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Back to Search Results  |  Modify Search  |  New Search

Preclinical Development of Reverse-Engineered Vitreous Substitutes

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Institution Receiving Award: VANDEVENTER PLACE RESEARCH FOUNDATION
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PUBLIC ABSTRACT
Objectives and Rationale: The vitreous gel fills the space between the lens and the retina and is the largest tissue of the eye. It is mostly water (99.9%), with the rest being mainly collagen and hyaluronic acid. Collagen, like gelatin, is a rigid fiber that provides stiffness and prevents swelling; hyaluronic acid is a soft, flexible, water-absorbing, and syrupy polymer. The vitreous plays a central role in the growth and overall health of the eye. Ocular and orbital traumas involving the vitreous are an increasing problem encountered by our veterans and soldiers involved in modern warfare. In addition, both soldiers and civilians suffer from devastating vitreous related diseases; for example, age-related macular degeneration, vitreous hemorrhage, retinal detachment, and proliferative diabetic retinopathy. Treatment of these conditions often requires surgery involving removal and replacement of the vitreous. Current vitreous substitutes are not physiological and are often associated with glaucoma and cataracts. In addition, they prevent wounded soldiers from being airlifted to safer places, because the gasses expand during flight. Our biomimetic vitreous substitute is made of a rigid, collagen-like polymer and a hyaluronic acid-like polymer that is soft and syrupy. In addition, the two polymers have several “sticky” groups that can form a permanent bond. In a preliminary 1-month rabbit study, we tested a two-component biomimetic vitreous substitute that exhibited good biocompatibility. Now we propose to test two additional biomimetic hydrogels with ability to inhibit cell proliferation in tissue culture and then select one for further testing in rabbits and mini-pigs. Thus, we will have two formulations for further animal studies, one that has already been tested in the 1-month rabbit study and a second that is the better performer in the tissue culture studies.

Applicability and Potential Impact: Each year, an estimated one million vitrectomies are performed worldwide, with over 300,000 of these being performed in the USA. For Warfighters, our improved vitreous substitute will benefit the treatment of ocular trauma sustained on the battlefield, particularly from blast injuries. In the civilian population, it will greatly alleviate age-related and chronic eye conditions, such as those associated with diabetes.

Benefits and Risks: Current vitreous substitutes have numerous disadvantages and side effects: (1) They are not permanent; some need a second surgery for removal. (2) Gases are replaced by bodily fluids that cannot tamponade the retina or absorb shock. (3) None of the substitutes matches the refractive index of the vitreous. (4) All of them distort vision. (5) Sometimes patient positioning is required over weeks, and some substitutes may necessitate travel restrictions. Our biomimetic substitute sets into a gel immediately, will tamponade the retina, and should have none of the above limitations. It will eliminate vision impairment after surgery by matching the vitreous’ optical, physical, and viscoelastic properties and will eliminate the need for secondary or tertiary surgery to remove the substitute. These advantages, coupled with the gel’s generating osmotic pressure, should significantly reduce re-detachment of the retina. Also, because our material is a biomimetic gel, it will expand our knowledge of how the structure of the vitreous is related to the vitreous properties; for example, the role of osmotic pressure as a stimulus for growth of the eye. We could further expand the role of the hydrogel to serve as a depot for delivery of drugs, proteins, and encapsulated cells capable of making drugs and proteins. We can also expand this same concept to repairing and rehabilitating patients with spinal cord injury and articular joint damage. Upon successful completion of this pre-clinical research, the US Department of Veterans Affairs and Washington University will aggressively seek to license the technology to the private sector.

Back to Search Results
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