Following a penetrating eye injury or surgical procedure, ocular antigens normally sequestered within the eye behind the blood-retinal barrier, become exposed to systemic immune detection. The eye does not have a lymphatic system which restricts ocular antigens from eliciting a local immune response. Instead, peripheral antigen presenting cells, such as macrophages and dendritic cells, phagocytose injury exposed ocular antigens. The protein components are processed into antigenic peptides for HLA class II presentation to CD4+ helper T cells in peripheral lymph nodes or the spleen.
The penetrating eye injury disrupts the blood-retinal barrier and allows leakage of ocular antigens into the systemic environment. Peripheral antigen presenting cells, such as macrophages and dendritic cells, alerted by tissue damage are recruited to the site of damage where they phagocytose ocular antigens normally sequestered within the eye. The activated antigen presenting cells migrate to the cervical lymph nodes or spleen where they present antigenic peptides derived from ocular proteins to autoreactive CD4+ helper T cells.
Peripheral antigen presenting cells, such as macrophages and dendritic cells, process phagocytosed proteins into peptide antigens that are displayed on HLA class II receptors which can be detected by antigen-specific CD4+ helper T cells. Normally, no CD4+ helper T cells should recognise ocular protein peptides since autoreactive T cells are deleted in the thymus. However, in rare instances an autoreactive T cell may escape the thymus or the peptide may resemble a similar peptide encountered previously through infection with a pathogen (molecular mimicry). Autoreactive T cells that respond to the ocular antigenic peptide, clonally expand and migrate to the site of inflammation. Indeed, HLA class II alleles such as DRB1*0404, DRB1*0405 and DQA1*03 are associated sympathetic ophthalmia that implies an autoimmune CD4+ helper T cell mechanism.
Activated immune cells upregulate cell surface receptors that allow them to extravasate from the blood circulation into inflamed tissue. Vascular endothelial cells also upregulate the ligands for these receptors to facilitate this process when stimulated by inflammatory cytokines such as IL-1 and TNF-α. Autoreactive CD4+ helper T cells penetrate the blood-retinal barrier of the damaged eye where they detect immunogenic ocular antigens and mount a pro-inflammatory immune response. Released cytokines recruit additional immune cells that overwhelm the immune privilege status of the eye and cause immune-mediated damage unless treated with anti-inflammatory drugs. Later, infiltration of autoreactive CD4+ helper T cells can promote inflammation of the undamaged eye (sympathetic eye), possibly due to upregulation of membrane receptors on local vascular endothelial cells by systemic cytokine stimulation.
Autoreactive CD4+ helper T cells can infiltrate the undamaged eye (sympathising eye) and mount an immune response to immunogenic ocular antigens previously detected in the injured eye. This is likely due to cytokine (IL-1 and TNF-α) driven upregulation of surface receptors on vascular endothelial cells in the sympathising eye that promote extravasation of peripheral immune cells. Activated T cells also secrete cytokines that recruit additional immune cells including antigen presenting cells that can take up ocular antigens and stimulate new autoreactive T cells. Immune-mediated damage can blind the sympathising eye unless the damaged eye is removed or immunosuppressive therapy is started.