Tear fluid biomarkers in ocular and systemic diseases

Lila Amer

Introduction

The complex composition of tear fluid presents as a future biomarker for systemic and ocular diseases. By analyzing the proteomics, glycomics, lipidomics and metabolics of tears, diseases can be pre-ordinately diagnosed. Tear collection is inexpensive, non-invasive, and easily replicated. Using the Schirmer's tear collection method, the components of tears extracted from the eye of a diseased patient can be compared to the tears of a healthy human eye. This comparison allows for the identification of abnormal levels of chemicals or hormones on the surface of the eye. Because ocular health is impacted by disparity in other regions of the body, tear fluid shifts in its hormones and chemicals in accordance to the imbalance of homeostasis. The elevated or depleted levels of these substances in the tear fluid can be identified using a mass spectrometer and gel electrophoresis machine. This experiment aims to identify the specific characteristics that verify tears as a biomarker. It is hypothesized that human tears possess traits capable of being used as precursors to diseases. Establishing the connection between tear fluid and bodily diseases allows for the research of tear fluid as a biomarker. This form of diagnosing systemic and ocular diseases allows for predictive and preventive medicine.

Review of Literature

As defined by the National Institute of Health, a biomarker is

A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to therapeutic intervention.

In accordance, the US Food and Drug Administration describes biomarkers as

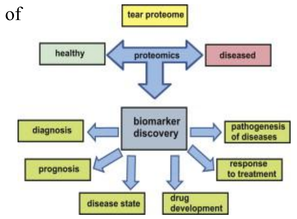
Any measurable diagnostic indicator that is used to assess the risk or presence of disease.

The diagnosis process usually starts with a patient presenting with a set of symptoms commonly associated with a specific disease. Chemical, hormone and physical exams lead to the actual diagnosis. Prognosis, or the prediction of the disease's outcome, is followed with a course of treatment. Treatment revolves around severity and stage. Depending on how far along the disease has progressed impacts the course of treatment. Doctors use biomarkers to catch. Due to their inexpensive, noninvasive nature and complex chemical makeup, tears pose as a promising future biomarker *(Investigation of the global protein content from healthy human tears)*. Blood is an example of a biomarker. Similar to how blood tests evaluate blood cell levels, tears tests would also be administered to monitor the components of tears. Accuracy is determined by consistency, so tear analyzing would be a regular.

A manuscript detailing the extensive characterization of human tear fluid has already been published by Marianne Dor, author of the *Investigation of the global protein content from healthy human tears.* Upcoming research in ophthalmology revolves around comparing healthy tears to diseased tears. The applications are extensive, involving systemic, neurological and optical diseases *(Tear fluid biomarkers in ocular and systemic disease: potential use for protective, preventive and personalized medicine)*. Ophthalmologists and researchers alike are calling upon more scientists to pursue tear research in an effort to raise awareness to the pertinence of tear tests in the diagnosis process.

Purpose

This experiment aims to expedite the healing process by introducing alternative methods to diagnosing diseases. By producing a systematic review of current tear research, these alternative methods can be identified. Using tears as biomarkers opens up an entirely new field of research responsible for monitoring both systemic and ocular diseases.

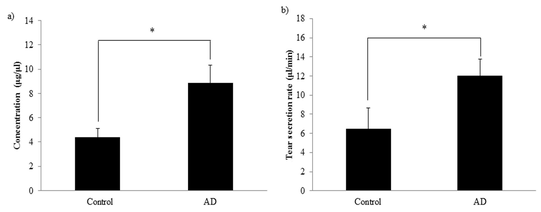


Current Studies

Tears are inexpensive, noninvasive and highly expressive; all the qualities of a biomarker. The increasingly prevalent presence of cancer calls for new methods of identification, and tears may be the answer. Researcher Evans Fockler has identified lacryglobin as a possible marker for breast cancer. Lacryglobin is a protein secreted by the lacrimal glands that is closely associated with cancer tissue in patients with breast cancer. In addition, to its breast cancer applications, lacryglobin was excessively present in patients with colon, prostate, lung and ovarian cancer. By monitoring lacryglobin levels in tears of patients with a family history of cancer, the cancer could be caught early and treated before it progressed to an untreatable state.

Expected Results

By determining compositional changes to tear profiles, progression of disease can be monitored, allowing for personalized prognosis and treatment. Both of these factors improve patient quality of life. It is expected that the tears of a diseased patient will present with abnormal levels of chemical or hormones.



Pictured above is the protein concentration in tears of patients with and without Alzheimer's disease.

Tear Fluid

Tear fluid covers the anterior surface of the cornea and serves critical functions in maintaining the homeostasis of the ocular surface. Produced by the lacrimal glands located in the upper lateral region of the orbit, tears are aqueous based substance responsible for hydrating and lubricating the surface of the eye. Tears supply nourishment and protect against foreign particles. The typical volume of tears in normal eyes ranges from 3.4 to 10.7 µl per eye.

Function of Tear Components

Tear **proteins** perform numerous functions, including antimicrobial defenses, lubrication, wound healing and regulation of the inflammatory response.

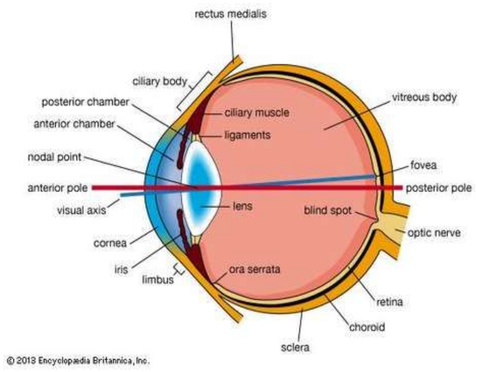
The **lipid** layer stabilizes the tear film by reducing stress, i.e surface tension, and by controlling water evaporation from the surface. The lipid layer is in contact with the eyelid skin acting as a barrier to the aqueous layer. Lipids also form a watertight seal when the lids are closed.

The **glycosomes** in tears contribute to maintaining the highly extended and rigid structure of mucins; structures responsible for protecting the eye on a molecular level. Mucins and glycans work together to clear debris and protect against pathogens with their antibacterial properties.

Metabolic wastes our as a by-product of cellular respiration; a process used to provide cells with energy in the form of ATP

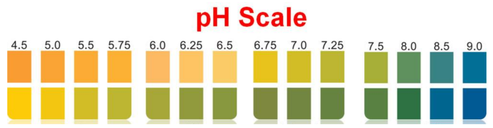
Tear Content	
Proteins	1543
Lipids	~600
Glycosomes	N/A
Metabolic wastes	N/A

Structure of the Human Eye



Future Studies

Proteins, lipids, sugars and metabolic wastes are the focus of this experiment. However, tear research involving tear fluid pH has yet to be explored. Analyzing the acidity and alkalinity of tears is an additional way of identifying abnormal traits as a result of an imbalance in homeostasis.



Methodology

Tears contain lipids, glycols, proteins and metabolic wastes. Referred to as the "-omics", the study of each of these factors was the basis of each reviewed article. Tears from a patient suffering from a disease are extracted using the Schirmer's strip method. A mass spectrometer is used to ionize the collected chemicals and sort the ions based on their mass-to-charge ratio. Proteins, the main tear component that presents with abnormalities when diseased, is processed through a spectroscopic analytical procedure used to measure the concentration of proteins in a solution. This procedure is commonly known as a protein assay. The gel electrophoresis machine separates macromolecules like DNA and RNA according to size and charge. This method continues the breakdown of proteins. The values of lipids, glycols, metabolic wastes and proteins collected from each diseased patient are compared to the tears of a healthy individual. A difference in composition suggests an imbalance of homeostasis. An imbalance in homeostasis indicates illness. It is because the body systems are interconnected that scientists are able to relate abnormalities in the eye, such as glucose levels, to otherwise unrelated systemic conditions, like diabetes. In so, tears are a viable systemic and ocular biomarker.

The average amount of tear fluid collected from various regions of a feline eye using the Schirmer's tear strip collection method.

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Contact information

Email- lamer7310@gmail.com
Phone Number- (845) -532-7310