Pipeline Therapies for Parkinson's Disease

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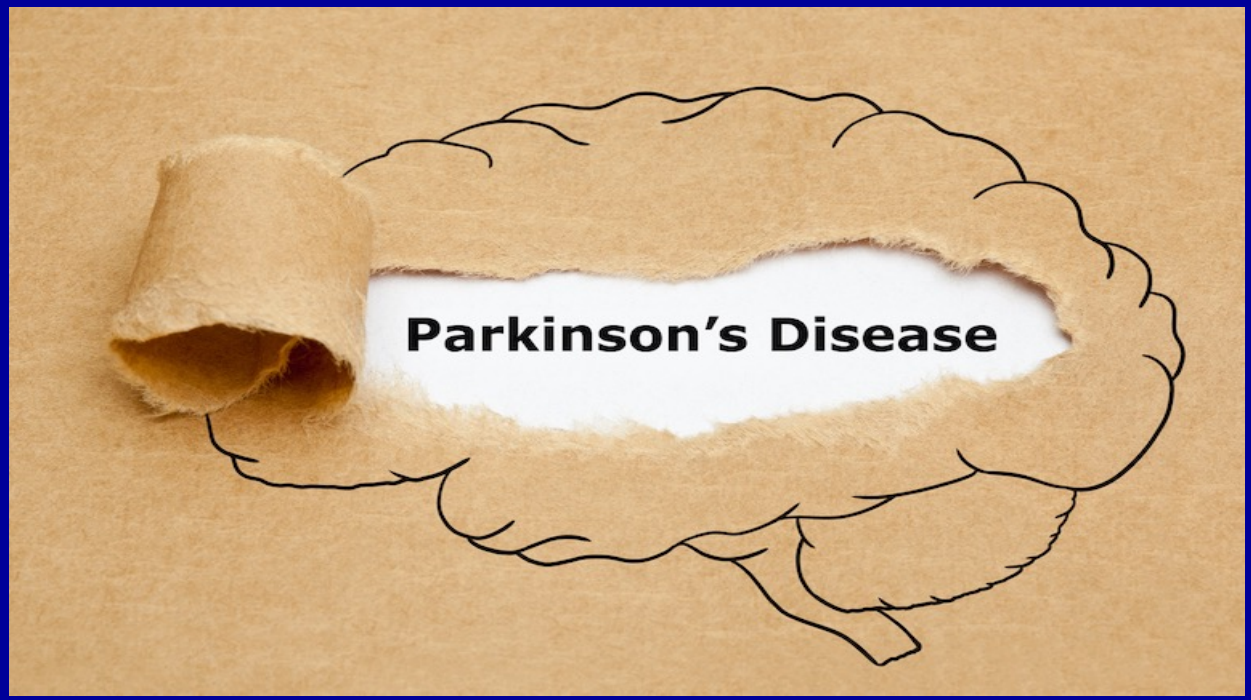


Clinical trials 101

- How do we categorize trials?
  - Symptomatic treatment vs disease modifying
  - Mechanism of action of a compound
  - Phase studies

    phase 1 safety

    Phase 2 efficacy

    Phase 3 long term large study

Two Main Types of Therapy

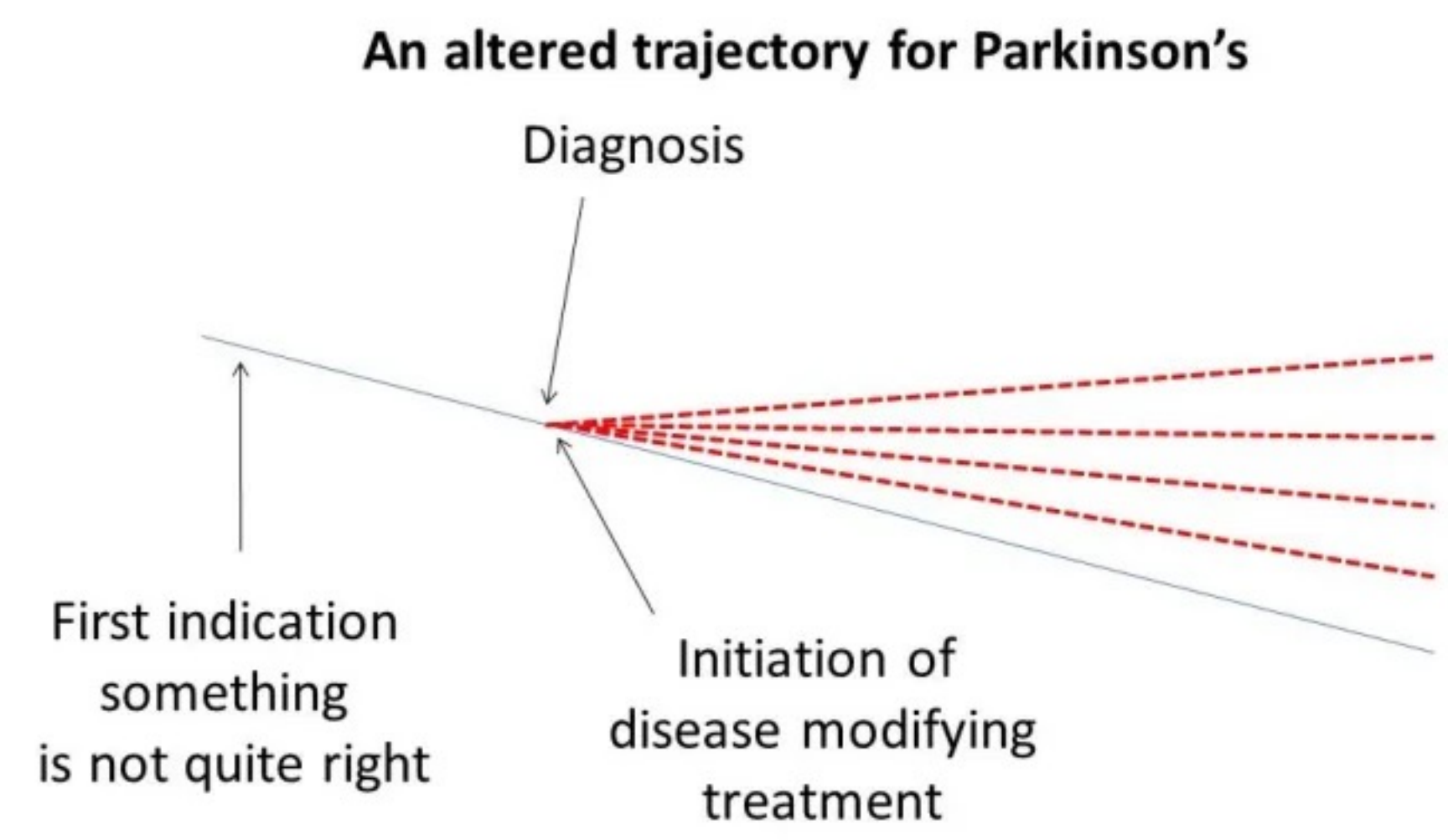
- Knee pain analogy
  - **Symptomatic therapy**: regardless of cause, Tylenol or ibuprofen helps
  - **Disease modifying therapy**: fix the source of the pain (arthritis, torn meniscus) stops further deterioration of that knee

Symptomatic

- Changing brain chemical transporters
  - Dopamine
  - Serotonin
  - Acetylcholine/glutamate

  - Changing brain functional network
    - Deep Brain Stimulation
    - MRIgfUS

Disease modifying



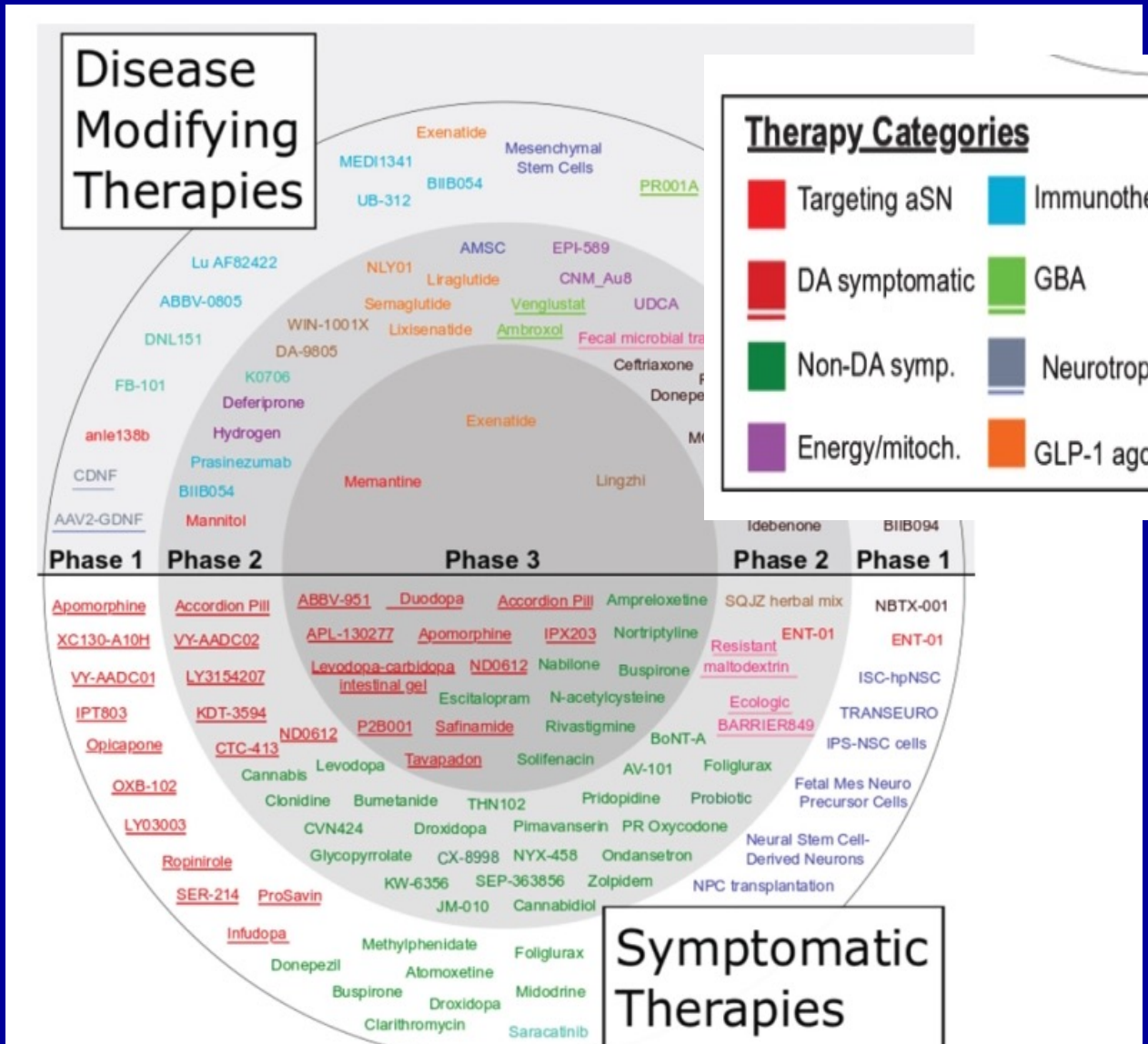
Mechanism of Action

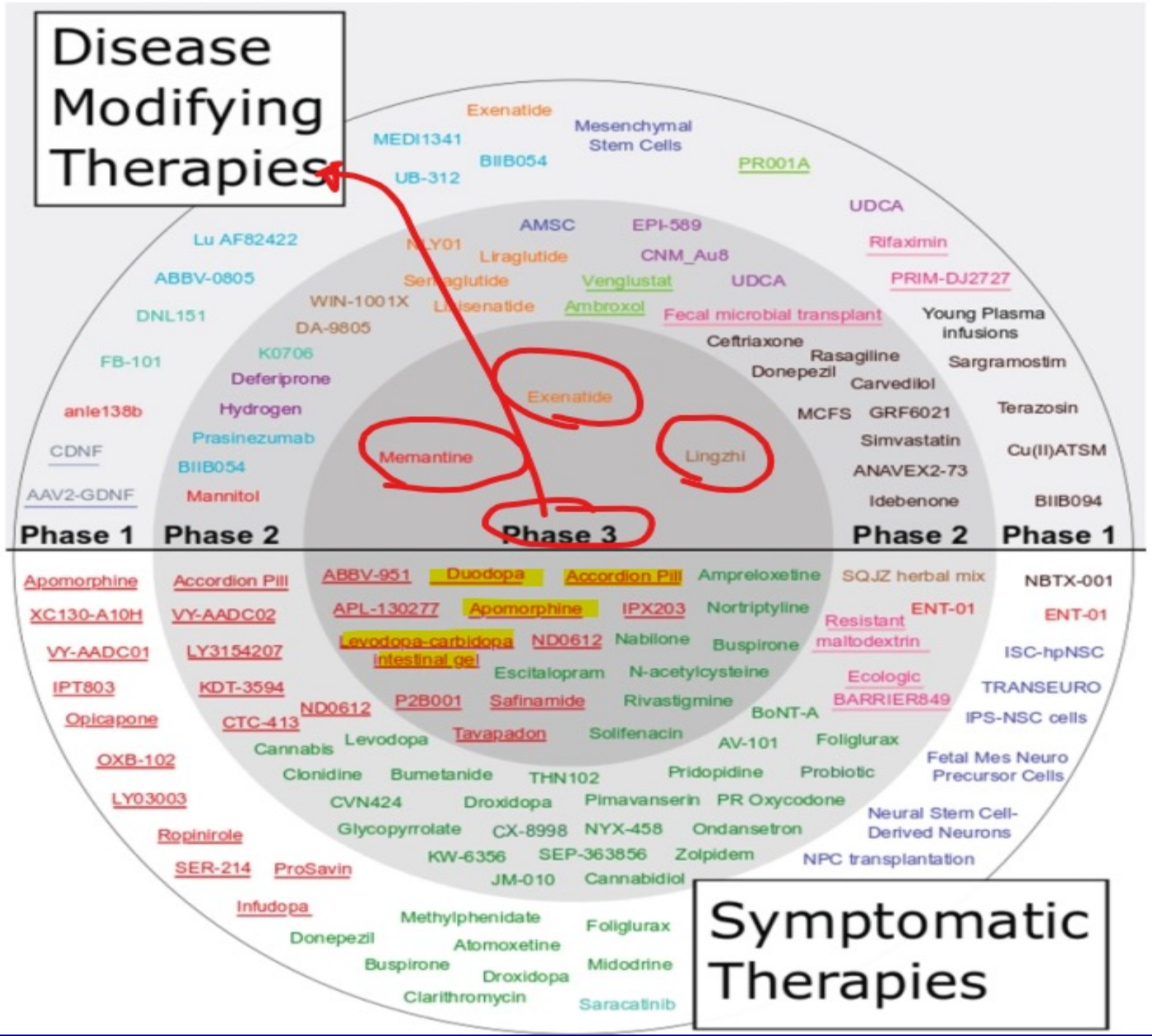
- *Antioxidants* – reducing oxidative stress
- *Botanicals* – herbal extracts
- *Cell therapy* – cell transplantation or peripheral delivery of cells.
- *Dopaminergic symptom relief* – agents that mimic the chemical dopamine.
- *Energy and mitochondria* – restoring mitochondrial function.
- *GBA* – enhancing the activity of glucocerebrosidase.
- *GLP-1 agonists* – a class of diabetes drugs.
- *Immunotherapy* – antibody-based agents.

Mechanism of Action

- *Kinase inhibitors* – blocking certain kinase activity.
- *Microbiome/GIT* – focused on the gastrointestinal tract.
- *Neurotrophic factors* – delivery of GDNF or CDNF.
- *Non-dopaminergic symptom relief* – symptomatic therapies not involving dopamine.
- *Targeting alpha synuclein* – agents inhibiting alpha synuclein aggregation.
- *Other* – where there was only one treatment for a specific MOA.

THE PIPELINE




Disease Modifying Therapies
Exenatide
Mesenchymal Stem Cells
MEDI1341
BIIB054
PR001A
UB-312
UDCA
AMSC
EPI-589
Lu AF82422
Rifaximin
Liraglutide
CNM_Au8
ABBV-0805
Venglustat
UDCA
PRIM-DJ2727
WIN-1001X
Ambroxol
Fecal microbial transplant
Young Plasma infusions
DNL151
DA-9805
Ceftriaxone
FB-101
K0706
Rasagiline
Sargramostim
Donepezil
Deferiprone
Carvedilol
Exenatide
anle138b
Hydrogen
MCFS
GRF6021
Terazosin
Prasinezumab
Simvastatin
Memantine
Lingzhi
CDNF
Cu(II)ATSM
BIIB054
ANAVEX2-73
AAV2-GDNF
Mannitol
Idebenone
BIIB094
Phase 1
Phase 2
Phase 3
Phase 2
Phase 1
Apomorphine
Accordion Pill
ABBV-951
Duodopa
Accordion Pill
Ampreloxetine
SQJZ herbal mix
NBTX-001
XC130-A10H
VY-AADC02
APL-130277
Apomorphine
IPX203
Nortriptyline
ENT-01
ENT-01
Resistant maltodextrin
VY-AADC01
LY3154207
Levodopa-carbidopa intestinal gel
ND0612
Nabilone
Buspirone
ISC-hpNSC
Escitalopram
N-acetylcysteine
IPT803
KDT-3594
Ecologic BARRIER849
TRANSEURO
P2B001
Safinamide
Rivastigmine
ND0612
BoNT-A
Opicapone
CTC-413
IPS-NSC cells
Tavapadon
Solifenacin
Levodopa
AV-101
Foliglurax
Cannabis
OXB-102
Fetal Mes Neuro Precursor Cells
Clonidine
Bumetanide
THN102
Pridopidine
Probiotic
LY03003
CVN424
Droxidopa
Pimavanserin
PR Oxycodone
Neural Stem Cell-Derived Neurons
Glycopyrrolate
CX-8998
NYX-458
Ondansetron
Ropinirole
KW-6356
SEP-363856
Zolpidem
NPC transplantation
SER-214
ProSavin
JM-010
Cannabidiol
Infudopa
Methylphenidate
Foliglurax
Donepezil
Atomoxetine
Buspirone
Midodrine
Droxidopa
Clarithromycin
Saracatinib
Symptomatic Therapies

repurposed/refashioned

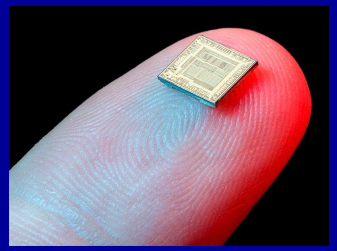
KYNMOBI™
(apomorphine HCl) sublingual film
10 mg • 15 mg • 20 mg • 25 mg • 30 mg

ts (34% of trials)

ONCE DAILY AT BEDTIME
GOCOVRI®
(amantadine) extended release capsules
68.5 mg | 137 mg

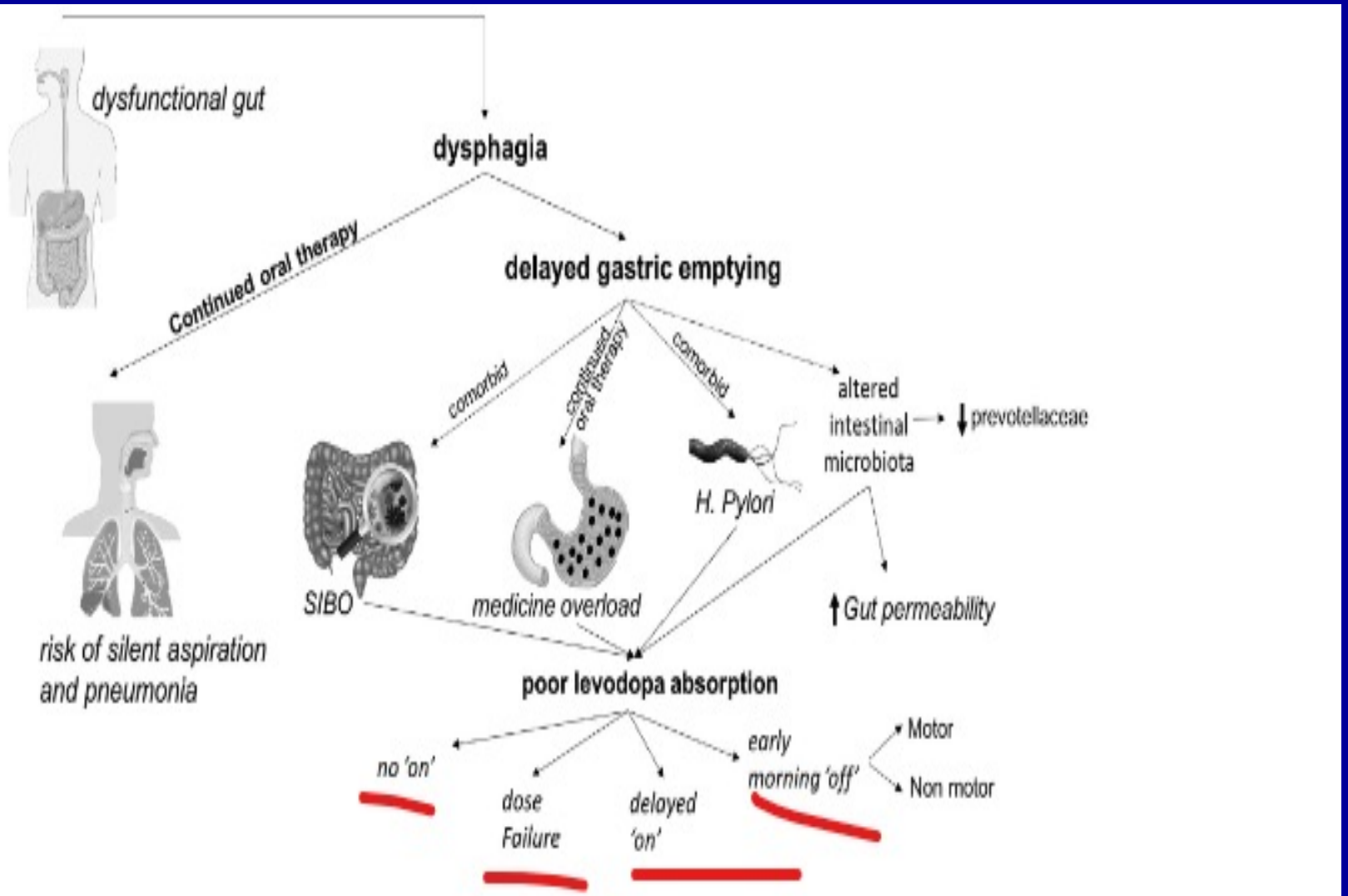
Ongentys®
(opicapone) caps

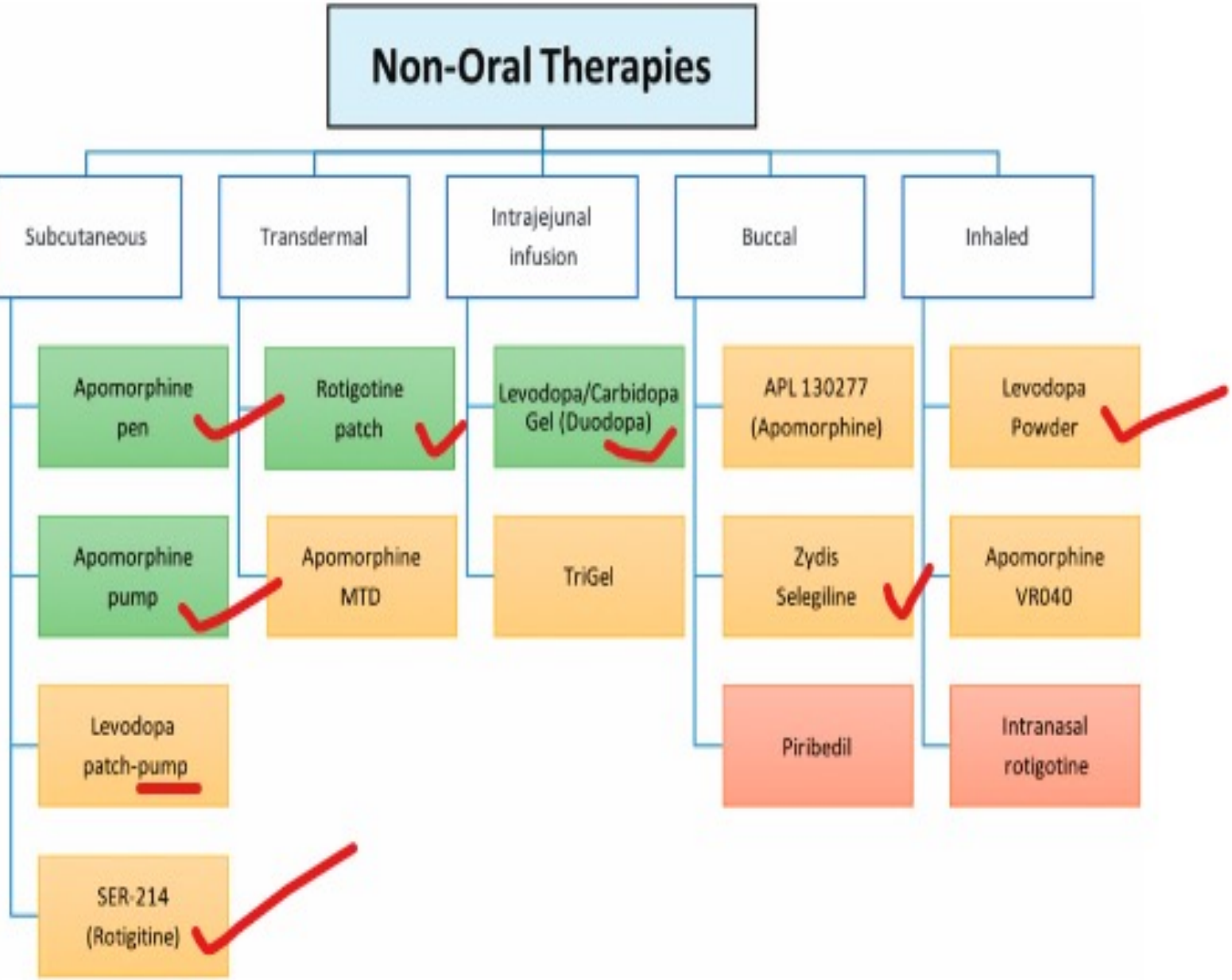
Honorable mention



- DBS technology
- Drugs that bypass the gut
- Alpha synuclein drugs
- Ultrasound therapy
- Stem cells
- Transdifferentiation

Get it in somehow!

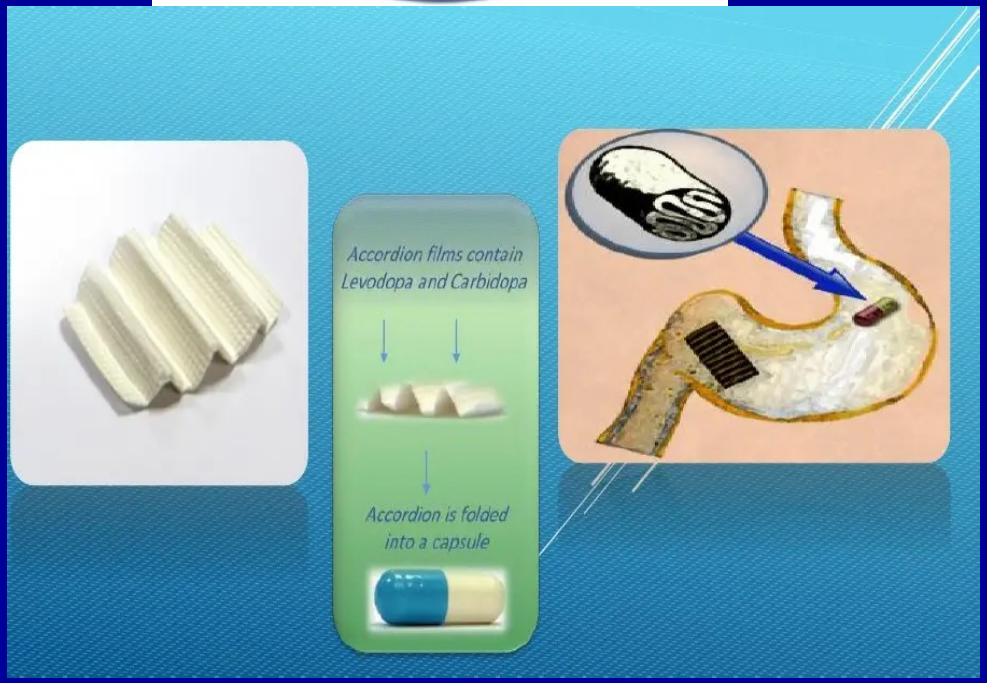



Non-Oral Therapies
Subcutaneous
Transdermal
Intrajejunal infusion
Buccal
Inhaled
Apomorphine pen
Apomorphine pump
Levodopa patch-pump
SER-214 (Rotigitine)
Rotigotine patch
Apomorphine MTD
Levodopa/Carbidopa Gel (Duodopa)
TriGel
APL 130277 (Apomorphine)
Zydis Selegiline
Piribedil
Levodopa Powder
Apomorphine VR040
Intranasal rotigotine

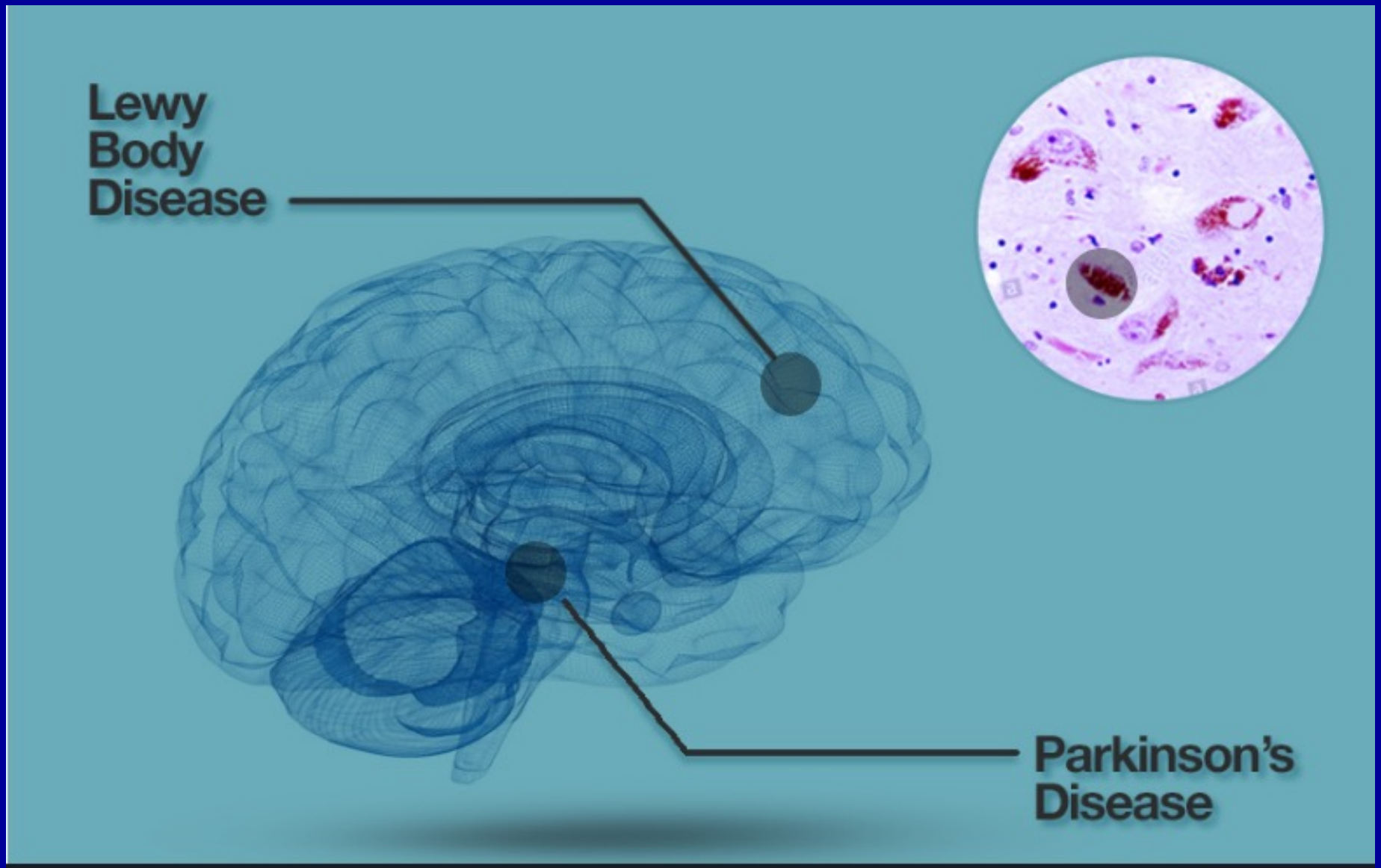
Levodopa delivery

- **patch/pump**

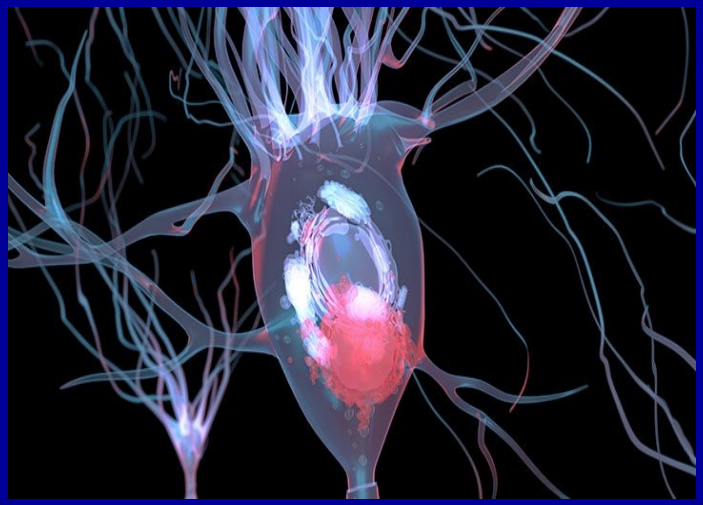
- **Accordian pill**

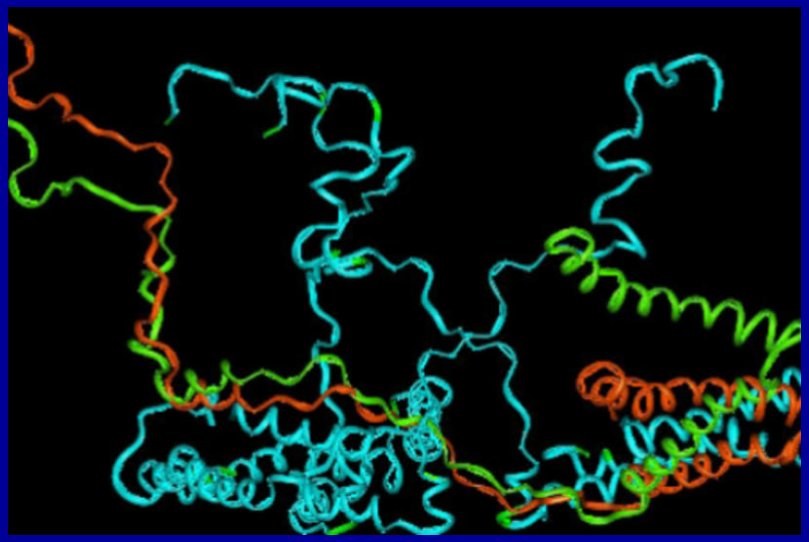


Lewy Bodies = alpha synuclein



clumps of “toxic” alpha synuclein





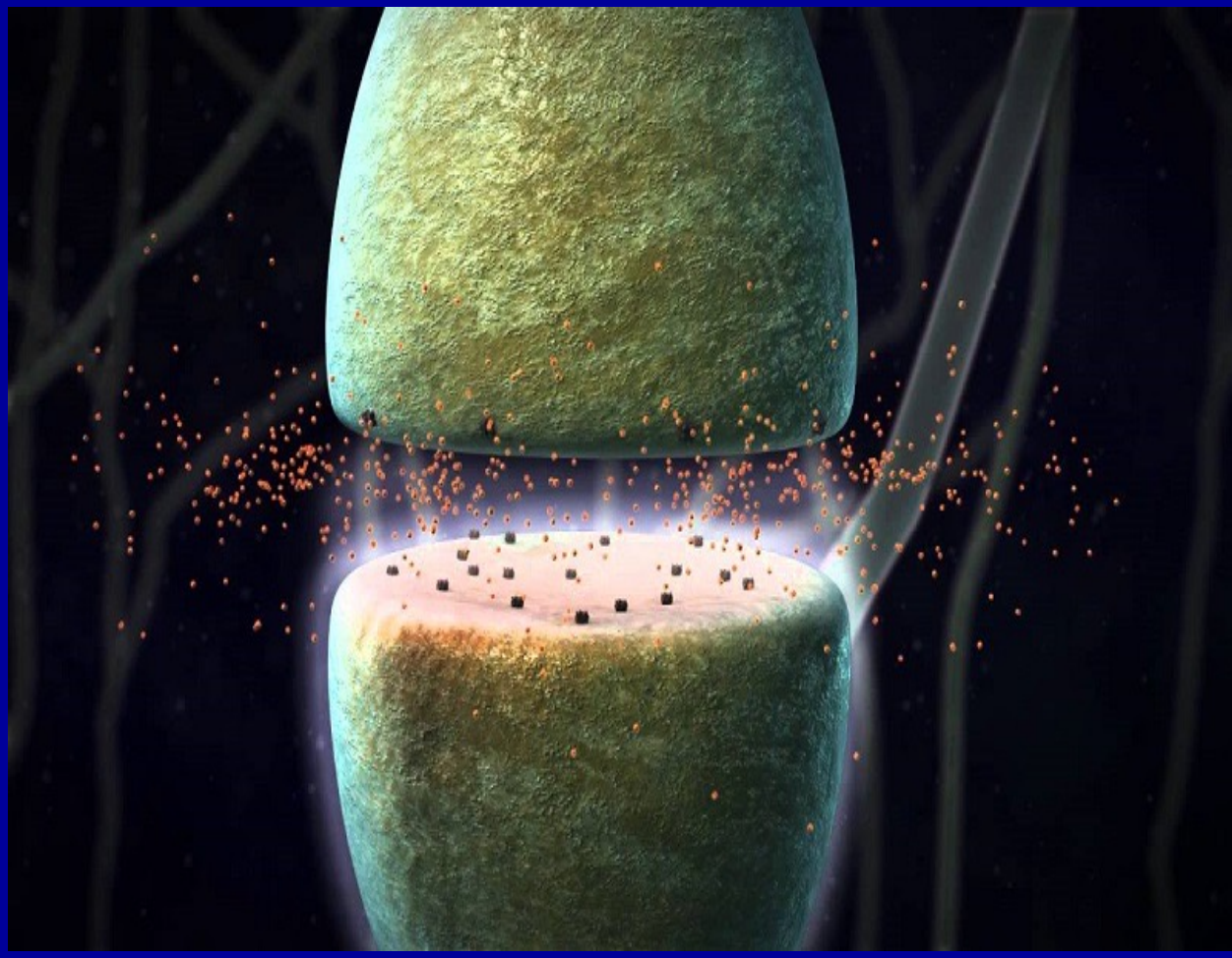
Toxic

-destroy the cell

-interferes with synapse

-can spread out of cell and injure other cells (prion-like)

-inhibits axonal transport



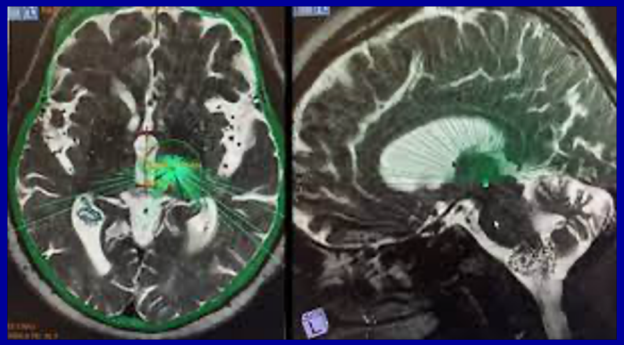
Some ASN busters

- Prothena/Roche 

- Biogen 

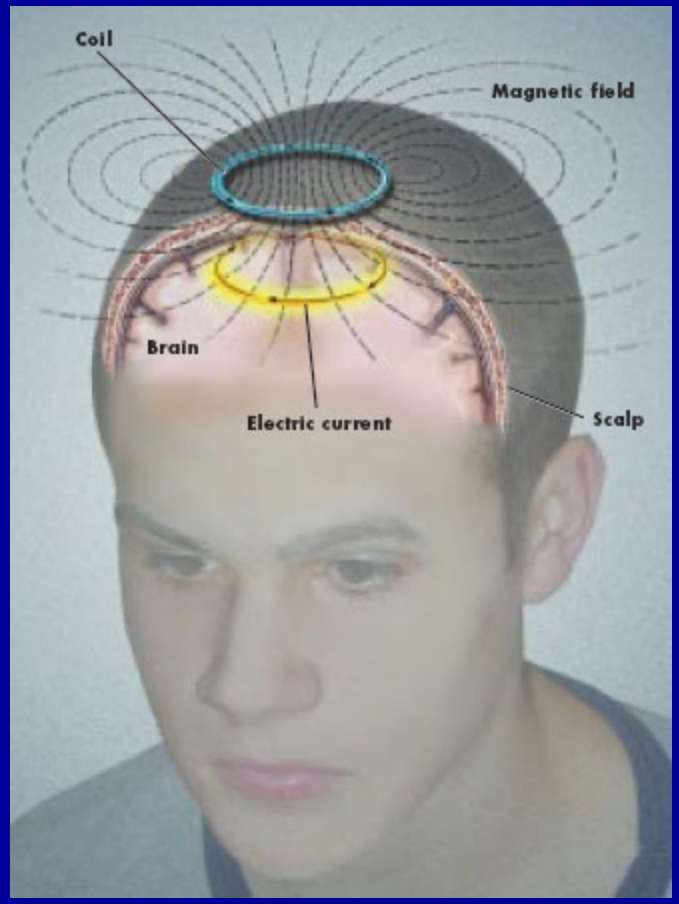
- Proclara
- Modag
- Prasinezumab
- AstraZeneca/Takeda – (MEDI1341)
- AFFiRis _ vaccine ASN

MRIgfUS (ultrasound ablation)

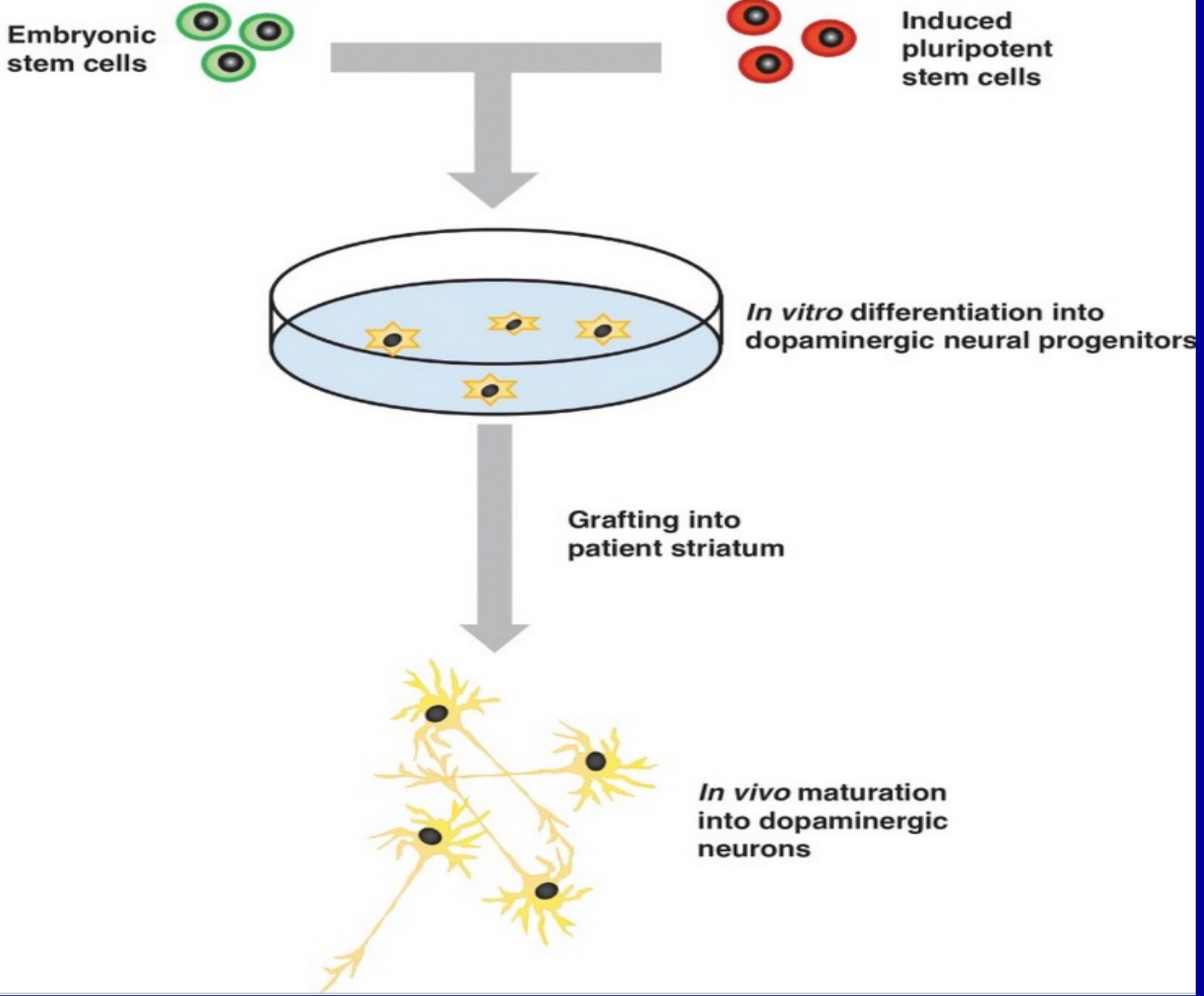


Magnetic Stimulation

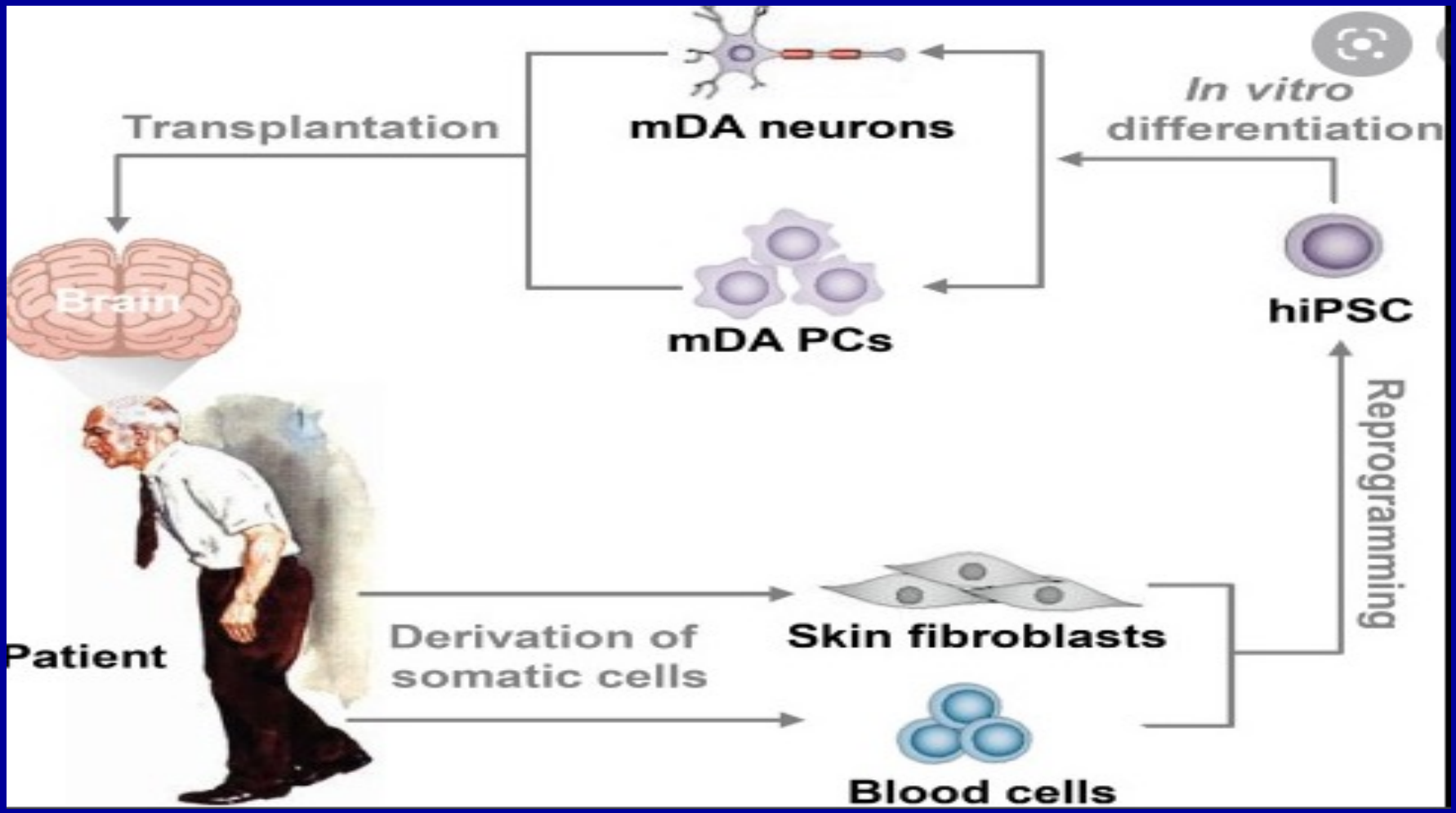
- Not electroconvulsive
- It's a magnetic device
- 8 positive, 6 neg trials
- OCD, depression, almost PTSD



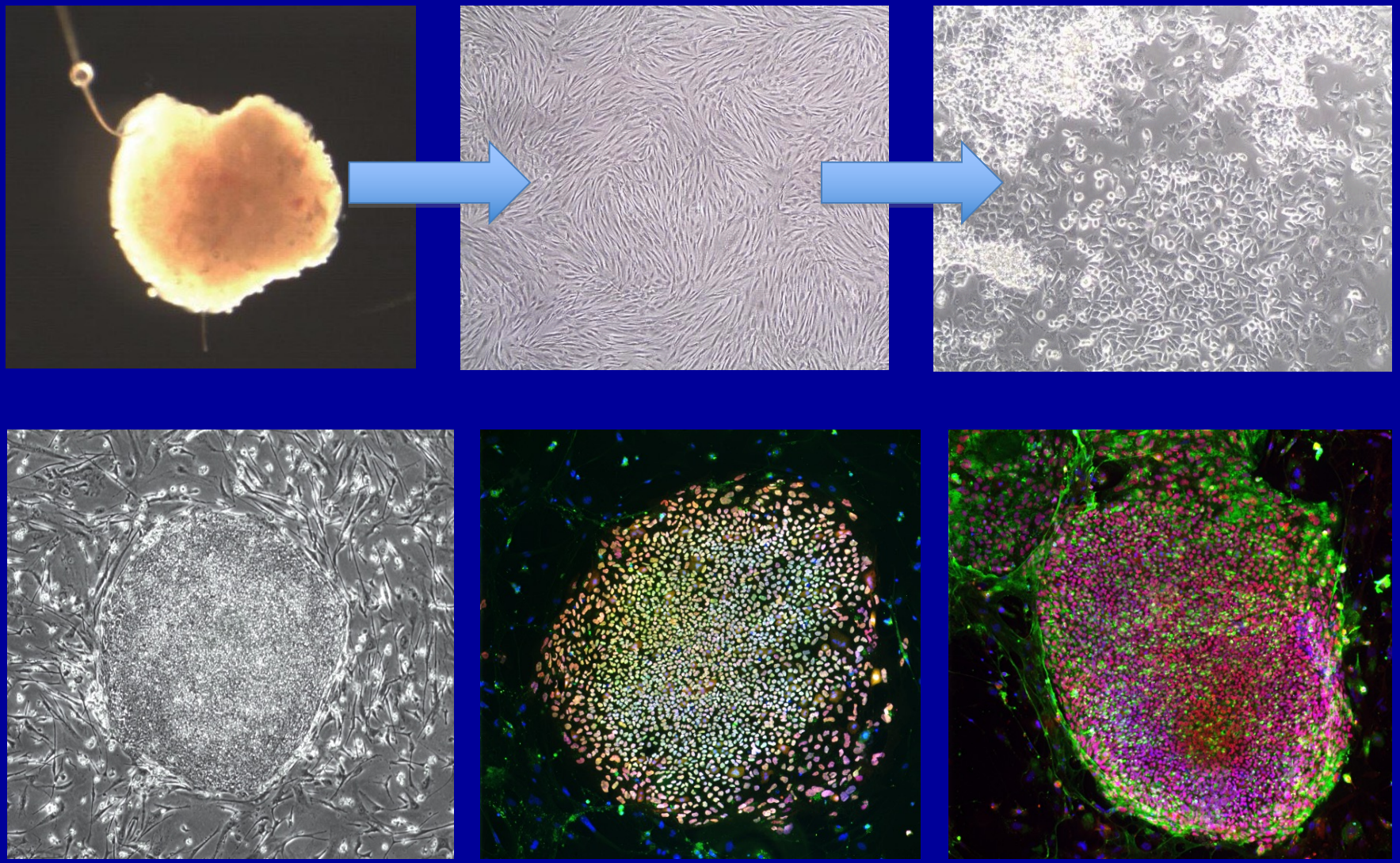
“Stem Cell” Therapy

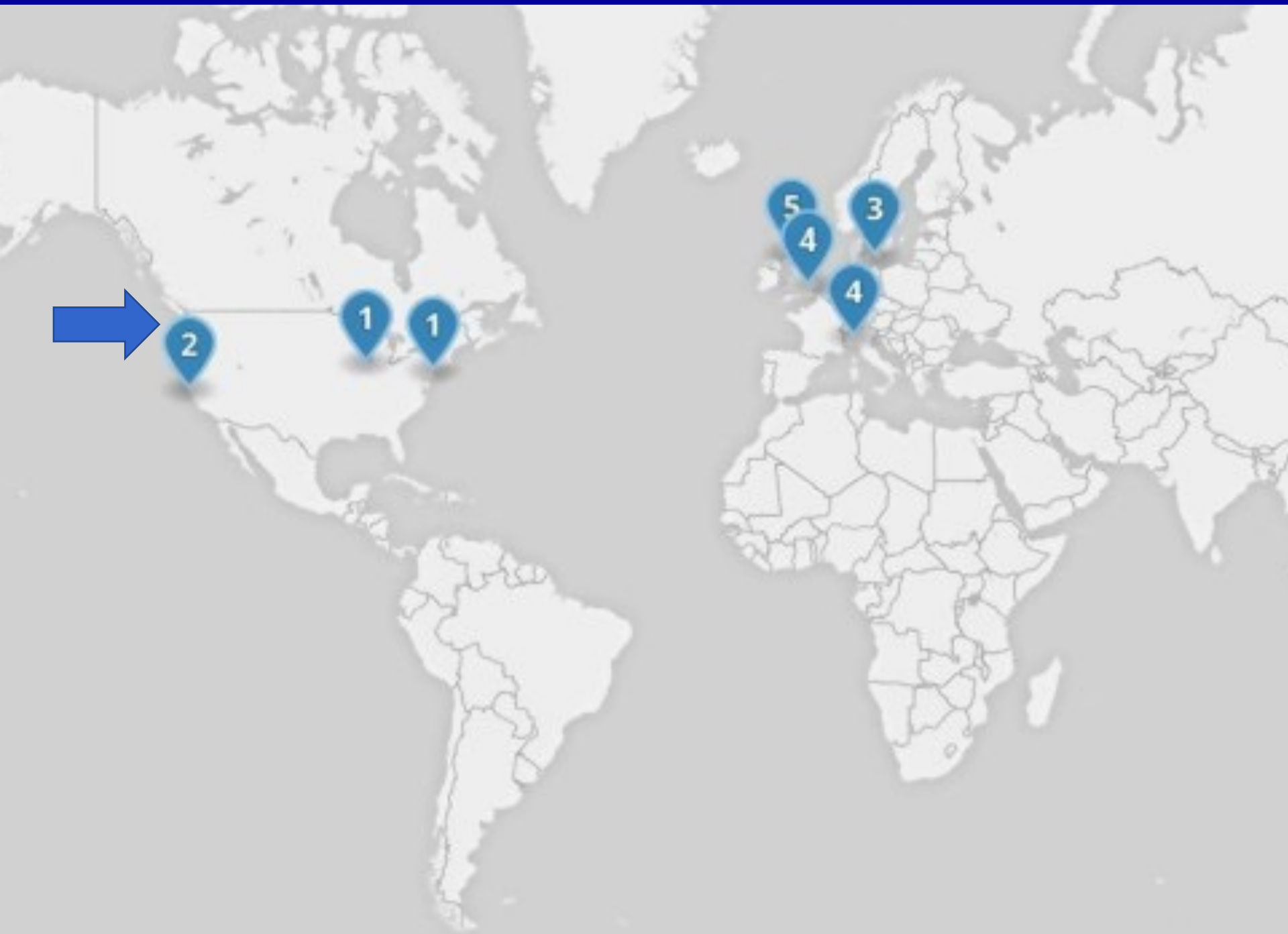

Embryonic stem cells
Induced pluripotent stem cells
In vitro differentiation into dopaminergic neural progenitors
Grafting into patient striatum
In vivo maturation into dopaminergic neurons

Patient derived stem cells

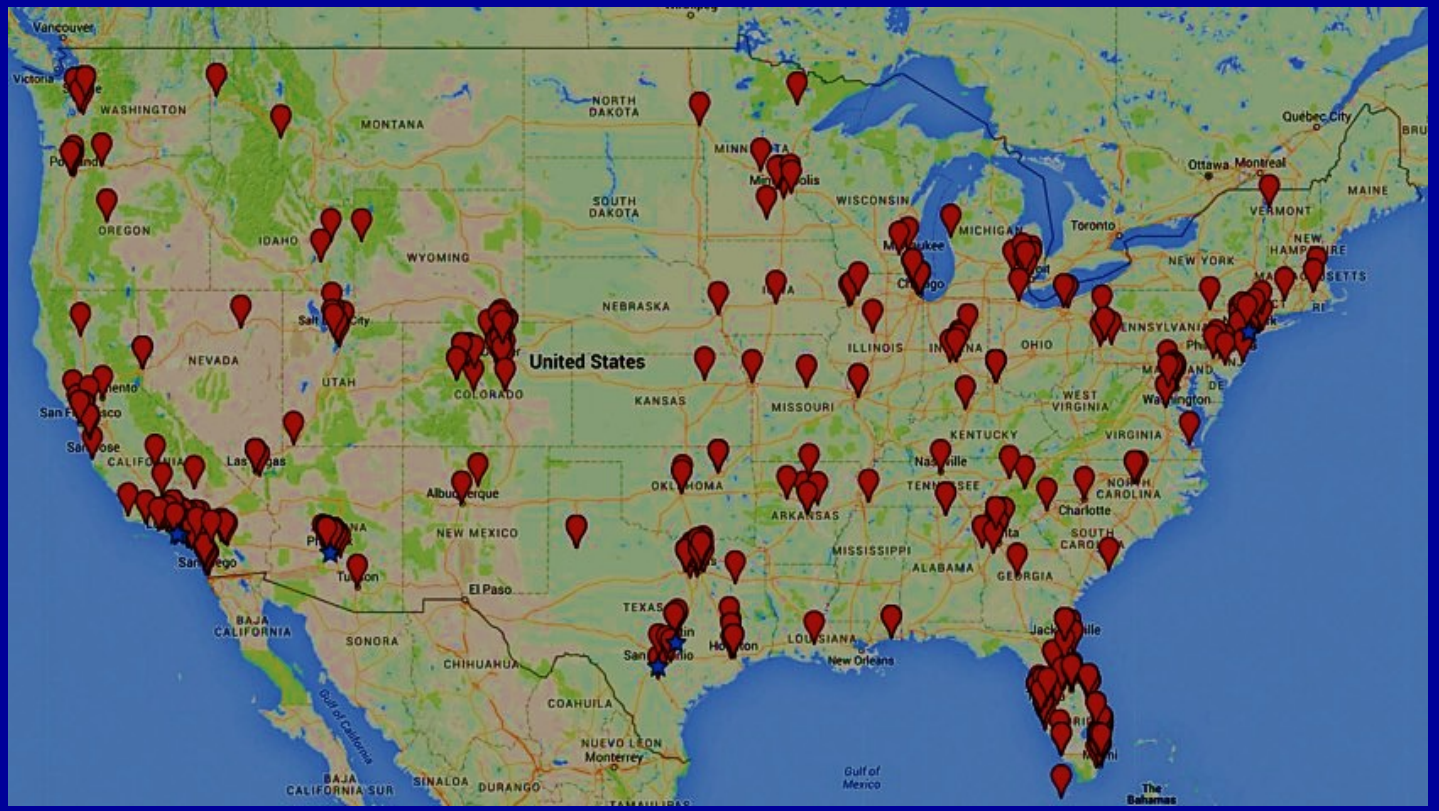


Evolution of Patient Stem Cells




5
3
4
4
1
1
2

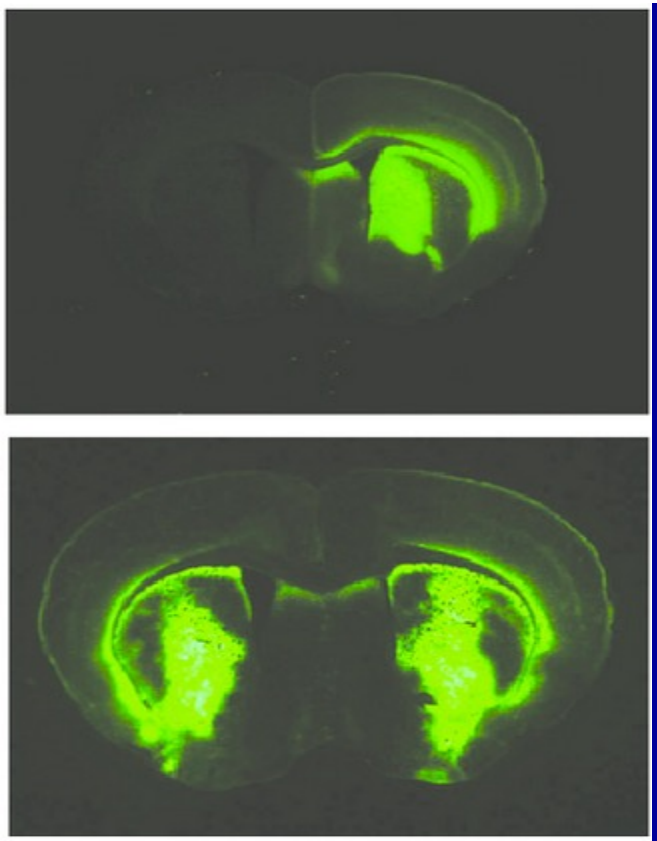
Stem cell “tourism”



Xiang-Dong Fu, Phd, UCSD

One-Time Treatment Generates New Neurons, Eliminates Parkinson's Disease in Mice

Inhibiting a single gene converts many cell types directly into dopamine-producing neurons



Unmet needs

- A drug that slows or stops the disease
- Non motor symptoms
  - Sexual
  - Sleep
  - Psychiatric
  - Autonomic
  - Cognitive

Resources

YOUR DOCTOR

Thanks! Empowerment for Parkinson's

The Parkinson's Association of San Diego Invites You to a Day Not to Be Missed!

PARKINSON'S ASSOCIATION OF SAN DIEGO

Wednesday, December 1, 2021
7: 45 AM – Registration Opens
8:45 AM - 3:45PM - Program

Marina Village Conference Center
1936 Quivira Way
San Diego, CA 92109

Come for a fun day of learning, sharing and empowering yourself and each other.

Cost: $20 per person
Includes light breakfast and lunch. Scholarships available!

Your safety matters. Proof of vaccination required upon check-in. We ask participants to follow CDC, state, and local mask guidelines at the time of the event.

SEE FULL AGENDA ONLINE AT PARKINSONSASSOCIATION.ORG

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COMMUNITY RESOURCES

EXPLORE NEW TOPICS

CAREGIVER SUPPORT

EXHIBITOR RESOURCE FAIR

Register now, space is limited!

- **By Phone:** 858-215-2570
- **By Mail:** Complete the registration form on the back of this flyer.
- **Online:** parkinsonsassociation.org

Empowerment for Parkinson's

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EMPOWER : MIND : BODY : SOUL

Personalized iPSC-Derived Dopamine Progenitor Cells for Parkinson's Disease

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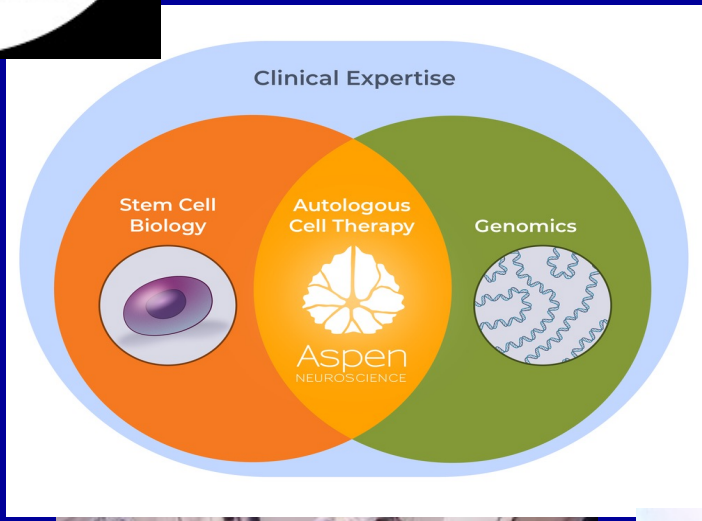
Aspen
NEUROSCIENCE



Summit4StemCell
New Hope for Parkinson's