Ophthalmic biomarkers
Future potential
Ophthalmic biomarkers to become routine part of practice in the future. Priscilla Lynch reports

The role of diagnostic biomarkers in ophthalmology is continuing to evolve and they will soon become a routine part of clinical practice, with many more exciting potential developments on the way, said speakers during a dedicated session on 'Biomarkers: from inflammation to genetic disease,' held during the 38th Congress of the ESCRS.

Biomarker tests are increasingly being used in diagnosis of disease, but also have significant potential for disease monitoring, predicting disease progression and assessing therapy success, thus facilitating more personalised treatment, noted session co-chair José Benítez-delCastillo MD, PhD, Spain.

However, key challenges include knowing when and how exactly to use such tests, specificity, costs, and the need to identify many more useful biomarkers.

A number of expert speakers during this session emphasised the role of inflammation as the key pathway in many ocular surface disorders, noting the emergence of useful inflammatory biomarkers in recent years.

Rohit Shetty MD, India, spoke about his research on identifying biomarkers in a range of eye conditions, eg, tear fluid diagnostic tests for inflammatory markers in keratoconus such as LOX enzyme and collagen levels. While these tests are easy to use, point of care and translation kits are needed to fully realise their potential, he said.

The future of successful biomarker use is going to include combining imaging, demography, molecular markers and predictive modelling with "artificial

intelligence to ensure we have a very, very robust point of care kit", Dr Shetty concluded.

Elisabeth Messmer MD, Germany, speaking about detection of inflammation in dry eye, noting that while inflammation is a significant pathogenetic factor, it can often be subclinical, thus making diagnosis a challenge: "So we need to test for inflammatory markers in the tear film (eg, MMP-9) as direct evidence of inflammation, or hyperosmolarity of the tear film as indirect evidence of inflammation."

However, inflammation is also the key pathway in allergy, and differentiating dry eye disease from allergy remains a diagnostic challenge, she acknowledged.

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Marc Labetoulle MD

A number of 'bed-side' tear film tests are currently available, which are helpful to identify patients with significant ocular surface inflammation and autoimmune disease, which may facilitate clinicians to commence ani-inflammatory treatment, Dr Messmer said. None of the currently available tests are perfect, however, and more work needs to be done on improving accuracy and refining the use of such tests, she said.

Also speaking during this session was Marlies Gijs PhD, the Netherlands, who gave a fascinating overview of ongoing research on the potential for diagnosis of neurodegenerative diseases through the eye.

Given the close relationship between the brain and the eyes, ocular symptoms and changes in functional vision can be among the first early signs of many neurogenerative diseases like Alzheimer's and Parkinson's disease. Thus there is increasing interest in the potential of noninvasive eye-based scans and tear fluid analysis to help diagnose these serious diseases earlier, and allow a better chance at successful treatment, she explained. There have been some useful

early lab findings to date, but a lot of work remains to be done before such diagnostics will become commercially available.

Meanwhile, Marc Labetoulle MD, France, discussed optimising detection of ocular viral infections, in particular the creation of biomarkers for adenovirus and herpes simplex keratitis.

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PCR testing on tear samples has emerged as a more accurate diagnostic test in HSV keratitis, though it has some practical limitations, he noted. “Probably in the future we will combine the presence of antibodies in the tears with PCR in the tears as we will have two clues for the diagnosis. This combination has a very high positive predictive value; 90.9% in a study from Shoji (2016), and confirmed by another study by Qiu (2017).”

Dr Labetoulle predicted that within five-to-10 years, all ophthalmic practices could have their own mini diagnostic “labon-a-chip machines”. “These would be a combination of microfluidic technologies and in-home portable PCR machines, which could help us in the future with one tear to test many biomarkers, and to finally search for several infectious agents.”

The final speaker in this session, Jesús Merayo-Lloves MD, Spain, spoke about moving biomarkers from the laboratory to clinical practice, and the challenges therein. It is a long, demanding process to bring potential biomarkers to market, and promising study results and clinical validation does not always translate into successful creation of a commercial product. Finding interested companies willing to produce and market potential products is a particular challenge, he said, discussing his own research attempts to develop biologicals and biophysical biomarkers for keratoconus, dry eye disease and corneal innervation and sensitivity.