STUDY OF THE ROLE OF P2Y RECEPTORS IN THE DEVELOPMENT OF EXPERIMENTAL AUTOIMMUNE UVEITIS

RELVAS L.J.M., VILLERMAIN F.

Affiliation Institution: Department of Ophthalmology, CHU St Pierre et CHU Brugmann

Promotor of the Project: WILLERMAIN F., MD, PhD

BACKGROUND AND AIM

During autoimmune uveitis (AU), retinal specific auto-reactive T lymphocytes (TL) are activated, alter blood retinal barrier and penetrate the eye where they start an inflammatory reaction. Nucleotides, normally present at low concentration in extracellular media, can act as a danger signal, through P2 receptors activation and might be implicated in AU. In this work we would like to investigate if the expression of the nucleotide receptor P2Y2 has any role in experimental autoimmune uveitis (EAU)

METHODS AND MATERIAL

EAU will be induced in WT and P2Y2 KO mice by IRBP peptide 1-20 injection. 12 days later, TL from spleen and lymph nodes will be purified and restimulated by IRBP. TL proliferation will be measured by thymidine incorporation and cytokines secretion by ELISA. TL from the 2 groups of mice will also be adoptively transfered in WT mice. Similarly, TL from WT mice will be adoptively transfered in WT and P2Y2 KO mice. EAU development will be graded by clinical and histological scores.

RESULTS

TL generated in KO mice proliferate and produce less IFNγ and IL-17, after IRBP restimulation than TL generated in WT mice. Accordingly, adoptive transfer of TL generated in KO mice induce significantly a lower grade of disease than those generated in WT mice. Finally, adoptive transfer of TL generated in WT mice induce disease of significantly lower grade in KO mice recipient than in WT mice recipient. CONCLUSION Our preliminary data shows that P2Y2 KO mice have a defective immune response after immunisation and develop lower intraocular inflammation following adoptive transfer with TL. Altogether this suggests that P2Y2, as danger receptor signals, play an important role in the development of uveitis.

REFERENCES

(1) Koevary SB – Ocular immune privilege: a review. Clin Eye Vis Care. 2000; 12(3-4):97-106
(2) Boeynaems JM, Communi D, Gonzalez N, Robaye B – Overview of the P2 receptors. Semin Thromb Hemost. 2005; 31:139-149.
(3) Relvas LJ, Bouffioux C, Marcet B et al – Danger signals and blood retinal barrier activation: extracellular nucleotides stimulate interleukin-8 production by ARPE cells. Invest Ophthalmol Vis Sci. 2009; 50(3):1241-6. [Epub 2008 Nov 21.]