

ROLE OF METALLOPROTEASES IN RETINAL DEGENERATION INDUCED BY VIOLET AND BLUE LIGHT

C. Sanchez-Ramos^{1A}, J.A. Vega², M.E. del Valle², A. Fernandez-Balbuena¹, C. Bonnin-Arias¹, J.M. Benitez-del Castillo¹.

A: Optic II, Neurocomputation and Neurobotic Group, 1: Univ Complutense Madrid, Spain; 2: Morphology and Cell Biology, Universidad de Oviedo, Oviedo, Spain.

XIII International Symposium on retinal Degeneration. Sichuan Ophthalmology Academy, Emeishan, Sichuan, China. Septiembre 2008

celiasr@opt.ucm.es

Introduction:

Light exposure produces three types of detrimental effect on the retina:

- Photomechanical
- Photothermal
- Photochemical.

Age-related Macular Degeneration (AMD) and other retinal diseases are known to be associated with light intensity, the (short) wavelength of light and the exposure time.

The enzymes metalloproteases (MMPs) are involved in degeneration processes and are responsible for degrading the basal membrane and extracellular matrix. The synthesis of these proteases in phototoxic processes mediated by light is supported both by experimental and clinical data.

Patients with AMD show the build-up and deposition of extracellular matrix molecules beneath the pigment epithelium (drusen) and this has led to the proposal that these formations could be linked to deficient MMP production by the pigment epithelium.

Objectives:

To examine the effects of phototoxic light exposure on the retina and preventing such effects through the use of intraocular lenses that block the blue portion of the visible light spectrum.

To contribute to existing knowledge of metalloprotease regulation in light-induced retinal degeneration.

Materials and methods:

Adult pigmented rabbits were exposed for 2 years to circadian cycles.

Of light of varying spectral composition

- Yellow intraocular lens
- Transparent intraocular lens



Image 2. Yellow intraocular lens

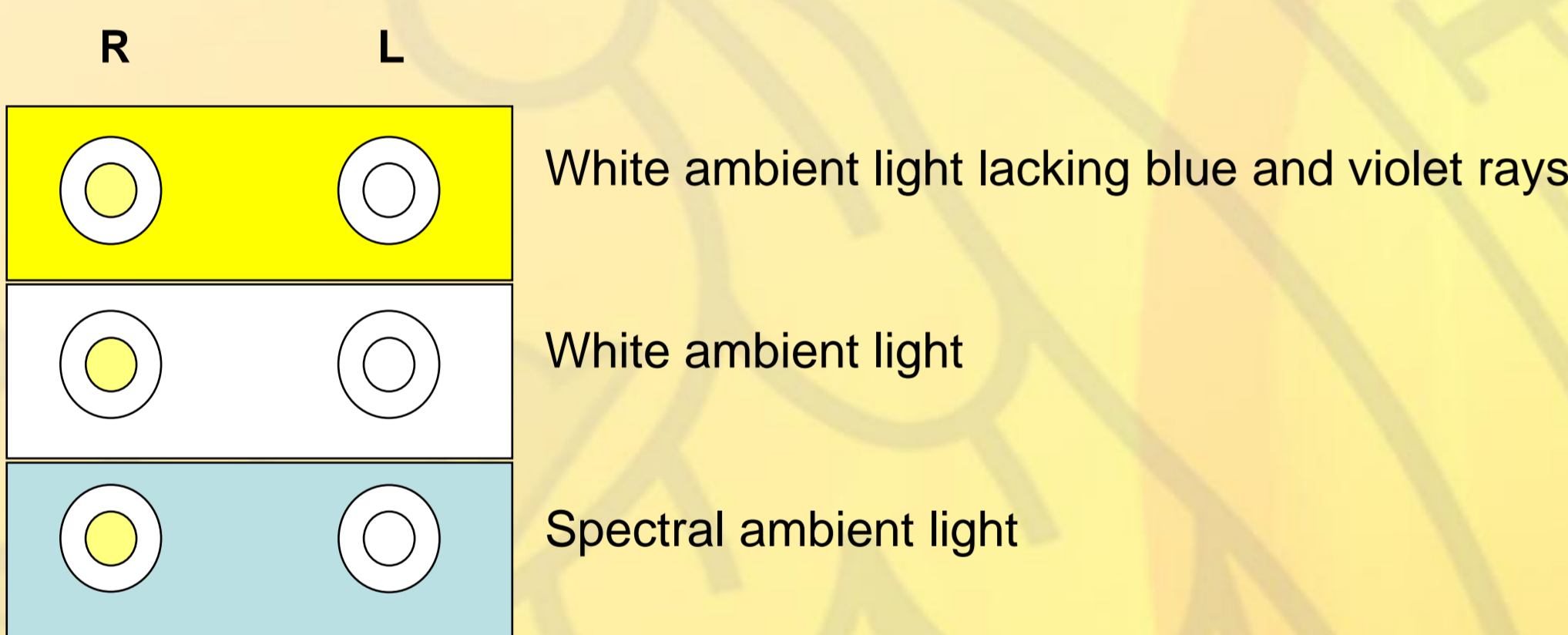


Figura 4. Diagram showing the types of ambient light (yellow, white and blue) the rabbits were exposed to and the intraocular lenses (left eye I transparent, right eye D yellow) implanted in the rabbits.

Clave	Intervención		Exposición	Tiempo
	OI	OD		
I3	T	A	Amarilla	2 años
G1	T	T	No expuesto	2 años
G3	T	A	Blanca	2 años
G5	T	A	Amarilla	2 años
G6	T	A	Azul	2 años
E2	T	A	Azul	2,5 años

Table 1. Used animals

Primers used:

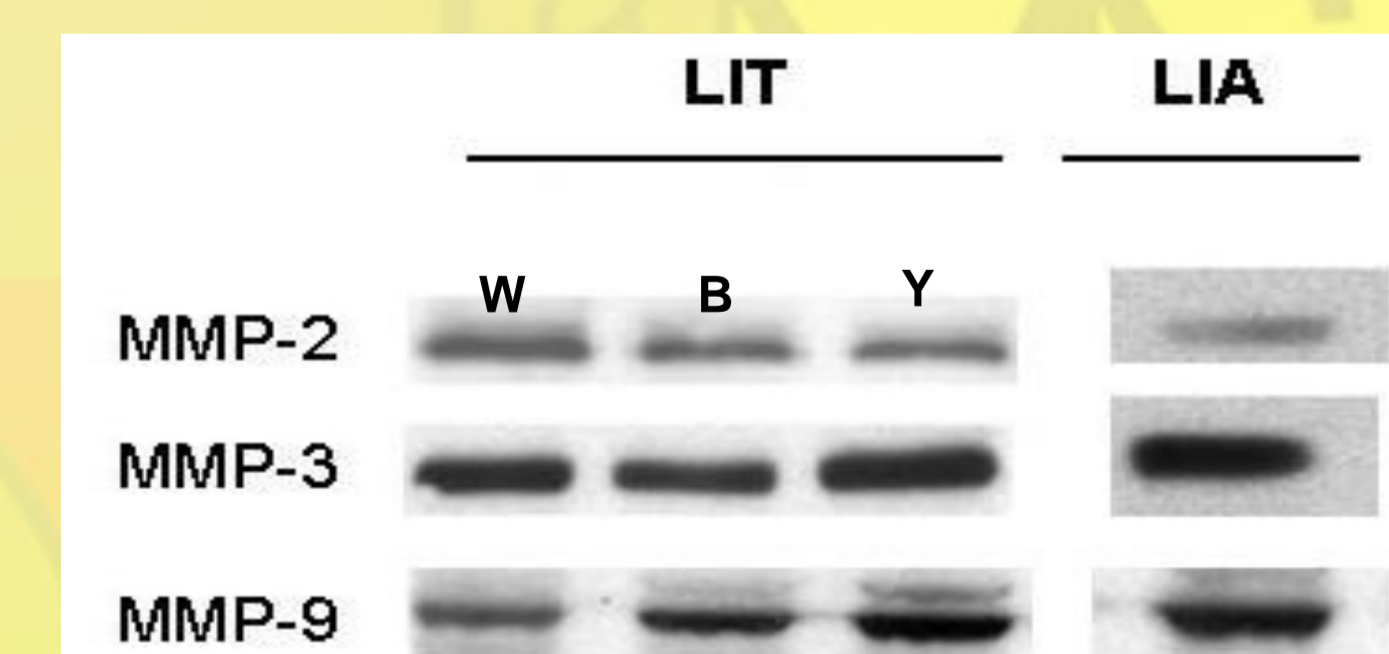
MMP-2: up: 5'-CCA CTG CCT TCG ATA CAC-3', down: 5'-GAG CCA CTC TCT GGA ATC TTC AAA-3'

MMP-3: up:5'-GCT TTG AAG GTC TGG GAG GAG GTG-3',down: 5-CAG CTA TCT TCC TGG GAA ATC CTG-3'

MMP-9: up: 5'-GTT CCC GGA GTG AGT TGA-3', down: 5'-TTT ACA TGG CAC TGC AAA GC-3'



Results:



Appears 5. Expression of the genes MMP-2, MMP-3 and MMP-9 in the retina of rabbits exposed to permanent lighting for 2 years.

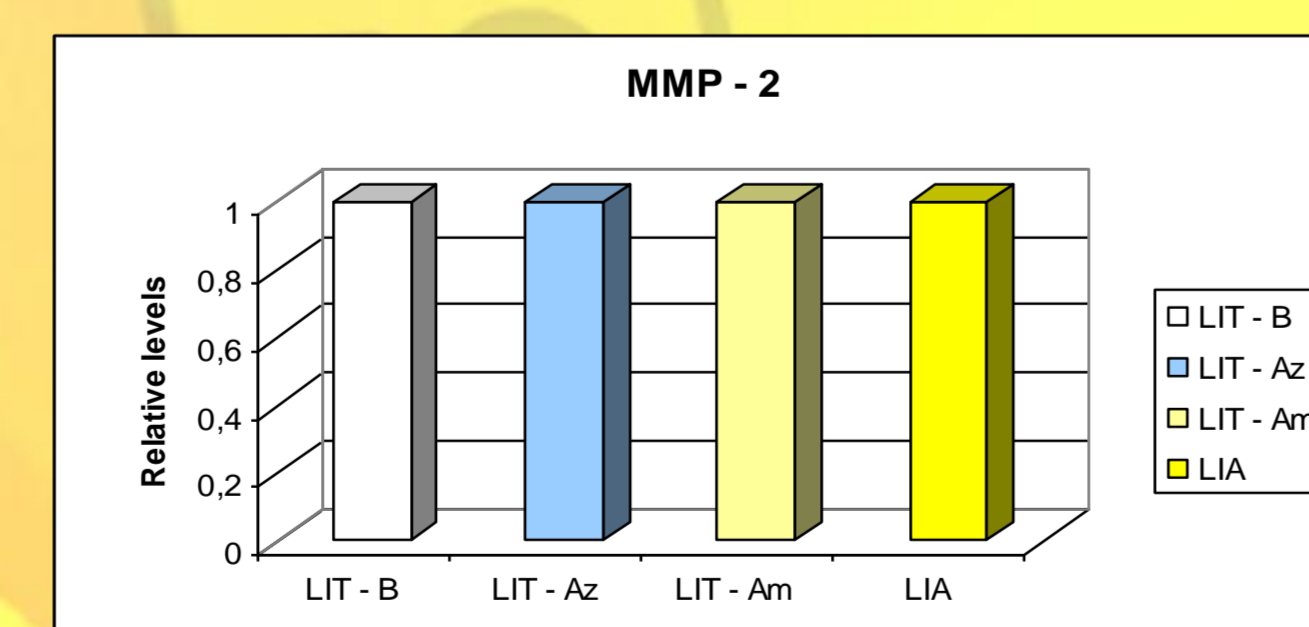


Table 2. Results MMP-2

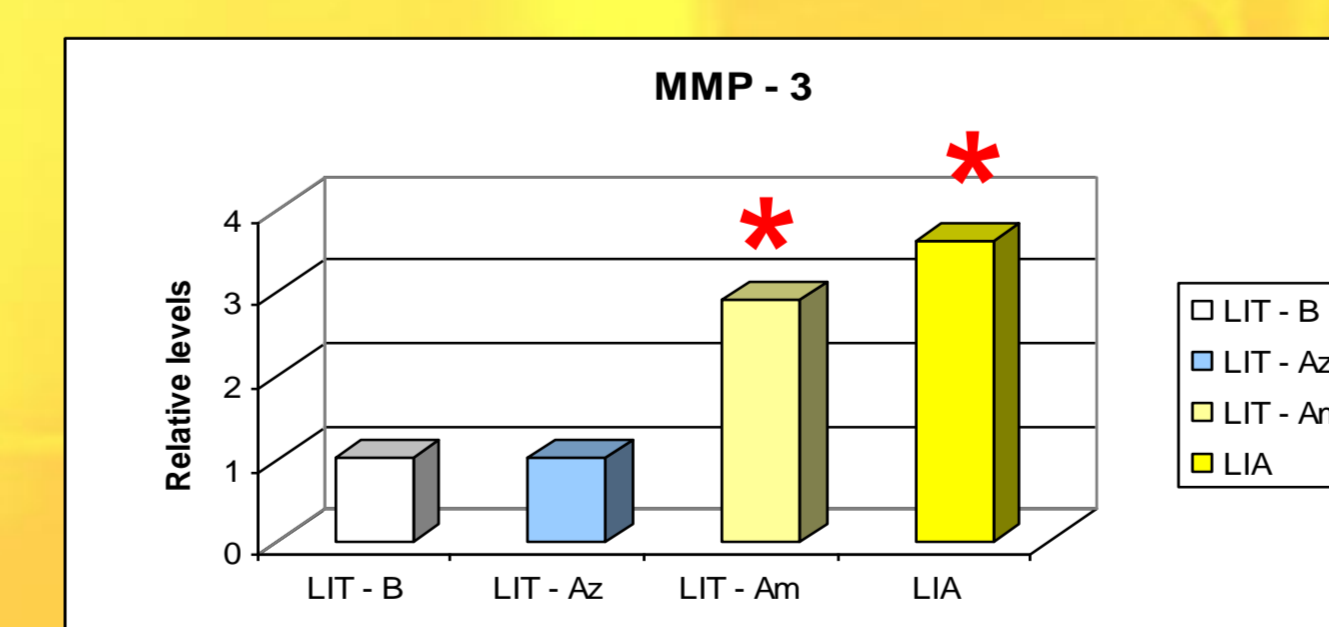


Table 3. Results MMP-3.

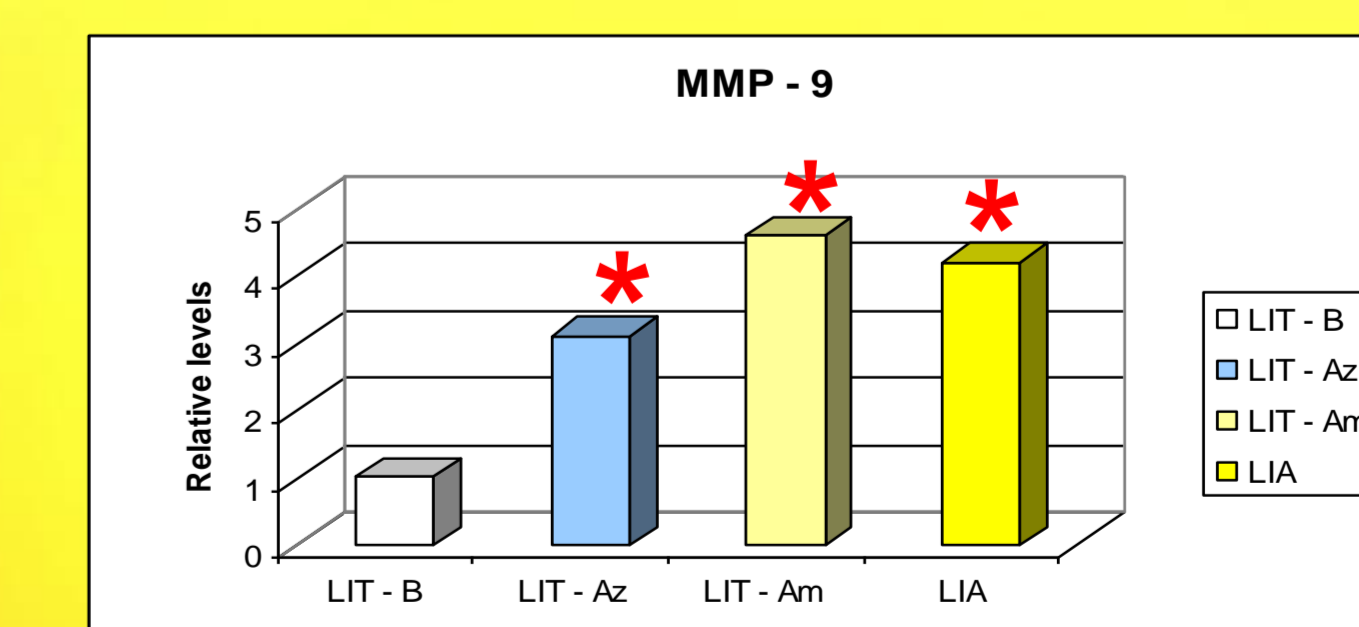


Table 4. Results MMP-9.

Conclusions:

Our findings indicate:

Exposure to long periods of light increases the expression of some MMPs and this could have harmful effects on the retina since it indicates damage to the extracellular matrix.

Increased MMP expression could determine the faster turnover of the extracellular matrix to avoid the formation of matrix deposits.

Light exposure or the intraocular implant of a yellow lens do not modify MMP-2 expression.

In animals exposed to light lacking the blue portion of the spectrum and in animals implanted with a yellow intraocular lens, MMP-3 expression was 2.9 and 3.6 times higher than in controls, respectively.

Similar behaviour was observed for MMP-9 expression which was upregulated in: animals exposed to blue light (3.1 times), animals exposed to white light lacking the blue portion of the spectrum (4.6 times) and animals fitted with a yellow intraocular lens (4.2 times).

References:

- Margrain TH, Boulton M, Marshall J, Sliney DH. Do blue light filters confer protection against age-related macular degeneration? *Prog Retin Eye Res* 2004; 23: 523-531.
- Elliot S, Catanuto P, Stetter-Stevenson W, Cousins SW. Retinal pigment epithelium protection from oxidant-mediated loss of MMP-2 activation requires both MMP-14 and TIMP-2. *Invest Ophthalmol Vis Sci*. 2006; 47:1696-1702
- Flaxel C, Bradle J, Acott T, Samples JR. Retinal pigment epithelium produces matrix metalloproteinases after laser treatment. *Retina*. 2007; 27:629-634
- Haeseleer E, Palczewski K. Calmodulin and Ca2+-binding proteins (CaBPs): variations on a theme. *Adv Exp Med Biol*. 2002;514:303-317
- López-Otin C. Overall CM Protease degradomics: a new challenge for proteomics. *Nat Rev Mol Cell Biol*. 2002; 3:509-519
- Margrain TH, Boulton M, Marshall J, Sliney DH. Do blue light filters confer protection against age-related macular degeneration? *Prog Retin Eye Res* 2004; 23: 523-531.
- Papp AM, Nyilas R, Szepesi Z, Loncz M, Takács E, Abraham I, Szilágyi N, Tóth J, Medveczky P, Szilágyi L, Juhász G, Juhász G. Visible light induces matrix metalloproteinase-9 expression in rat eye. *J Neurochem*. 2007; 103: 2224-2233
- Plantner JJ, Jiang C, Smine A. Increase in interphotoreceptor matrix gelatinase A (MMP-2) associated with age-related macular degeneration. *Exp Eye Res*. 1998; 67:637-645
- Plantner JJ, Smine A, Quinn TA. Matrix metalloproteinases and metalloproteinase inhibitors in human interphotoreceptor matrix and vitreous. *Curr Eye Res*. 1998; 17:132-140