PROJECT ALS
THERAPEUTICS
CORE
AT COLUMBIA

Overview and Services

Overview and Structure.

- Seven-unit, multidisciplinary approach to ALS translational research
- Integrates the preclinical ALS expertise of Columbia's Motor Neuron Center with the clinical research infrastructure of Columbia's Eleanor and Lou Gehrig ALS Center
- Scientific Directors: Serge Przedborski, MD, PhD; Neil Shneider, MD, PhD; Hynek Wichterle, PhD
- Core units: Clinical research/development; in vitro screening; in vivo evaluation; viral vector development/validation; custom antibody development; neurolipidomics; in vivo electrophysiology
- Flexible collaboration model:
    - Study plans are custom-developed around each partner's specific aims, stage of development, and in-house capabilities
    - Collaborations can be structured as service agreements, with no intellectual property concerns
    - Core services are subsidized through funding provided by Project ALS, allowing collaborators cost-competitive access to deep ALS expertise and a wide range of ALS patient samples and disease models
        - Select Core services, including in vitro drug screening, are available at no cost to collaborators
- Directors of Internal and External Operations (Emily Lowry, PhD and Erin Fleming, respectively) facilitate and execute on study plan, provide regular updates, and consult as-needed on questions or issues that may arise throughout collaboration
- Case studies detailing prior / current collaborations available upon request

Units and Resources.

Clinical research and development

Director: Jinsy Andrews, MD, MSc

+Access to a renewable, customizable source of patient samples (cell lines, biofluids, postmortem tissue) for preclinical studies

+ Development and execution of early-phase clinical studies in a carefully characterized ALS patient population

In vitro screening

Director: Emily Lowry, PhD

+Robust human iPSC-derived motor neuron screening platform for high-throughput screening for potential ALS drugs with neuroprotective effects against ER stress, oxidative stress, protein misfolding, and other ALS-related phenotypes

+Analysis includes quantification of motor neuron survival, morphology, cell body size, neurite outgrowth, and other parameters

In vivo evaluation

Director: Emily Lowry, PhD

+Non-regulatory toxicity and pharmacokinetic studies in wild-type mice to evaluate solubility, stability, CNS penetrance, PK and toxicity of candidate therapies

+Through well-established partnerships with medicinal chemists with expertise in CNS drug development, optimization of compounds that exhibit strong neuroprotection but insufficient CNS penetrance

+Long-term safety and efficacy studies in multiple ALS mouse models

Antibody development

Director: Susan Morton

+ Generation of novel antibodies for immunohistological examination of post-mortem ALS brain and spinal cord, mouse tissue, and biochemical characterization of protein complexes

+Custom antibody resource for phamacodynamic target validation

+Novel antibodies in development for improved detection of motor neurons and quantification of neuromuscular junctions

Viral vector development and validation

Director: Francesco Lotti, PhD

+Viral vector production for novel genetic targets in ALS

+Development of virally-mediated constructs for relevant animal models of ALS will serve as positive controls in the in vivo evaluation unit

Neurolipidomics

Director: Estela Area Gomez, PhD

+Profile lipid signature in a variety of ALS patient biofluids to build on pilot studies and thoroughly assess its value as a potential diagnostic, prognostic, and therapeutic biomarker for ALS

+Implement parallel lipidomic assessments for ALS efficacy studies in the *in vivo evaluation* unit

In Vivo Electrophysiology

Director: George Mentis, PhD

+Characterize physiological, synaptic, and motor circuit defects in the Core's ALS animal models