A MOLECULAR MARKER FOR DRY EYE

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In 1989 I began my Ph.D. thesis in the Molecular Biochemistry and Biology Dept. IV of the Veterinary College of the Complutense University in Madrid. My thesis was about a type of molecule known as diadenosine polyphosphate, which attracted my interest because they behaved as neurotransmitters in the central nervous system (1). Although not very well known, these molecules seem to participate in an important number of biological processes. From the molecular viewpoint, diadenosine polyphosphates are compounds made up by two adenosines joined by a chain of phosphates. These biomolecules are usually identified by means of their short form «ApnA» where n is the number of phosphates bridging both adenosines.

When, for a number of apparently random reasons, I started to work in the University School of Optics in the above mentioned University, I began to ponder the possibility of researching the role of these molecules in the eye. I started studying the role of these substances in the regulation of intraocular pressure (IOP) and their presence as natural components of aqueous humor. Quite early in my investigation it became clear that these substances could act as natural IOP regulators (2). However, even though this is a relevant function, one of the most surprising finding about the action of ApnA in the eye was the role it plays on the ocular surface.

Firstly, it was satisfying to confirm that both in animal models as in humans, diadenosine polyphosphates and particularly Ap3A and Ap4A are intrinsic components of tears (3). It has been observed that the superficial lesions produced by a foreign body heal faster when Ap4A is present because this compound accelerates the migration of corneal epithelial cells, rapidly closing corneal wounds (4). This finding is of great interest because Ap4A could be used for facilitating scarring after refractive surgery.

However, in what concerns the eye surface, the dry eye is doubtlessly a hot, complex and controversial topic due to its diverse etiology and difficult diagnosis arising from the low correlation between signs and symptoms. Accordingly, this pathology which is endured by so many people does not have an efficient treatment for many reasons, including the difficulty in its diagnosis (5-7).

Recently, studies made in a high number of patients with dry eye syndrome have proved significant variations in the concentration of Ap4A regardless of whether patients have normal or low lacrimation. It is relevant to note that the levels of Ap4A are up to 5 times above normal levels in patients with dry eye and normal lacrimation. This increase is even higher in dry eye individuals with low tear production. In these cases the Ap4A are increased over 100 fold (8).

The increased presence of said dinucleotide in tears responds to a surprising process. Ap4A is released into tears from the eye surface, the cornea conjunctiva, as a consequence of the massage performed by the eyelid on the eye. Contrary to what could be expected, i.e., a release of Ap4A together with the tear from the main lachrymal gland or the nerve terminations which innervate the cornea (as occurs in the central nervous system), all studies indicate that said release does not depend on either of these two factors but directly on the degree of the patient’s discomfort. We all use our eyelids with greater frequency when feeling discomfort in the eyes (9), thus releasing greater quantities of Ap4A (8).

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Currently, the difficulty in diagnosing dry eye does not allow a reliable approach for treatment. This is evident when we observe the lack of active principles for resolving this pathology (10). Products based on cyclosporine, which approach the dry eye syndrome as an inflammatory process, or the highly vaunted Prolacria (2% diquafosole), which has given great results in clinical essays and will soon be on the market, together with artificial tears, comprise the small amount of treatment options we have at this point in time.

Measuring the Ap4A levels in tears is an objective method which allows for a reliable diagnostic of dry eye. We trust that, in the same way that the identification of said molecule can contribute to an improved quality of life of our patients after receiving more specific treatment by eye professionals, this molecule may also help pharmaceutical labs to develop new drugs with higher efficiency rates in dry eye syndrome treatments.

REFERENCES