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Advances in Tear Research: Tears as Useful Biomarker

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Abstract

The clear watery liquid secreted by the lachrymal glands is made up of water, electrolytes, proteins, lipids, and mucins that form layers on the surface of eyes. The quantity or quality of tears declines such that the eyes don't stay lubricated and results in dry eye and many other Patho-physiological disorders. The different types of tears-basal, reflex, and emotional-vary significantly in composition. Recently, like other biofluids tears can also be used as biomarker because tears contain a specific chemical, the alpha-synuclein, which can be used as biomarker for the diagnosis of Parkinson's disease. The cells taken from the lachrymal glands now can be developed into organoids which can be transplanted if the original were damaged.

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Introduction

Eyes are among the most unique organs in the body. The eyes are the window to the world as well eyes can be a window into the body. The human eye is made up of lots of highly specialized tissues so as to maintain transparency that enables us to see. A thorough examination of the eye uncovers clues about the state of the whole body. As we age, the composition and structure of the eyes changes. One of the main areas where this happens is in the lens.

In addition to visual processes, light also plays an important role in physiological responses; in turn there is change in behavior [1,2]. Our experiments with ophthalmic mutant rats also showed that the loss of vision also hampered their physiological activities, and their rhythm city was also disturbed [3].

We are constantly making tears by the gland namely, the lachrymal gland, located above each eyeball, behind the bony orbit of the eye [4]. This normal tear production is called basal tearing. It is normal to have the occasional watery eye from basal tears. In certain situations, such as in response to certain stimuli or in response to emotions, the eye will also make extra tears. These tears are called; reflex tears or emotional tears [5,6].

There are three types of tears, which vary in their composition:

i. **Basal Tears,** shed constantly and provide cushion the eye, supply the tissue with nutrients and remove debris and have lots of salt ions and other electrolytes, as well as proteins with antimicrobial properties. These proteins include lipocalin, which binds and disrupts certain compounds in microbes, and lysozyme, an enzyme that kills bacteria by breaking down their cell walls. people produce about 1 to 4 microliters of tears a minute - or about 1.44 to 5.76 milliliters per day - on average. However, this volume can vary significantly depending on what we are doing.

ii. **Reflex Tears,** which are produced in response to irritants, such as smoke, or the chemicals released on chopping onions. They have higher water content, and a lower concentration of fats and proteins, than basal tears do.

iii. **Emotional Tears** that people shed in sadness after a breakup or in joy when seeing a friend after years spent apart. These tears carry higher concentrations of hormones typically released due to emotions, compared with reflex tears.

Structure of Tears

Maintaining tear structure is important for the tears covering the eyes to function normally. Tears have two distinct layers from the outer surface (Figure 1).

Lipid Layer

The lipid layer is secreted by the Meibomian glands on the edges of our eyelids. This layer prevents the evaporation of tears by covering the outer surface. If Meibomian gland function declines due to aging or inflammation, the secretion of oily substance can decrease, or the composition can change so that

the oily substance changes its property to resemble wax, and gland openings can become obstructed. If this happens, tear stability declines, resulting in dry eye syndrome [7-9]. This type of abnormality is called Meibomian gland dysfunction and is often seen in older patients.

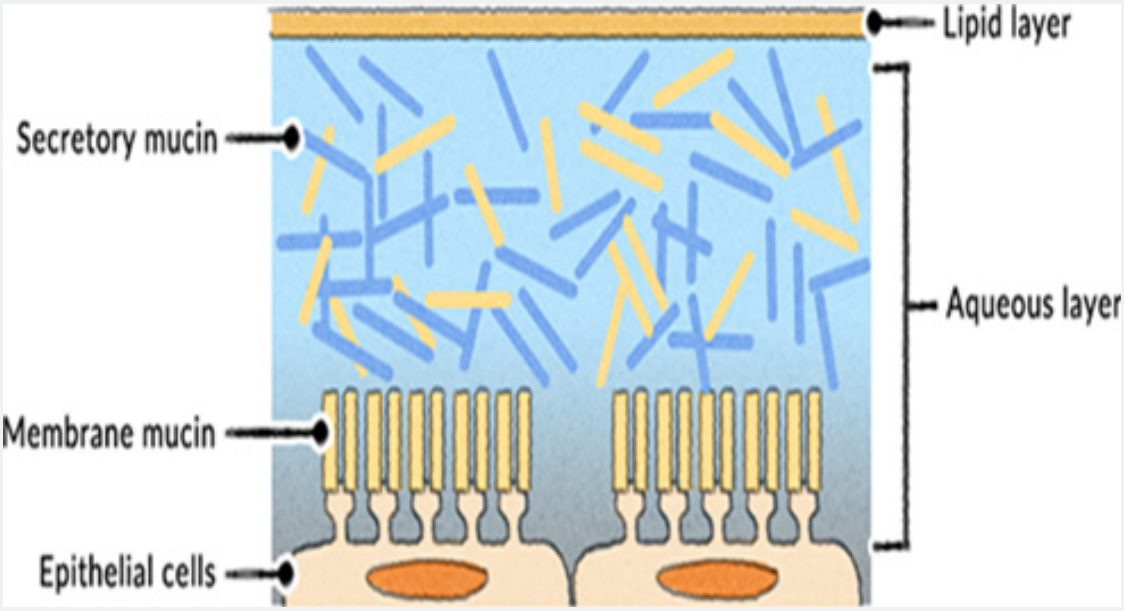

Figure 1: Schematic Diagram of the Eye Surface.

Aqueous Layer

This layer makes up the majority (95%) of tears and contains various substances including proteins. It performs the key functions of tears, such as supplying nutrients to the cornea, preventing infection and healing damage. It is secreted by the lacrimal gland on the underside of the upper eyelid. In addition, mucus which is secreted by the goblet cells on the surface of the eye, helps distribute tears across the surface of the eye uniformly. Infected mucin is the one which plays an important role in tear stability [10].

Tears drain from the eyes via tear ducts. But because emotional and reflex tears are typically released in a flood, not in a trickle, these can often spill out of the eye rather than draining normally [11]. Upon being made, all these tears are added to a thin film that covers and nourishes the cornea of the eye. This tear film has three distinct layers (Figure 1). On the outside is an oily layer produced by the meibomian glands in the eyelids [1] that stops the eyes from drying out. The next layer is watery and lubricates the eye (Figure 1); it's made mostly by the lachrymal gland, which also adds proteins, oxygen and electrolytes. The inner layer, closest to the cornea's surface, contains a slime-like protein called mucin, which helps the tear film stick to the eye's surface [9].

Babies Start Making Tears at Later Age

Babies' eyes aren't completely dry at birth, but they have minimal moisture. Newborns start making more tears once their lachrymal glands are fully developed. This typically happens sometime after two weeks of age. The ability to produce tears continues to increase over the next several weeks [12] premature babies take a bit longer to start producing noticeable tears.

After two to three months, tear production will ramp up so that tears become visible during crying. When a baby cries, the lachrymals glands produce excess tears that drain into the tear ducts and spill out over the eyelids. This overflow of tears from the eyes is what we call "Real Tears."

Functions of Tears

The fluid that makes up our tears contains water for moisture and oils for lubrication and to prevent tear liquid from evaporating. Tears also contain mucus so they can spread evenly across the surface of the eyes. Plus, that mucus contains antibodies and special proteins for resistance to infection. Tears can improve vision, hydrate the eyes, and sharpen focus. They protect the eyes and keep out debris from them. Tears also transport oxygen and nutrients to the surface of the eyes [13].

On blinking the eyelids, a film of tear fluid coats the surface of the eye at a certain thickness and is maintained for a while. This is called tear stability. Tears not only keep the eye moist but also have an important role in maintaining the healthy functioning of the eye.

i. **Preventing Dryness Tears** prevent dryness by coating the surface of the eye, as well as protecting it from external

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irritants [12,14].

ii. **Supplying Oxygen and Nutrients** There are no blood vessels on the surface of the eye, so oxygen and nutrients are transported to the surface cells by tears.

iii. **Preventing Infection** Foreign bodies that enter the eye are washed out by tears. Moreover, tears contain a substance called lysozyme, which has an antibacterial action, and works to prevent invasion and infection by microbes.

iv. **Healing Damage** to the surface of the eye Tears contain components that heal damage to the surface of the eye.

v. **Creating a Smooth Surface** on the eye Tears lubricate and smooth the surfaces of our eyes so that light is refracted correctly, enabling us to see clearly.

vi. **On Ageing Tear Glands Stop Working** due to which some diseases can also increase the likelihood of having dry eyes [7-9], such as Sjögren's syndrome [15-17], an autoimmune condition in which the body's own immune cells damage the lacrimal glands that moisturize the eyes.

If the quantity or quality of tears declines such that the eyes don't stay lubricated, those results in addition to dry eye; many Patho-physiological disorders have been described for dry eye. Tears in old age are one of them. This may be due to various etiological factors and mechanisms for eyelid abnormalities, naso-lachrymal drainage pathologies, neurological causes, corneal disorders, irritation of lashes and hyper secretion of tears [18]. Dry eyes are considered to be the most common of all in causing excess of tears. Recent advances related to the cause and target oriented treatment of the tears have also been discussed that will open new avenues for further research. People with Sjögren's syndrome cannot even produce reflex tears [16-18].

Biomarker of Parkinson's Disease

Recently it is shown that tears contain a specific biomarker the alpha-synuclein of Parkinson's disease (PD) the company named AXIM Biotechnologies developed tear-based diagnostic tests for PD [19-21], These studies used a more cumbersome method to detect the presences of α-synuclein, the company noted. Total tear protein content is then quantified via a bicinchoninic assay followed by alpha-synuclein detection using a plate reader. In addition, the company noted that additional studies have indicated that total lactoferrin (Lf), an antimicrobial protein that is a component of the immune system, is reduced in patients with PD

Tear Glands in a Dish

Scientists used their expertise to work out culturing conditions for cells from mice and human lachrymal glands without lachrymal ducts. They were also successful in stimulating tear production, they then exposed their organoids to several chemicals, including the neurotransmitter norepinephrine, that relay messages between nerve cells and glands [22]. And when the team transplanted the organoids into mice, the assemblages matured and developed duct-like structures containing proteins found in tears.

Transplant Potential

Eventually, now it is possible to provide material for transplants these organoids derived from human cells, to replace diseased or damaged tear glands. Earlier this group also developed salivary gland organelles that will be tested in clinical trials starting this summer for people who suffer from dry mouth, a condition that can cause tooth decay and difficulty in chewing and tasting.

Salivary-gland trials [23] could serve as a testing ground to work out methods that could then be adapted for future tear-gland transplants. the work that Clevers' team has done in characterizing tear glands - including creating a detailed cell-by-cell map of the structures and their organoids [23,24] has demonstrated that the glands are more heterogeneous than was previously appreciated and could send researchers back to reinterpret old data. That has implications for a lot of studies [24].

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