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## An Induced Pluripotent Stem Cell Patient Specific Model of Complement Factor H (Y402H) Polymorphism Displays Characteristic Features of Age-Related Macular Degeneration and Indicates a Beneficial Role for UV Light Exposure

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**Key Words.** iPSC • AMD • RPE • UV Exposure

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We read with great interest Hallam and colleagues' article regarding the beneficial effects of ultraviolet (UV) exposure in their patient-specific in vitro model of age-related macular degeneration (AMD) [1]. In light of recent evidence proposing an active and deleterious role of UV exposure within AMD pathogenesis [2] their findings raise interesting questions, which may have clinical relevance in our understanding of the photobiological mechanisms affecting the aging macula and pathogenesis of AMD. We are interested in both their methodology and findings and would like to raise a number of issues.

When irradiating their model, the authors have cited 390–410 nm as the “ultraviolet” wavelength the tissue was exposed to. It is worth noting that although UV-C (<280 nm) does not reach the surface of the Earth in solar radiation, the eye is exposed to UV-B wavelengths (280–315 nm) and UV-A (315–400 nm) through ambient exposure to sunlight. However, above 400 nm is visible light [3]. In light of this, we would be interested to learn how this narrow emission band was achieved, as the authors have not described their UV source, or how its spectral output was gated.

Moreover, the means of quantifying the reported irradiance of 0.0045 mW/cm<sup>2</sup>, and its relevance as a stressor, has not been clearly outlined by the authors. Whether or not this intensity of UV could reasonably expect to reach the retina of the general public is left unclear, it is important to note that the vast majority of UV

radiation that falls upon the eye is absorbed by the cornea, lens, and vitreous humor with only a fraction reaching the retinal basement membranes [4]. It is intriguing nonetheless, that long-wave UV decreased drusen volume in the high-risk cells, and we agree with the authors' statement that this finding should be investigated further to isolate the mechanism of action. However, any broad statements, that exposure to UV radiation is beneficial to those at high risk of AMD, should be considered carefully to ensure they are in keeping with the best available evidence.

There is a pressing need to standardize experimental models that seek to explore UV-RPE interaction, and we should be grateful to the authors for addressing the issues raised. This will provide the level of detail required for others to replicate experiments and compare datasets, which is necessary in exploring this field further.

It is in light of these concerns that we kindly invite the authors to expand upon the UV irradiance apparatus used in their manuscript, and the steps taken to validate its use within an in vitro context.

### DISCLOSURE OF POTENTIAL CONFLICTS OF INTEREST

The authors indicated no potential conflicts of interest.

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