Editorial

There is no longer any doubt that inflammatory processes are highly involved in the pathogenesis of various ocular diseases. Autoimmunity, inflammation and infection may initiate a large spectrum of pathologic processes or contribute to their progression. In light of the recent introduction of novel therapeutic interventions in ophthalmic disorders, it is necessary to revisit experimental models of ocular inflammation and discuss the relevance of each of them to human diseases.

In September 2007, a workshop on animal models of ocular inflammation was held in Paris, under the auspices of the International Ocular Inflammation Society, and was attended by more than 40 participants. The number of attendees and the presence of expert immunologists, molecular biologists, geneticists and physicians, dealing with specific aspects of diseases, were major steps towards a multidisciplinary and translational approach, which attempted to build a bridge between basic research and patient care. The workshop was organized in 3 different sessions dedicated to age-related macular degeneration, uveitis and other major ophthalmic diseases such as diabetic retinopathy, ocular lymphoma, inflammatory glaucoma, optic neuropathy and corneal graft rejection. We would like to thank Uwe Pleyer, the Editor-in-Chief of *Ophthalmic Research*, who allowed us to dedicate a special issue to the summary of major discussions of this meeting.

The role of chemokines has recently been reported in the pathogenesis of age-related macular degeneration. Raoul et al. showed that the drusen-like appearance in CX3CR1 knockout mice consists of subretinal lipid-bloated microglial cells, rather than a gradual accumulation of extracellular debris from the retinal pigment epithelium and choroid. Chan et al. generated and analyzed

double knockout mice for CCL2 and CX3CR1, showing that chemokines, A2E and endoplasmic reticulum proteins may be implicated in the pathogenesis of age-related macular degeneration. Using another knockout strategy, Nandrot et al. identified a critical role of $\alpha v \beta 5$ integrin receptors and their ligand MFG-E8 in synchronizing retinal phagocytosis.

Miyamoto et al. described a model for retinal edema using human ARPE-19 cells and showing that VEGF alters the external epithelial blood-ocular barrier through VEGFR-1. Optic neuritis is another critical issue in patients with multiple sclerosis. Guy described the role of mitochondria and oxidative stress, and the effects of modulating antioxidant gene expression in the murine model of experimentally induced autoimmune encephalomyelitis. Touitou et al. summarized different models of intraocular lymphoma and presented data on therapeutic targets in this malignancy.

The major part of the workshop was dedicated to experimental uveitis. Caspi et al. elegantly revisited the mouse model of experimental autoimmune uveoretinitis by dissecting its mechanisms. Wildner et al. used the rat model of experimental autoimmune uveoretinitis to determine a molecular mimicry between environmental molecules and retinal autoantigens. Induction of oral tolerance has been achieved and an international multicenter clinical trial is currently under evaluation. The same model has been used by Saraswathy and Rao to show the effects of oxidative stress in the initiation of photoreceptor damage in the early phase of the disease and they reported occurrence of photoreceptor mitochondrial stress prior to any macrophage infiltration. Camelo et al. were able to modulate regional immune microenvironment by injecting VIP-loaded liposomes

intravitreally in rats. Features of experimental melanin-protein-induced uveitis were summarized by Smith et al. Interestingly, inflammation in this model shares the features of human acute anterior uveitis and recurrences are common.

Transgenic models of experimental uveitis were discussed by Gregerson et al., bringing evidence for the extrathymic generation of regulatory T cells specific to a retinal neo-self antigen. Some experimental models mimic human conditions. De Kozak et al. presented the pathological features of spontaneously occurring uveitis, mimicking birdshot retinochoroidopathy in HLA-A29 transgenic mice. Animal models of Vogt-Koyanagi-Harada disease and sympathetic ophthalmia were summarized by Yamaki and Ohno. Salient features of these animal models, pertinent human uveitis entities with their clinical and histopathologic features and relevant comments of expert panel members were summarized by Bodaghi and Rao.

Other animal models were also described. Deeg discussed the spontaneous occurrence of uveitis with its recurrences in the horse model. Epitope spreading seems to play an important role in this model. Animal models in large animals with recurrent uveitis are convenient for long-term studies due to their relatively long life span, access to blood or cell samples and ocular imaging for studying disease kinetics. LeHoang et al. described the clinical and angiographic features of autoimmune uveoretinitis and vasculitis in cynomolgus monkeys immunized with human S antigen. Interestingly, a single injection induced a chronic and recurrent disease similar to human retinal vasculitis.

The role of pathogens in inducing ocular inflammation is no longer controversial. Rosenbaum et al. present-

ed an endotoxin-induced model of uveitis in both rats and mice. Muramyl dipeptide is another bacterial cell component that may induce experimental uveitis. This molecule activated the intracellular protein NOD2, and mutations in the NOD2 gene were associated with uveitis in patients with Blau syndrome. Rosenzweig et al. used intravital microscopy to show ocular inflammatory responses in a murine model of proteoglycan-induced spondylitis. Fujimoto et al. presented an experimental system in which microbial Toll-like receptor ligands stimulated naive CD4 cells specific against hen egg lysozyme capable of inducing uveitis in eyes expressing this lysozyme, thus showing that microbial products can trigger pathogenic autoimmunity.

More than many other areas of medicine, we are blessed with numerous experimental models of ocular inflammation. Not recognizing a mechanism or its consequences does not mean that it is not present with significant implications. Thus, we should not be concerned predominantly with the clinical ophthalmological phenotypes but divide them up based on disease mechanisms. Different diseases may share a final common pathway and phenotypic expression of the disease. Approaches based on disease mechanisms should be emphasized in understanding the ophthalmic diseases and in therapeutic interventions or prevention of the disorders.

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