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Use of tears as a source of biomarkers for disease

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The tear film is a relatively uncomplicated body fluid that has the potential to contain biomarkers for various diseases. Tears contain around 1500 proteins. Tears might be useful in the diagnosis and/or management of various diseases including dry-eye disease, keratoconus, diabetes and cancer. Whilst the proteome of tears is less complicated than that of plasma/serum, there are challenges when using tears. Several proteins, called regulated proteins, are released into the tear film with the aqueous component and their concentration does not change between the three tear types. Other proteins, such as sIgA, are constitutively produced and their concentration drops in reflex tears. Other proteins leak into the tear film from the ocular vasculature and so become more concentrated in closed-eye tears. Therefore, it may be important to control and time tear collection, and to analyze at least one prominent protein of each tear type so that you can control for different types of tear collection. We published the first 2D-gel proteomic analysis of tears in 1997. During this study we identified that tears contain lacryglobin, also known as mammaglobin B. Mammaglobin B has been reported to be a marker in plasma for metastatic breast cancer. Lacryglobin is phosphorylated in tears, and lacryglobin is expressed in primary and metastatic cancer cell lines and tissues but not in normal breast tissues. In tears, lacryglobin was present in patients with various cancers (83-100%) compared to tears from controls (60%). Using tears from dogs with various cancers including breast cancer, we found that a protein presumptively identified as lacryglobin was over-expressed in tears of dogs with cancer. We have recently shown using MRM analysis that the concentration of MUC16 (also calledCA125) in tears is significantly increased in patients with metastatic breast cancer compared to healthy age-matched controls. We have examined tears of contact lens wearers using MRM/MS or ELISA and shown that concentration of sPLA2 and lipocalin increased in contact lens discomfort, along with changes to the tear lipidome. Using combinations of ELISA, LC-MS/MS and antibody arrays has shown that tears of people with Keratoconus have reductions in lactoferrin, immunoglobulin receptor, fibrinogen, cystatin S, cystatin SN, but increased cathepsin B, MMP-1,-3,-7,-13, IL-4,-5,-6,-8 and TNF-α,-β. Using antibody arrays and western blotting, tears of diabetics have increased levels of cytokines IP-10 and MCP-1,but the ratio of anti-angiogenic/angiogenic cytokines IFN-γ/MCP-1 and IL-4/MCP-1 were significantly reduced. Tear concentrations of AGE modified proteins were significantly elevated in DR and DNR groups. These findings will be presented and their significance discussed.

Biography

Mark Willcox, a Professor at the School of Optometry and Vision Science, is to be awarded a Doctor of Science (DSc) from UNSW Australia based on his published work and contributions to the body of scientific and clinical literature. He will receive this award during graduation on the 9th of November 2015, as well as giving the occasional speech to the graduating students. Professor Willcox graduated from The University of West England with a BSc in 1983, and from The University of Manchester with a PhD in 1987. He is now one of the foremost experts in the research areas of Ocular Microbiology, Antimicrobial Contact Lenses, Inflammatory Mediators and Keratitis, and Tear Film and Ocular Surface Cells.

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