Eye Imaging to Develop a Non-Invasive Biomarker for Amyotrophic Lateral Sclerosis

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Background
- Amyotrophic lateral sclerosis (ALS) is an incurable rapidly progressive neurodegenerative disease that causes degeneration of motor neurons and death.1
- The pathological hallmark of ALS is the presence of axonal spheroids in motor neurons in the spinal cord.2
- Current biomarkers for ALS are expensive and difficult to implement in clinics and clinical trials.3
- The retina and optic nerve are extensions of central nervous system (CNS) and provide valuable insight into CNS diseases.
- Our team recently demonstrated existence of retinal spheroids in retina of post-mortem ALS eyes compared to age-matched controls.4
- 10% of ALS cases are familial and SOD1 mutations are present in about 19% of these cases.5
- SOD1 transgenic mice are a well-established animal model to study ALS, as they replicate the ALS in patients.6

Purpose
- To determine if hyperreflective profiles exist in SOD1 transgenic ALS mouse model.
- To characterize retinal hyperreflective profiles in ALS mouse models.

Materials and Methods
- Experiments were performed after Keenan Research Centre Animal Care Committee approval.
- SOD1 transgenic mice (n = 8, 40/40) and WT mice (n = 35, 40/40) (C57Bl/6 strain)
- Muscle weakness was monitored using a scoring system of ALS related clinical findings.
- At age of 2 months, in vivo imaging was performed weekly under general anesthesia (2% isoflurane) using Spectralis system (Heidelberg Engineering, Germany) that combines confocal laser scanning ophthalmoscope (cLSO) Blue Reflectance-IR (488nm) InfraRed-IR (820nm), and Optical Coherence Tomography (OCT, 870nm).
- A 250 lens and a contact lens with a curvature of 1.7 were used during imaging.

Results

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Table 1: Number of hyperreflective profiles and statistical analysis in SOD1 mouse compared with control mice at age 20 weeks.

Figure 2. Retinal images of ALS and control mice (OD) at age 20 weeks. (a) Fundus image of ALS AF1 mouse shows Hyperreflective profiles (Arrow heads). (b) Fundus image of Control C11 mouse shows Hyperreflective profiles (Arrow heads) [6–6 Zoomed in fundus images of AF1, C11 and C1M1, (g–h) OCT scans of AF1, C11 and C1M1 retina. Hyperreflective profiles are in the inner most layer of retina (arrowheads). Blood vessels are shown by stars.

Figure 3. Average hyperreflective profiles over time significantly increase in female SOD1 mice compared to female control (P<0.001).