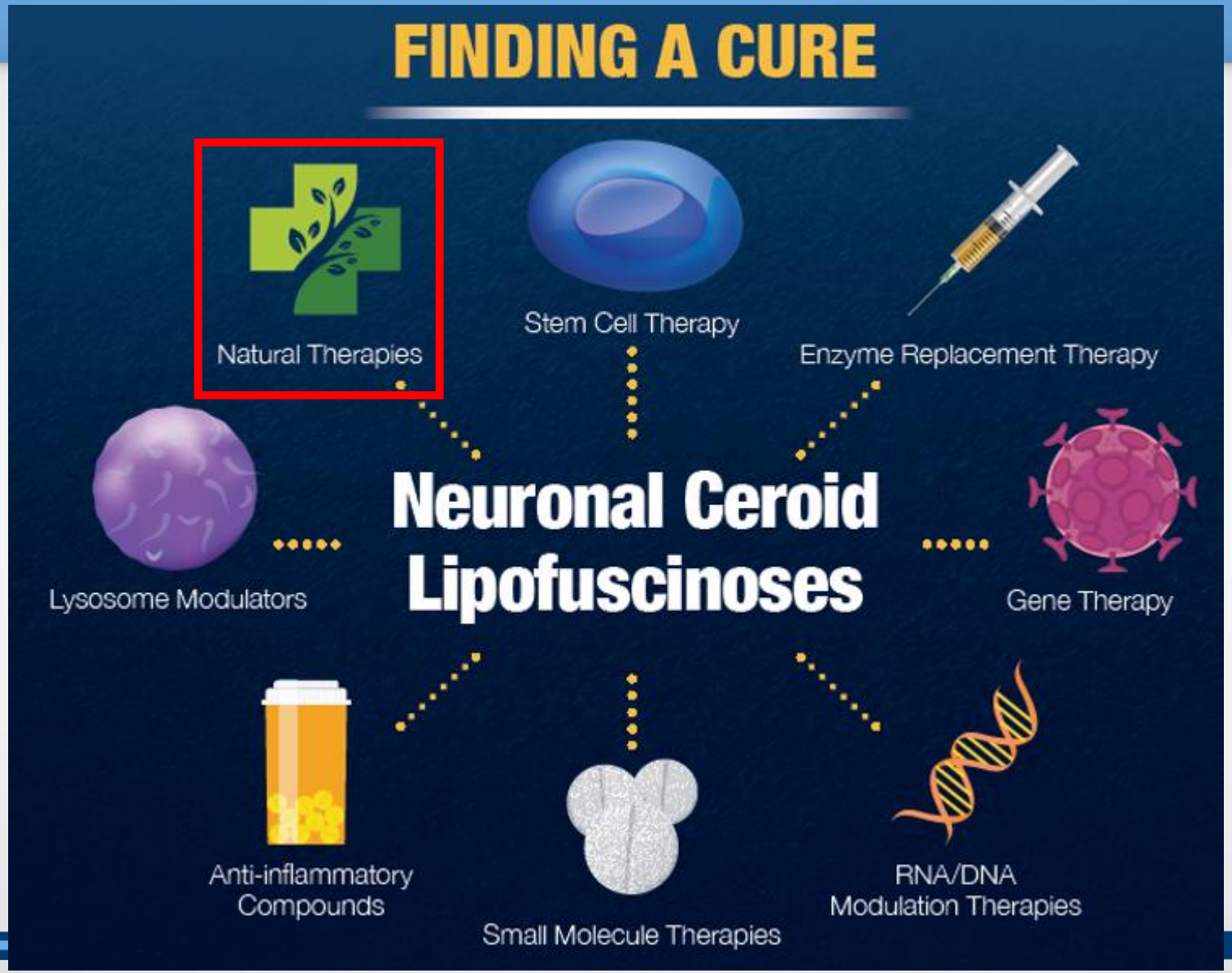
Lysosome Modulators

We know in all Batten disease that lysosome function is compromised….SO LETS FIX IT.

- pH modulation
- Calcium modulation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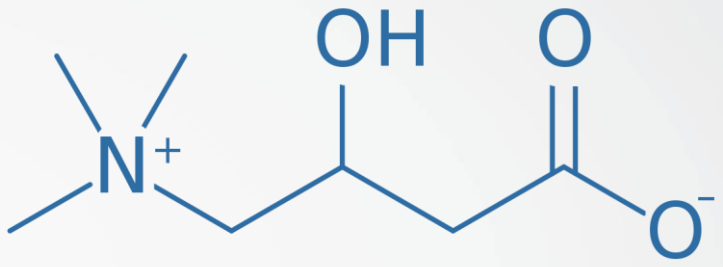
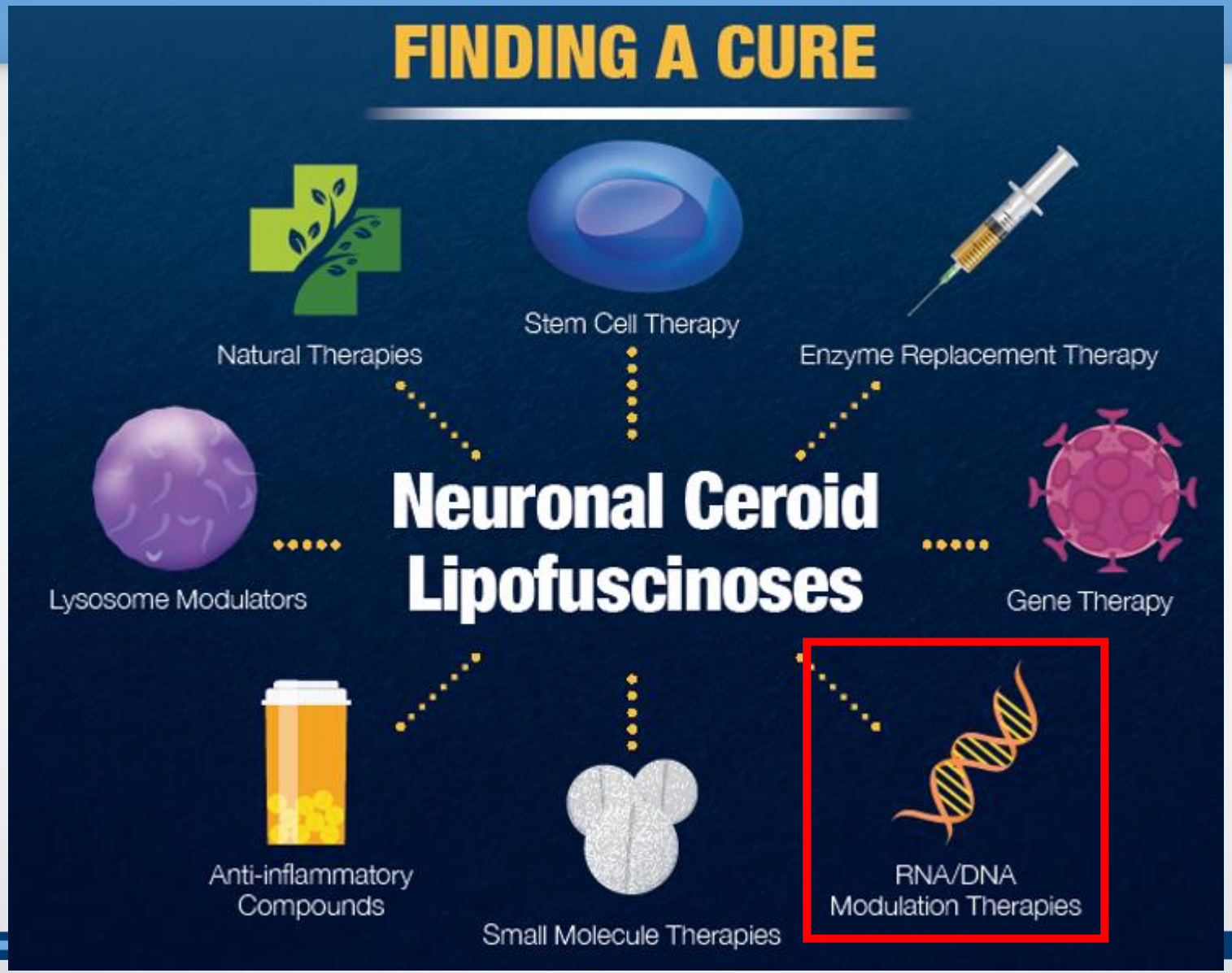
Natural Therapies

Symptomatic Treatments

- Carnitine



- Fish Oil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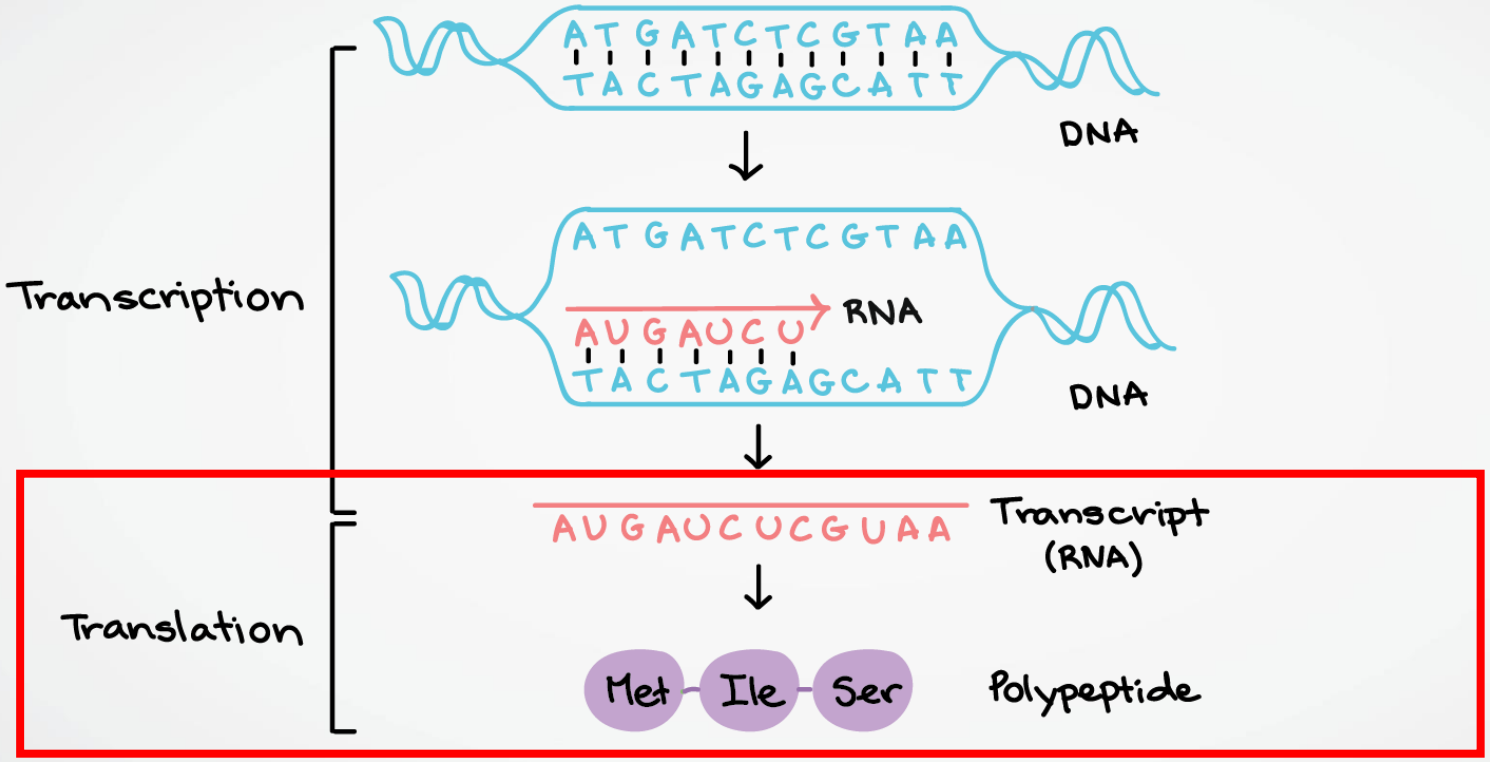
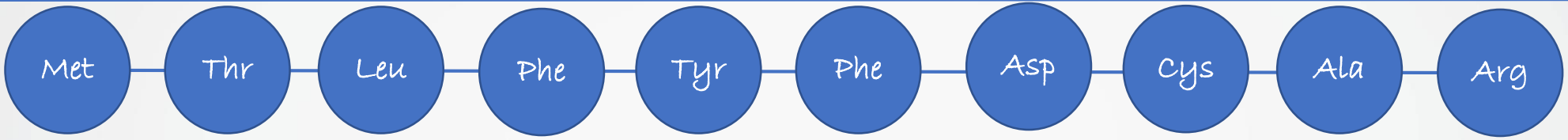
RNA/DNA Modulation



https://www.khanacademy.org/science/biology/gene-expression-central-dogma/transcription-of-dna-into-rna/a/overview-of-transcription

RNA/DNA Modulation

AUU AUG ACG UUA UUC UAC UUU GAU UGU GCG AGA UAG C



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RNA/DNA Modulation