between patterns on fundus AF images and maps of retinal sensitivity derived from microperimetry testing.
Methods: Fifty eyes of 25 patients with Stargardt disease underwent functional testing using fundus controlled perimetry (MAIA, CenterVue, Italy). A confocal scanning laser ophthalmoscope (HRA2, Heidelberg Engineering, Germany) was used for recording NIR- and SW fundus AF. Disease-related patterns on AF images were categorized as follows: 1) no pattern, 2) granular pattern, 3) bright > dark flecked pattern, 4) dark > bright flecked pattern, 5) dark pattern and 6) atrophic lesions. Retinal sensitivity along a horizontal line of 15° eccentricity through the fovea was compared between these regions.
Results: Pattern-related retinal sensitivity was not different between both eyes of each patient (ANOVA; p=0.16 and p=0.54 for SW- and NIR-fundus AF, respectively). Borders between consecutive patterns on NIR-fundus AF images were more eccentric compared to equivalent borders on SW- fundus AF images. For both SW- and NIR fundus AF retinal sensitivity was different between patterns (ANOVA, p<0.0001; post hoc test, p<0.0001 to p=0.047) except for the comparison between patterns 1 and 2 (p=0.06 and p=0.98 for SW- and NIR fundus AF, respectively), as well as between patterns 2 and 3 (p=0.42 and p=0.05 for SW- and NIR fundus AF, respectively). The largest drop in retinal sensitivity was observed at the border to regions with predominantly dark pattern in both SW- and NIR-fundus AF (mean retinal sensitivity [dB±SEM], SW fundus AF: 1 = 23.33±0.81, 2 = 19.94±1.45, 3 = 16.60±1.53, 4 = 9.27±1.43, 5 = 4.13±1.18, 6 = 0.58±0.35; NIR fundus AF: 1 = 24.08±0.58, 2 = 23.66±0.67, 3 = 19.38±1.33, 4 = 12.62±1.48, 5 = 2.97±0.67, 6 = 0.71±0.41).
Conclusions: Structure-function correlations reveal consistent functional deficits of fundus AF patterns in Stargardt disease. In both, SW- and NIR fundus AF the transition to a predominantly dark pattern is associated with a marked impairment of retinal sensitivity. Areas of equivalent patterns on NIR fundus AF images exceed those on SW fundus AF, suggesting superiority of NIR- fundus AF imaging to indicate early functional alterations.
Commercial Relationships: Philipp L. Müller, Carl Zeiss Meditec, Germany (F), Heidelberg Engineering, Germany (F), Optos, UK (F); **Martin Gliem**, Carl Zeiss Meditec (F), Heidelberg Engineering, Germany (F), Optos, UK (F); **Frank G. Holz**, Acucela (C), Acucela (F), Allergan (C), Allergan (F), Bayer (C), Bayer (F), Boehringer Ingelheim (C), Genentech (C), Genentech (F), Heidelberg Engineering (C), Heidelberg Engineering (F), Merz (C), Novartis (C), Novartis (F), Optos (F), Roche (C), Zeiss (F); **Peter Charbel Issa**, Heidelberg Engineering (F)
Support: ProRetina

Program Number: 5015
Presentation Time: 5:00 PM–5:15 PM
C20-D3-Vitamin A (ALK-001) rescues the phenotype of an *Abca4*$^{-/-}$ mouse model of Stargardt disease
Peter Charbel Issa[1, 2], Alun R. Barnard[1], Ilyas Washington[3], Robert E. MacLaren[1]. [1]Nuffield Laboratory of Ophthalmlolgy, University of Oxford, Oxford, United Kingdom; [2]Department of Ophthalmology, University of Bonn, Bonn, Germany; [3]Department of Ophthalmology, Columbia University Medical Center, New York, NY.
Purpose: To investigate the effect of C20-D3-Vitamin A (ALK-001) on the phenotype of the *Abca4*$^{-/-}$ mouse
Methods: *Abca4*$^{-/-}$ mice treated with ALK-001 for various amounts of time (3, 6, 7.5 and 9 months) were compared to untreated *Abca4*$^{-/-}$ mice and wild type (WT) controls reared on chow containing normal amounts of vitamin A. Quantitative fundus autofluorescence (AF) imaging and electroretinography (ERG) were assessed in vivo (n=10 per group) and assessment of bisretinoid (A2E) accumulation was then performed postmortem
Results: In all *Abca4*$^{-/-}$ mice that received ALK-001, lipofuscin-related fundus AF levels were significantly lower than in untreated *Abca4*$^{-/-}$ controls, in which AF levels were about twice those of WT controls at 9 months.The longer animals had stayed on ALK-001, the lower their AF signals. The most significant effect was observed in *Abca4*$^{-/-}$ mice maintained on ALK-001 for 9 months, with AF signals similar to those of untreated WT controls. When animals were crossed over from ALK-001 to normal chow, AF signals increased steeply. Absence of diet-related changes on scotopic and photopic ERG recordings between the same groups of 9 month-old animals indicated that ALK-001 was safe to the retina. Post-mortem analyses of eye cups revealed an about 8-fold increase of A2E in 9-month old *Abca4*$^{-/-}$ mice compared to WT controls, while treatment with ALK-001 from birth reduced bisretinoid concentration in eyes of *Abca4*$^{-/-}$ mice down to the levels measured in WT controls.
Conclusions: These experiments confirm that an increase in the concentration of ocular A2E levels is paralleled by an increase in fundus AF intensity, and that treatment effects of C20-D3-vitamin A (ALK-001) in mice can be monitored with measurement of A2E and AF intensity. Finally, the results demonstrate that ALK-001 can be administered safely in mice and rescues the phenotype of a mouse model of Stargardt disease by reducing the rate of formation of autofluorescent materials in the eyes, without negatively affecting the ERG recordings.
Commercial Relationships: Peter Charbel Issa, None; **Alun R. Barnard**, None; **Ilyas Washington**, Alkeus Pharmaceuticals (C), Alkeus Pharmaceuticals (P); **Robert E. MacLaren**, None
Support: NIHR Biomedical Research Centre, the Wellcome Trust, Medical Research Council, UK Department of Health, Special Trustees of Moorfields Eye Hospital, the Royal College of Surgeons of Edinburgh, ProRetina, National Institute of Health (Grant 1R01EY021207-01)

Program Number: 5016
Presentation Time: 5:15 PM–5:30 PM
High-Resolution Imaging in Stargardt Disease: Preliminary Observations In Preparation for Intervention
Michel Michaelides[1, 2], Fouad R. Zakka[3], Jonathan Aboshiha[1, 2], Yusufu N. Sulai[4], Thomas B. Connor[3], Dennis P. Han[3], Alfredo Dubra[3, 5], Joseph Carroll[3, 5], Adam Dubis[1, 2]. [1]Moorfields Eye Hospital, London, United Kingdom; [2]UCL Institute of Ophthalmology, London, United Kingdom; [3]Department of Ophthalmology, Medical College of Wisconsin, Milwaukee, WI; [4]The Institute of Optics, University of Rochester, Rochester, NY; [5]Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI.
Purpose: There is considerable well-documented inter-subject variability in Stargardt disease (STGD) in terms of age of onset, and both pattern and rate of degeneration. Because of this variability and the lack of robust natural history data, longitudinal deep phenotyping is needed to better characterise the disease process. Such studies will result in a better understanding of the cellular changes associated with each genotype, which is a prerequisite to planned therapies for STGD.
Methods: Eleven patients (ages 7 to 62) with molecularly confirmed STGD underwent examination and retinal imaging, including autofluorescence (AF) imaging, spectral domain optical coherence tomography (SDOCT), and confocal adaptive optics scanning light ophthalmoscopy (AOSLO). Serial imaging was undertaken over a period ranging between 3 months and 1 year. Retinal lamination was assessed using SDOCT, and AOSLO was used to probe integrity