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Presentation Abstract

Program#/Poster#:	2019
Abstract Title:	**Application of the TLR9 Ligand CpG DNA to the Injured Corneal Epithelium Induces Intraocular Inflammation**
Presentation Start/End Time:	Monday, May 03, 2010, 4:45 PM - 5:00 PM
Session Number:	272
Session Title:	Hot Topics in Infection and Immunity
Location:	Room 315
Reviewing Code:	169 corneal immunology – IM
Author Block:	*H.R. Chinnery[1], S. McLenachan[1], M. Degli-Esposti[1], J.V. Forrester[2], E. Pearlman[3], P.G. McMenamin[4].* [1]Centre Ophthalmology and Visual Sciences, Lions Eye Institute, Nedlands, Australia; [2]Div of Applied Medicine, Imm & Inf, University of Aberdeen, Aberdeen, United Kingdom; [3]Ophthalmology and Visual Sciences, Case Western Reserve University, Cleveland, OH; [4]Anatomy & Human Biology/Ct Ophth Vis Sci, Univ of Western Australia, Perth, Australia.
Keywords:	480 cornea: basic science, 556 inflammation, 593 microbial pathogenesis: experimental studies
Abstract Body:	**Purpose:** CpG oligodeoxynucleotides (ODN) are synthetic immunostimulatory sequences containing an abundance of CpG -DNA motifs similar to those found in high quantities in bacteria and viruses. Recognition of CpG DNA by TLR9 leads to activation of the innate immune system. We investigated the inflammatory response to CpG DNA in the mouse eye following its application to the injured corneal epithelium. **Methods:** The central corneal epithelium of C57Bl/6 mice (aged 6-12 weeks) was debrided using an Algerbrush. 20ug of CpG ODN 1826 (Type 'B'), or control (GpC) ODN was applied to the cornea. Mice were sacrificed at 0h, 0.5h, 2h, 6h, 24h, 72h or 7 days after treatment. Frozen eye sections or corneal, retinal and iris/ciliary body wholemounts were examined for infiltration of neutrophils and macrophages following immunostaining with anti-leukocyte antibodies (NIMP, Iba-1, MHC Class II and F4/80). Macrophages and neutrophils were quantified in the cornea and retina/vitreous. **Results:** In the cornea, neutrophils had infiltrated by 6h, reaching a peak at 24h and were absent by 72h. At 24h, F4/80+ macrophages were present in the corneal stroma, but their density increased over 6-fold by Day 7. A large influx of

neutrophils and macrophages were present in the anterior chamber, ciliary body, iris, vitreous and inner retina. Quantitation of neutrophils in the retina/vitreous in wholemounts revealed a small number of intravascular neutrophils by 6h (average 15 cells/mm^2), increasing to 800 cells/mm^2 by 24h. This had disappeared by 72h. In addition to resident Iba-1+ microglia in the ganglion cell layer and hyalocytes in the vitreous, there was an increased number of round Iba-1+ MHC Class II+ cells in the retina/vitreous of CpG ODN-treated eyes. This response was highly specific for CpG rich DNA, as similar topical exposure to (GpC) ODN did not induce any infiltration of inflammatory cells.
Conclusions: Widespread intraocular inflammation can be induced by the application of CpG ODN to the injured cornea. These findings indicate that DNA released during microbial keratitis can stimulate an inflammatory response in the retina. Future studies will examine the specific cell types mediating TLR9 responses in the eye and the molecular basis for these observations.

CommercialRelationships: **H.R. Chinnery:** None. **S. McLenachan:** None. **M. Degli-Esposti:** None. **J.V. Forrester:** None. **E. Pearlman:** None. **P.G. McMenamin:** None.

Support: NH&MRC Grant 572709