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OCULAR IMMUNE RESPONSE IN RETINA GENE THERAPY

Oral

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Purpose:

There is growing awareness that an ocular immune response may present as an adverse event following ocular gene therapy. Factors affecting host immune responses including the features of the viral vector, delivery method, promotor transgene characteristics, and ocular disease will be reviewed. Pathophysiology, consequences, and mitigation strategies will be discussed.

Methods:

The current literature on complications of ocular gene therapy will be reviewed.

Results:

There is a growing understanding that despite the immune privilege of the eye, innate and host adaptive responses may arise to challenge the durability of transduction efficiency. Treatment-emergent adverse events have occurred from the vector, surgery, and effect on the target tissue. Mitigation strategies include choice of vector, gene therapy payload, use of anti-inflammatory therapy, and surgical techniques that avoid the macula. It remains unclear what role the presence of serum neutralizing antibodies plays in the development of an ocular immune response.

Conclusions:

Ocular gene therapy holds great promise for the curative treatment of monogenic inherited retinal disease. The choice of vector, payload, patients, and disease selection has bearing on the immunogenicity and adverse events associated with clinically effective gene transfer. Scientific, ethical, and financial challenges to this technology still exist.