

Fellowship Program in ALS Translational Medicine

RATIONALE

This fellowship is designed to provide opportunity for clinically trained individuals to enter a physician scientist track for a academic career in translational neuroscience. In addition, it is also ideal for individuals who are already on a physician scientist track and now wish to differentiate into ALS, neuromuscular, or neurodegeneration. *The fellowship is designed to be highly flexible and lead in multiple directions* from clinical research, therapy design, clinical trials, biomarkers, cellular and animal models, or basic disease mechanisms -- *the exact directions the fellow will take is to be driven by their interests, successes and creativities.*

The program leverages unique clinical and basic research science strengths existing at UCSD in the UCSD Center for ALS Research and Therapy, a consortium of **clinical programs** in ALS, neurophysiology and neurodegenerations and of **scientific programs** in cellular and molecular biology, genomics, computational biology, stem cell biology, neurobiology and genetics. Fellows will receive substantial protected time to work in the extraordinary and highly collaborative UCSD medical research environment and are expected to partner creatively with physicians and scientists on disease pathobiology.

Upon completion of the fellowship, individuals will be positioned for independent research, academic, clinical or industry careers and will be competitive for various NIH mechanisms, junior faculty positions, or to start or join translational programs.

PROGRAM OVERALL GOALS AND OBJECTIVES

- Gain a thorough understanding of all clinical aspects of ALS, motor neuron disorders and the variants, including diagnosis, neurophysiology, medical management, multidisciplinary care, rehabilitative care, and palliative care
- Gain a thorough understanding of the onset and progression in terms of pathophysiology, etiopathogenesis, genetics, molecular neuropathology and molecular pathobiology, including association with FTD
- Learn ALS clinical trial methodology and Human Subjects Research
- Learn and participate in biobanking
- Learn about high throughput genomic technologies and how to apply them to unravel human disease
- Learn about new genetic therapies such as antisense oligonucleotides and how they can be applied to human disease
- Learn and understand basic research and critically read research articles
- Regular conferencing with basic science groups in molecular and cellular biology, genomics, genetics, neurodegenerations, and stem cell biology
- The candidates are expected to develop their own independent clinical and/or basic science research, which will be the major activity by the end of the first year and put the Fellow on the path to an academic career as physician scientist
- The fellows are expected to collaborate in a number of other research projects so as to develop a portfolio of research tools and projects to support their colleagues for everyone's betterment
- A wide variety of other activities related to neuromuscular diseases, neurophysiology, neurogenetics, and neurodegenerations are available at multiple UCSD sites and these

are available to the fellows to participate in *if they are of interest and will advance career prospects.*

SCHEDULES:

Overall Weekly Schedule: Block Diagram

	Mon	Tues	Wed	Thurs	Fri
AM	9:00 -10:30 AM: Ravits Lab Meeting [MTF] 10:30-Noon: Research	9:00-10:00 AM: Neurodegenerations Seminar [Skaggs] 10:00 AM-Noon: Research	9:00 AM-Noon: Research	9:00 AM-Noon: Research 8:30 AM-Noon (one day per month): MDA Clinic [Hillcrest]	8:30-9:30 AM: Neuroscience Grand Rounds [CNCB] 9:30-Noon: Research
PM	1:00-4:00 PM: Research 4:00-6:00 PM: Cleveland Lab Meeting [CMME]	1:00-6:00 PM: ALS Clinic [Hillcrest]	1:00-5:00 PM: Research	1:00-6:00 PM: Neuromuscular Clinic [Perlman]	1:00-6:00 PM: Research 3:00-5:00 PM (once per month) Joint Neurodegenerations Research Group Meeting [SCRM]

Year 1 Schedule:

- 2-3 half-day clinics per week
- 3-4 weekly conferences
- 1-2 half days per week in translational activities (mainly biobanking and clinical trials)
- Rest of time is independent research
- Participation in resident didactics when appropriate (CPCs, didactic conferences, special rounds etc.)

Year 1 Goals:

- Clinical competency in diagnosis, management, multidisciplinary care, palliative care, end of life care, and communication with ALS patients and families
- Competency in clinical research including bioethics, research compliance, informed consent, standards of research, and ALS clinical trials methodologies
- Competency in biobanking methodologies
- Competency in methodologies and challenges in biomarker discovery
- Competency in genomics and whole genome technologies
- Establishment of major research project for year 2 and beyond
- Teaming with other translational fellows and with basic scientists

Year 2 Schedule:

- Three tracks will be available:
 - Clinical Academic track: 4 half-day clinics per week, emphasis on phenotypes, onset/progression, measurements of disease progression, clinical standards, clinical pathways, diagnosis, multidisciplinary care, palliative care, patient education, quality of life instruments, instruments for provider assessment and feedback, coordination and interplay of lay organizations, follow-up care, care-

giver and family support, community resources, interfacing with outside providers and health care organizations

- Translational/Reverse Translational track: 2-3 clinics per week, emphasis on multidisciplinary care, biosamples, clinical trials, genetic studies, imaging, pre-symptomatic carriers, biomarker discovery.

 - Science track: 1-2 clinics per week, biosamples, experimental models, molecular pathology, genomic profiling, cell culture models, therapy modulation esp. molecular pathway modulation and antisense oligonucleotides, antisense oligonucleotides optimization, animal models (partnering with basic science labs)
- Continued participation in 3-4 weekly conferences
 - Partnering with other programs in Neurodegeneration, Movement Disorders, Neuromuscular, Neurophysiology, and Basic Sciences as related to chosen track
 - Independent research in chosen track
 - Grant and manuscript writing

Year 2 Goals:

- Same as Year 1
- In addition:
 - Mentoring 1st year fellows
 - Teaming with basic science groups
- Original research with expectation of presentations, abstracts, manuscript productivity by the end of this year

Approximately 30% of the fellowship time involves clinical responsibilities, 10-20% of the time is conferencing (~half of this is “educational” and half is working team conferences), and the remainder is flexible for independent research and study. The environment of the fellowship and the research collaborations is designed for the fellows to think creatively and learn independently.

FACULTY RESEARCH ACTIVITIES (SUMMARY)

- Biobanking to include blood, autopsies, skin biopsies
- Pre-FALS prospective observational study of ALS gene carriers (UCSD is in process of joining University of Miami for this study)
- ALS Clinical Trials
- Molecular pathology
- ALS RNA biology, esp by way of transcriptome profiling esp fibroblasts cultures
- miRNA regulation in ALS
- Biomarker discovery
- C9ORF72 profiling
- C9ORF72 gene knockdown by ASOs
- Whole genome technologies including bioinformatics applied to disease pathobiology
- Intra-arterial therapy delivery

FACULTY

Clinical Faculty:

- John Ravits, MD
- Irene Litvan, MD
- Doug Galasko MD
- Eddie Koo, MD, PhD
- Mark Tuszinski, MD, PhD

Science Faculty:

- John Ravits, MD
- Don Cleveland, PhD
- Clotilde Lagier-Tourenne
- Larry Goldstein, PhD
- Martin Marsala, MD
- Al La Spada, PhD
- Gene Yeo, PhD