Meeting Objectives

- Discuss novel models to accelerate drug development for neurodegenerative diseases (NDs)
- Discuss proof of concept examples where genomics and large datasets have enabled progress in ND
- Prioritize elements of common utility
- Explore benefits and considerations for a neutral collective effort across NDs
- Discuss incentive structures to encourage alignment
- Propose an operational framework(s) to move from concept to reality

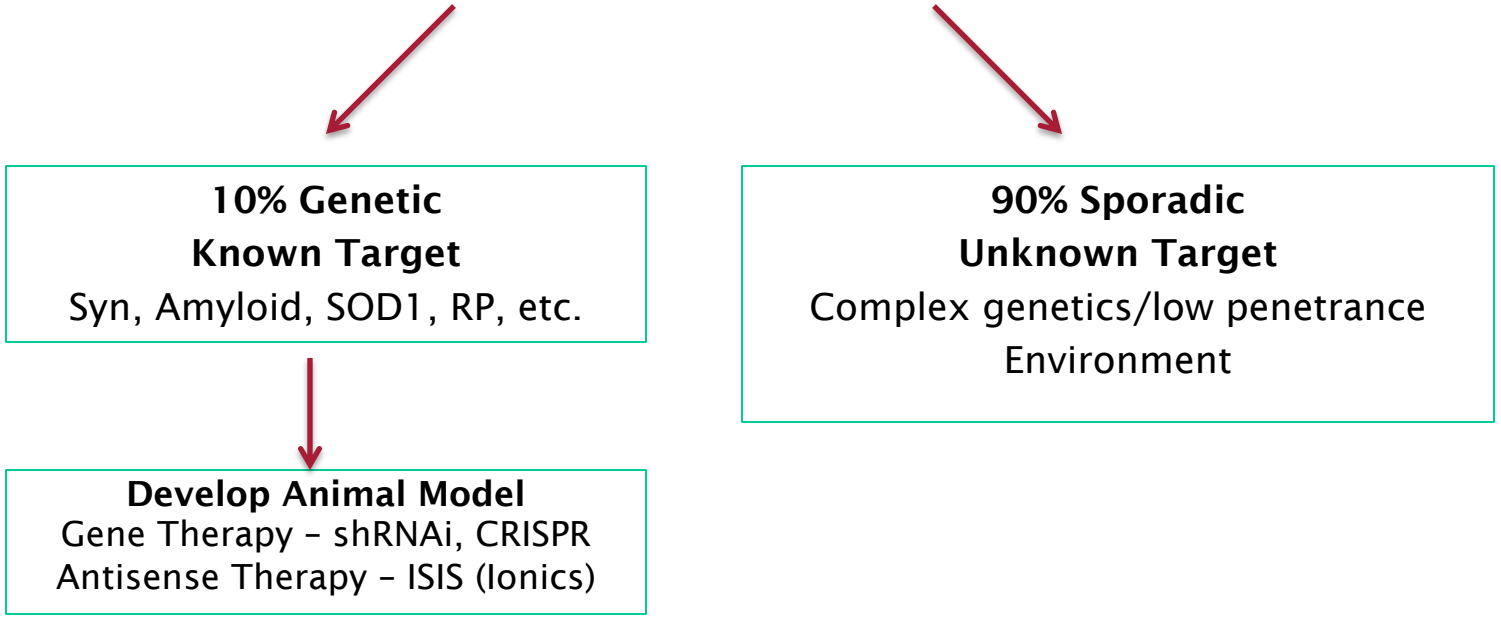
Examples of enhancing clinical trial efficiency

Once breast cancer has been diagnosed, doctors will create a personalized treatment plan that depends on...

- The tumor's subtype, including hormone receptor status (ER, PR) and HER2 status
- The stage of the tumor
- Genomic markers, such as Oncotype DX™ and MammaPrint™
- The patient's age, general health, menopausal status, and preferences
- The presence of known mutations in inherited breast cancer genes, such as *BRCA1* or *BRCA2*

Major Neurodegenerative Diseases

- Parkinson's disease
- Alzheimer's disease/FTD/Dementias
- Amyotrophic Lateral Sclerosis (ALS)
- Huntington's Disease



Major Neurodegenerative Diseases

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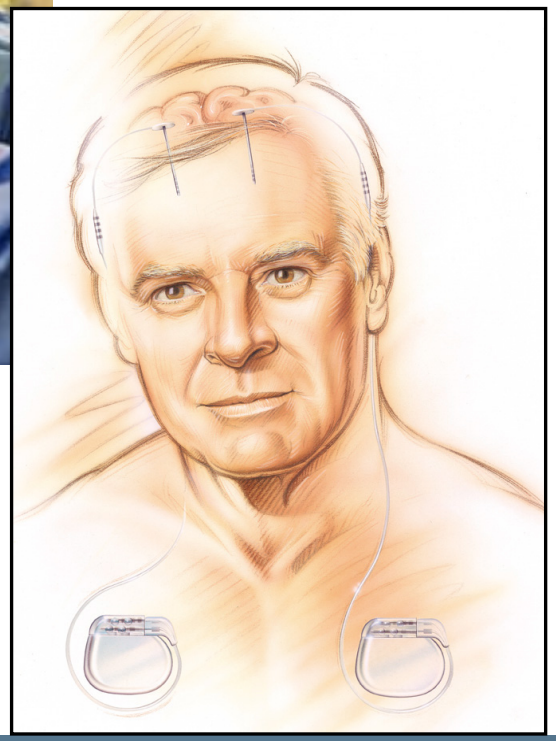
10% Genetic
Known Target
Syn, Amyloid, SOD1, RP, etc.

Develop Animal Mdoel
Gene Therapy – shRNAi, CRISPR
Antisense Therapy – ISIS (Ionics)

90% Sporadic
Unknown Target
Complex genetics/low penetrance
Environment

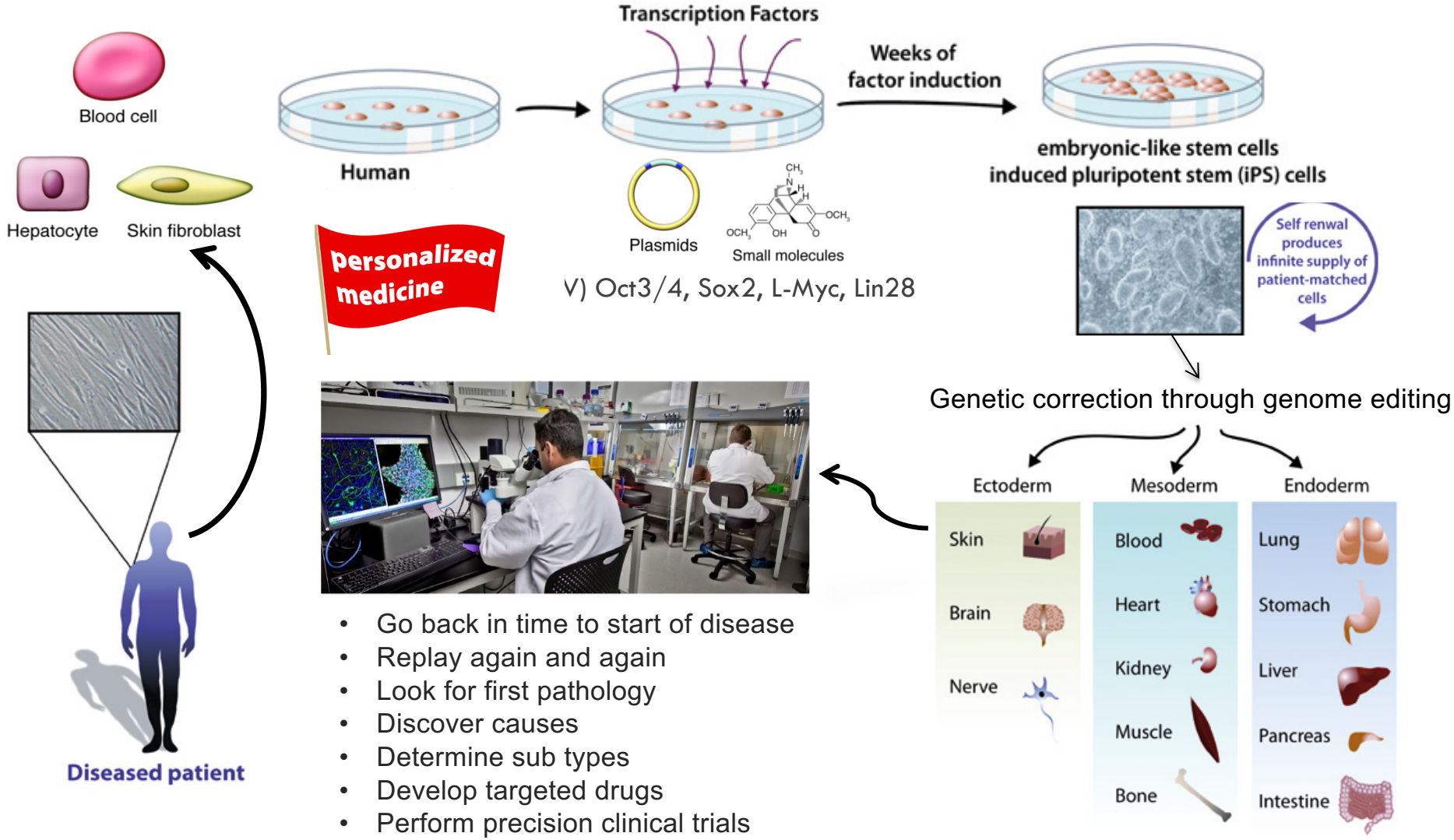
No Animal Model!!! Need iPSC model
Drugs/biologics to reduce pathology
Stem cell therapy
Growth factor therapy
Learn more about cause of disease

Deep brain stimulation – example of using clinical data to guide therapy for Parkinson's Disease



Adam Mamalak
Michele Tagliati

Induced pluripotent stem cells



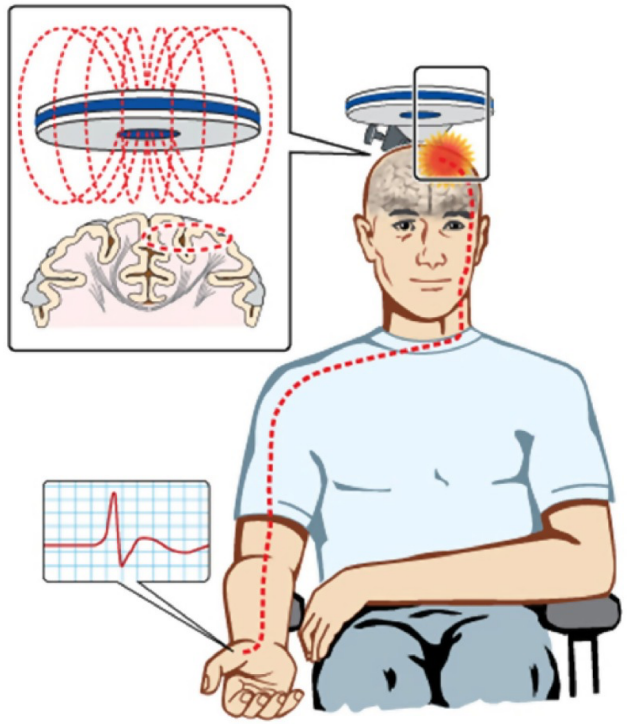
- Go back in time to start of disease
- Replay again and again
- Look for first pathology
- Discover causes
- Determine sub types
- Develop targeted drugs
- Perform precision clinical trials

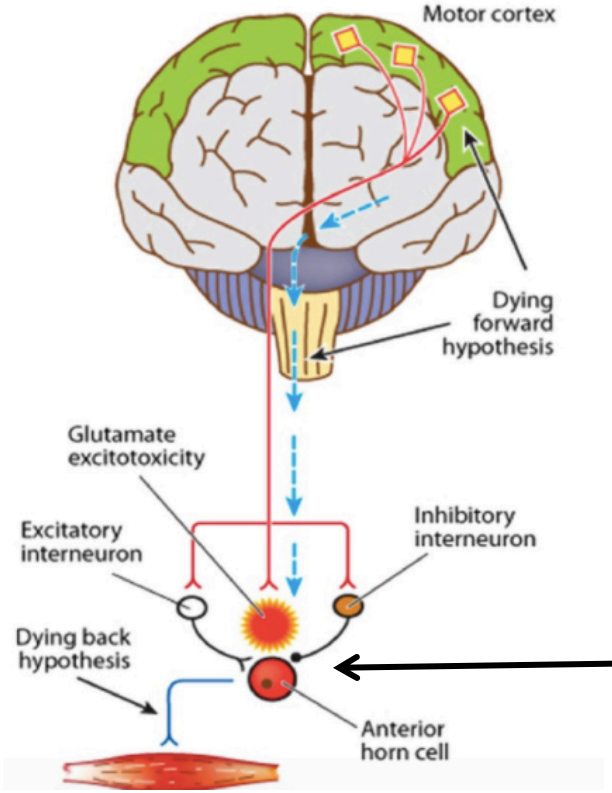
OPEN ACCESS

REVIEW

Transcranial magnetic stimulation and amyotrophic lateral sclerosis: pathophysiological insights

Steve Vucic,[1,2] Ulf Ziemann,[3] Andrew Eisen,[4] Mark Hallett,[5] Matthew C Kiernan[2,6]

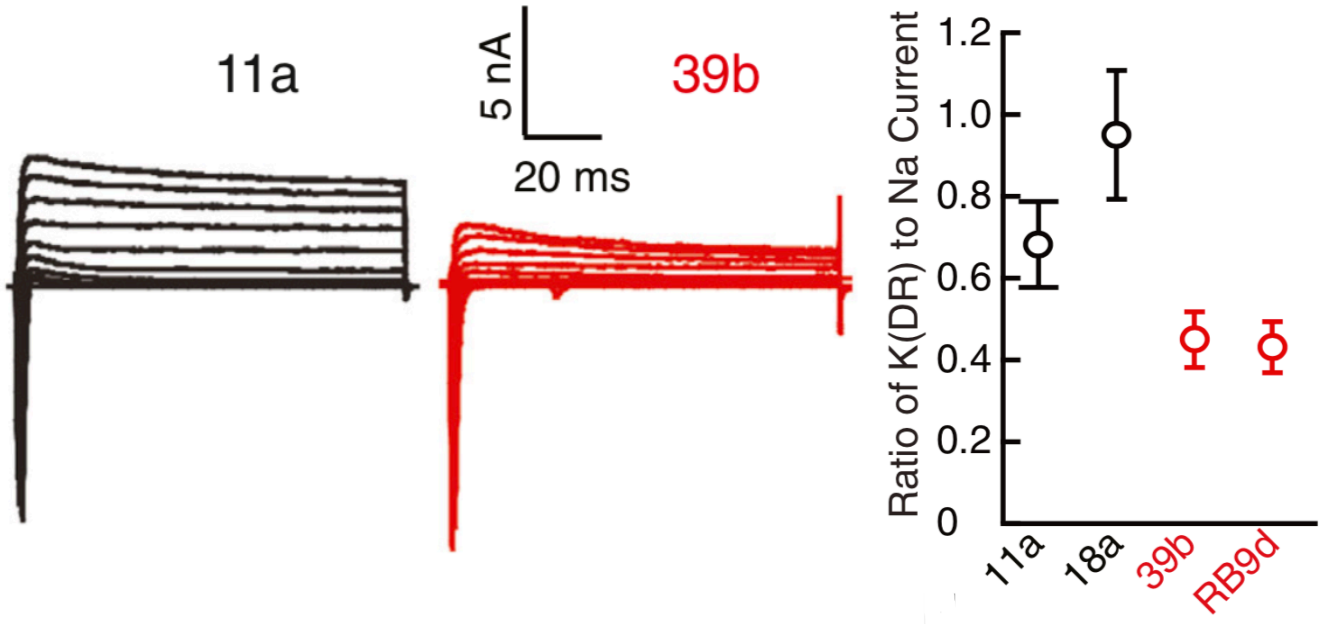




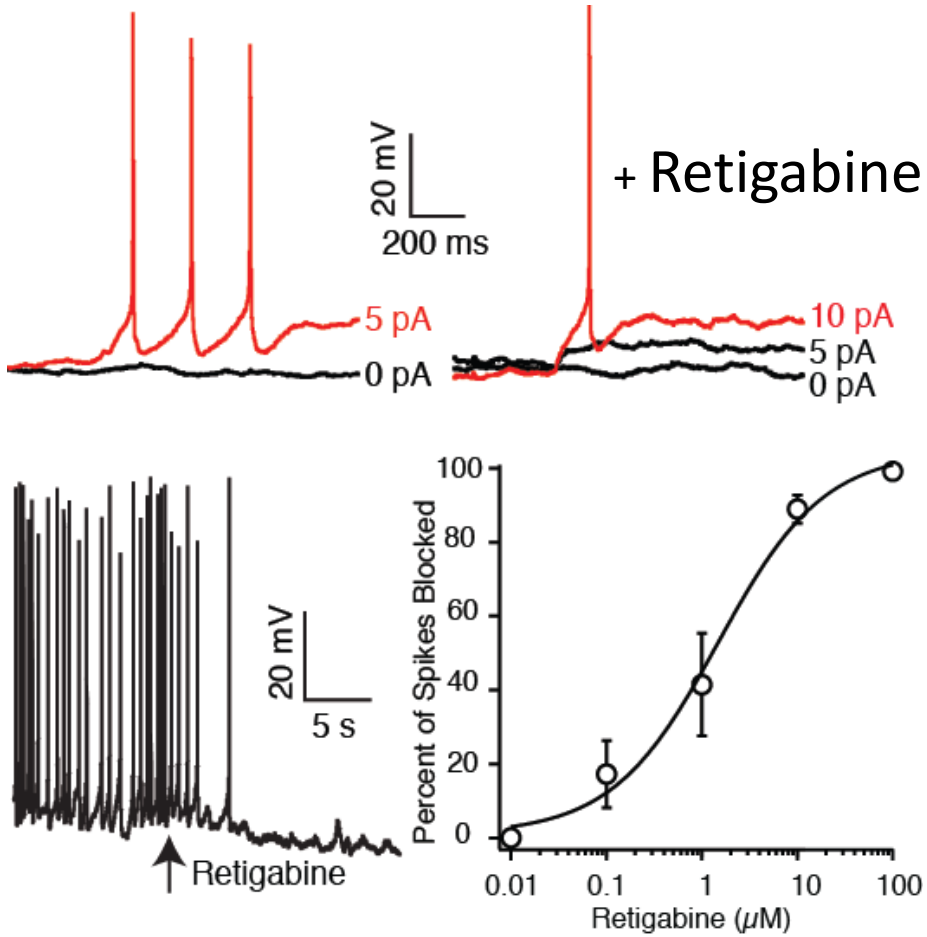
Rilozule *blocks release of glutamate*

iPSC derived motor neurons show hyper excitability

Voltage-Clamp



Retigabine (ezogabine) opens Kv7 Channels



Wainger et al. Cell Reports, 2014

Rapid Translation

- 2014: Published iPSC modeling of motor excitability and identified candidate drug
- 2015: Investigator's meeting with TMS and TT-NCS workshops
- 2015: Control subject recruitment to validate TMS and TT-NCS techniques at NEALS sites.
- 2016: Recruited first ALS patient for 12-site Phase 2 study with primary outcome: change cortical hyperexcitability during 10 week drug study
- 2018: finished Phase 2 study

First example of using iPSC data to inform a clinical trial

Wainger, Cudkowicz et al. Unpublished