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Abstract

Histology (H&E) and transmission electron microscopy (TEM) data are provided showing age-related changes in the retinal structure of sTg-IRBP:HEL mice. These include substantial photoreceptor loss, atrophy of the retinal pigment epithelium, Bruch’s membrane disruption and thickening, along with the presence of drusenoid deposits and changes in basal laminar infoldings. These features resemble some of those key characteristics found in the course of human dry (atrophic) age-related macular degeneration (AMD), particularly with regard to drusen. Hence, we believe the sTg-IRBP:HEL mouse model represents a useful and promising archetype for future study of the mechanism of drusen formation in AMD.

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**Value of the data**

- Despite being a leading cause of blindness in the UK, resulting in a gradual loss of (central) vision, as well as an economic burden, the underlying pathogenesis of especially dry AMD is not understood.
- The atrophic (dry) form of the disease is more prevalent, and there is no treatment available at the present time. The data in this DIB report offer a new model for dry AMD which will allow researching of therapeutic options.
- In contrast to their WT controls, sTg-IRBP:HEL mice exhibit age-related drusenoid deposits, resembling those seen in human dry AMD.
- This animal model is compatible with the clinical cardinal features of human dry AMD and may prove beneficial for future mechanistic AMD research and therapy.

1. Data

Single transgenic IRBP:HEL mice expressing hen egg lysozyme (HEL) under the retinal interphotoreceptor retinoid-binding protein (IRBP, RBP3) promoter, were generated as previously reported [2]. With age, these mice gradually lose the expression of interphotoreceptor retinoid-binding protein (IRBP; RBP3). In our experiments, we compared 60 day old (“adult”) or 240–300 day old (“aged”) wild type mice (WT; P60 and P240–300, respectively), with said transgenic animals of the same age groups for the cardinal features resembling human atrophic (dry) AMD. Central retinal evaluation by TEM revealed absence of age-related changes occurring in retinas of control adult (P60) WT mice (Fig. 1A-C), while in sTg-IRBP:HEL mice of the same age (Fig. 1D-F) drusen-like deposits were found that accumulated with age (Fig. 1F). These adult mice showed signs of slightly disorganized/shortened photoreceptor layers (Fig. 1D, E) and Bruch’s membrane thickening with extensive alteration in RPE basal infoldings (Fig. 1F, circle). In terms of retinal degenerative markers, aged control mice (P240–300, WT; Fig. 1G-I) were comparable to adult (P60) sTg-IRBP:Hel mice. In aged sTg-IRBP:HEL mice (P240–300) retinal degeneration became increasingly evident, with complete loss of photoreceptors (Fig. 1J, K) and large sub-RPE drusen-like deposits detected (Fig. 1L). These degenerative features are in agreement with those encountered in human atrophic AMD, thus we propose the sTg-IRBP:HEL mouse model as an accessible and useful vehicle for future AMD research. Data are summarised and described in Table 1, statistics are provided in Table 2.
2. Experimental design, materials, and methods

2.1. Animals

The generation of sTg-IRBP:HEL mice was previously described [2]. All procedures performed were in agreement with the regulations of the Animal License Act (UK) and followed the ARRIVE guidelines for animal husbandry. All mice were bred in established breeding colonies and maintained/housed in the Medical Research Facility of the University of Aberdeen. Mice genotypes were verified by a routinely used in-house PCR protocol.
2.2. Sample preparation for histology, and H&E staining

Wild type (WT; controls) and IRBP:HEL single transgenic (sTg) mice of two age groups were used (P60: post-partum day 60, "adult"; P240–300: post-partum day 240–300, "old"). Eyes were humanely killed and eyes removed immediately. Per age- and test group 2 to 4 animals were analysed. Eyes were fixed in 2.5% (w/v) glutaraldehyde (Fisher Chemicals, Loughborough, UK) and embedded in resin to be sectioned for standard H&E staining. Images were recorded using a ProgRes XT Core 5 colour digital microscope camera (JENOPTIK Optical Systems GmbH, Jena, Germany) with samples mounted on an inverted microscope (Axioskop40, Carl Zeiss, MicroImaging GmbH, Jena, Germany).

2.3. Sample preparation for TEM

As above, mouse eyes (WT and sTg-IRBP:HEL; P60 and P240–300, respectively) were collected and fixed in 2.5% glutaraldehyde (Fisher Chemicals, Loughborough, UK) and embedded in resin to be sectioned for standard H&E staining. Images were recorded using a ProgRes XT Core 5 colour digital microscope camera (JENOPTIK Optical Systems GmbH, Jena, Germany) with samples mounted on an inverted microscope (Axioskop40, Carl Zeiss, MicroImaging GmbH, Jena, Germany).

2.4. Statistical analysis

Statistics were performed using IBM SPSS Statistics 25.0. Based on the nature of the data available, the non-parametric procedure of Mann-Whitney U-test was used to compare data based on ranks.

Table 1 specifies photoreceptor inner- (PIS) and outer layer (POS), retinal pigment epithelium (RPE), and Bruch's Membrane (BM) thickness as presented in Fig. 1. Medians (50th percentile) and ranges (in brackets) of n = 3 measurements each are provided. Wild type (WT; controls) and IRBP:HEL single transgenic (sTg) mice of two age groups were used (P60: post-partum day 60, “adult”; P240–300: post-partum day 240–300, “old”).

|                | PIS/POS [µm] | RPE [µm] | BM [nm] |
|----------------|--------------|----------|---------|
| WT P60 (“adult”) | 180.6 (20.8) | 5.2 (0.3) | 376.3 (172.0) |
| WT P240–300 (“old”) | 118.1 (7.0) | 4.3 (1.7) | 537.6 (215.1) |
| sTg-IRBP:HEL P60 (“adult”) | 66.0 (6.9) | 3.9 (1.0) | 1075.0 (268.8) |
| sTg-IRBP:HEL P240–300 (“old”) | 10.4 (3.5) | 2.6 (0.7) | 806.5 (451.7) |

Table 2 compares mice groups based on age (P60 vs. P240–300: post-partum day 60, "adult" vs. day 240–300, "old"), or genotype (WT: wildtype vs. sTg-IRBP:HEL: single transgenic). P-values are provided; asterisks denote significant differences based on a ≥ 95% level of confidence. Medians (50th percentile) of n = 3 independent measurements per marker of interest were compared using the Mann-Whitney U-test.

|                | PIS/POS, p-Value | RPE, p-Value | BM, p-Value |
|----------------|------------------|--------------|-------------|
| WT P60 (“adult”) | 0.046*           | 0.043*       | 0.127       |
| WT P240–300 (“old”) | 0.050*         | 0.050*       | 0.050*      |
| sTg-IRBP:HEL P60 (“adult”) | 0.046*      | 0.046*       | 0.050*      |
| sTg-IRBP:HEL P240–300 (“old”) | 0.043*   | 0.178        | 0.513       |
Medians (50\textsuperscript{th} percentile) and ranges are presented in Table 1, along with \(p\)-values based on a \(\geq 95\%\) level of confidence in Table 2.

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**Transparency document. Supporting information**

Transparency data associated with this article can be found in the online version at https://doi.org/10.1016/j.dib.2018.12.007.

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