Dear editor,

We are pleased to submit an original research manuscript entitled “Eye movement biomarkers allow for the definition of phenotypes in Gaucher Disease” for consideration for publication in Orphanet Journal of Rare Disease.

This is an original study which examined eye movements in the lysosomal storage disorder, Gaucher disease. This study focussed initially on a subgroup of patients who have ‘neuronopathic’ disease or ‘type 3’ Gaucher disease, the early characteristic manifestation of neurological involvement is a horizontal saccade defect which is well described. We used a saccade measuring device, the EyeSeeCam, to evaluate saccades in this population (as has been shown previously) with an aim of describing the defect in more detail and initiating a baseline dataset from which we could determine if the EyeSeeCam could be used as a clinical trial outcome measure.

An unexpected and striking observation, during the study, was the finding of saccadic defects in a group of patients who have the non-neurological form of disease (type 1) Gaucher disease. Furthermore, these patients shared a *GBA1* mutation (compound heterozygous) which may have profound implications for genotype:phenotype relationships in this disease, a disease in which there are over 400 known pathogenic mutations. This is fascinating for the disease area and utilises clinical methodologies which can be used at the bedside, it may have wider implications which future studies will interrogate. Not only does this have implications for our understanding of the phenotypic spectrum of disease it also has implications for clinical trials, which currently, are dependent on the classification of disease by presence or absence of neurology. We may be moving into an era where genotype phenotype correlations can be used to determine clinical trial eligibility and precision medicine can be pursued more effectively.

Each of the authors has read and concurs with the content in the final manuscript and no significant conflicts of interest have been identified; the final author (ES) as detailed ES is general manager and shareholder of EyeSeeTec GmbH. The material within will not be submitted for publication elsewhere except as an abstract.

Many thanks for your consideration,

Yours Sincerely,



Dr Aimee Donald MBChB MRCPCH PhD