Annexin A2 in Proliferative Vitreoretinopathy

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PUBLIC ABSTRACT

Proliferative vitreoretinopathy, or PVR, is a potentially blinding disease that occurs in almost one-half of military personnel who have suffered a penetrating wound to the eye. It also may occur in patients who have had complicated eye surgeries. When there is a tear in the retina (the eye’s fragile internal lining that allows us to see) cells inside the eye begin to proliferate and, over time, can form a scar that pulls the remaining retina away from the back of the eye, further compromising vision. In this project, we wish to determine whether the development of PVR depends upon a protein called annexin A2, or ANXA2. We have created genetically engineered mice that have no ANXA2 at all. When we induce an eye injury in these mice with a substance called dispase, there is almost no PVR scar formation, whereas the scars that form in normal mice are dramatic.

We suspect that cells called macrophages, which clean up debris from injured tissue shortly after injury, may send molecular signals to other cells, called RPE cells, to start dividing, to migrate toward the center of the eye, and to start creating a scar. While scar formation can be a normal and productive response to an injury elsewhere in the body, it is detrimental inside the eye, where it can obscure vision or cause further damage to the delicate retina. In this project, we hope to determine how ANXA2 in macrophages, or possibly RPE cells, enables the PVR process. We plan to examine the PVR process in normal and ANXA2-deficient mice and to study macrophages and RPE cells harvested from those mice. In addition, in patients with PVR, we plan to study eye tissue that has been removed surgically as part of their treatment and would otherwise be thrown away. We hope that we can prove that ANXA2 is a major culprit in PVR, and we hope to show that by using an ANXA2 inhibitor immediately after eye surgery or eye injury, we can prevent PVR from occurring. If successful, this work would provide a new preventive treatment for PVR in patients who are at high risk for significant vision loss. While it is difficult to know for certain, we estimate that we could be well on our way toward developing new ANXA2 inhibitors at the conclusion of this 3-year study. That means that a new agent could be ready for patient trials about 3 to 5 years later. PVR is an increasingly common problem in service members who have suffered combat-related eye injuries as a result of their active duty. The current surgical treatments for this disorder are inadequate, and preventive therapies should be a high priority.
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