

# Research

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The Translational Neuromuscular Medicine Laboratory led by Dr. Crystal Yeo focuses on bridging the gap between clinical care and the basic sciences in neuromuscular disorders. We study the basic biological mechanisms of neuromuscular disease and their direct applications to patient care and drug discovery. We are committed to collaborations across many disciplines, including biochemistry, genetics, immunology, ageing, single-cell transcriptomics, proteomics, stem cell biology, high throughput screening, RNA therapeutics, muscle and nervous system imaging. We believe that fostering close collaborations between clinicians, basic scientists and the drug development industries is essential to advancing our understanding of clinical diseases and translating discoveries into clinical practice.

Our overall objectives are to discover novel biomarkers, therapeutic targets for drug development, and point of care diagnostics.

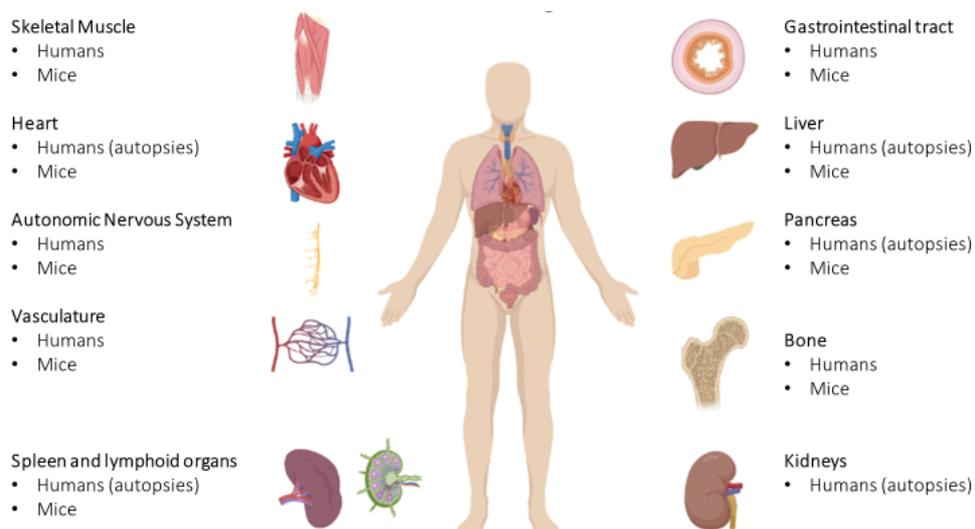
We are committed to being relevant to the current medical landscape and clinical needs, which are driven by these factors:

1. An ageing population and increasing usage of immunomodulatory treatments and biologics in the developed world, driving a significant healthcare burden of neurodegenerative and neuroinflammatory diseases in Asia, Europe and the United States.
2. Increasing evidence of peripheral organ contributions to neurodegenerative diseases, which imply that optimal clinical management would require a multi-system and multi-disciplinary approach.
3. Long-standing difficulties in accessing human brain or nerve tissue for treatment or biomarker measurements.

Our research focuses are in the following areas:

1. Understand systems-wide manifestations of neurological diseases

## **Overturning the Paradigm of Spinal Muscular Atrophy as just a Motor Neuron Disease (Yeo and Darras, Pediatric Neurology, 2020)**

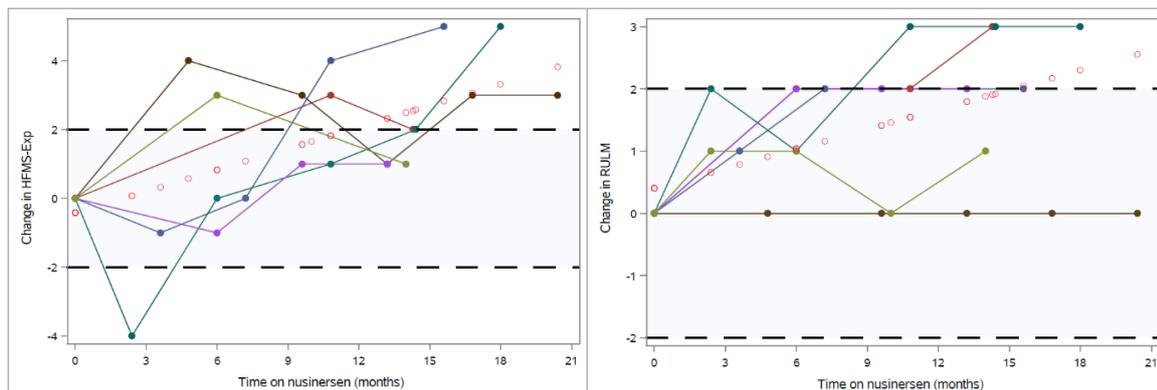


2. Discover important tissue-intrinsic and systems-wide signaling and metabolic pathways which drive disease
3. Discover common signaling and metabolic pathways in more than 1 neurodegenerative disease
4. Investigate non-cell autonomous influences of neuronal degeneration and loss
5. From (1) and (2), investigate novel biomarkers in blood and/or skin to monitor disease progression
6. From (2) and (3), investigate high-yield therapeutic targets for the development of drugs which can be used to treat diseases in more than 1 organ system, and across different neurological diseases.
7. From (4), investigate neurotrophic and tissue growth factors which can act downstream of faulty genes and complement gene therapies.
8. Robust and reliable dissection of peripheral tissue and immune responses in neurodegeneration

We use a range of techniques to investigate the basic molecular biology of disorders of the muscle, neuromuscular junction, nerve fibers, neurons, spinal cord and brain and the clinical implications:

1. Clinical trials and observational studies

#### ***Motor Assays in Adult Patients with SMA over Time on Nusinersen Treatment***



2. Electrophysiology including nerve conduction studies and electromyography
3. Neuromuscular ultrasound and neurohistopathology
4. High throughput screening using systems wide transcriptome and proteasome analysis
5. Robust dissection of phenotypes using spatial transcriptomics and single cell RNA-Seq
6. Preclinical modeling involving patient iPSC derived cell/tissue cultures and mouse models
7. Functional knockdown and repletion models using antisense oligonucleotides

We provide opportunities for people with neuromuscular diseases to volunteer by providing biosamples or enroll in clinical trials:

1. This is a collaboration which helps the translational medicine team to understand their diseases and reach the goal of finding a cure.
2. These biosample gifts will be shared widely to maximize the impact of these gifts.