ISWAVLD 2023

International Symposium of the World Association of Veterinary Laboratory Diagnosticians

29 JUNE-1 JULY 2023 Congress Centre Lyon

Towards the veterinary diagnostics of the future

Main topic :

The invention and development of a new diagnostic test for tuberculosis. A one health success story.

WOOD P. [1]

[1] *Monash University, Fitzroy, Australia*

In 1984 CSIRO was asked by the Australian cattle industry to develop a better test for bovine tuberculosis (TB), to help in the final stages of the national bovine TB eradication program, as there were challenges skin testing herds in the remote north of Australia.

Invention.

Early work focused on defining specific antigens for use in conventional antibody assays to compliment the tuberculin test which relied on a T-cell response however, this did not provide the accuracy required. We therefore looked at measures of T-cell responses like IL-2 release before settling on Interferon (IFN)-gamma. This required the collection of a heparinized whole blood sample which was included overnight with tuberculin antigens (PPD). The supernatants were then assayed for IFN-gamma using a bioassay. Early trials in experimentally infected cattle looked promising, so a patent was lodged, and we moved to determining if an EIA for IFN-gamma would provide the necessary sensitivity.

Using a human model to prove the overall concept.

The reagents for developing an EIA for bovine IFN-gamma did not exist, so we tested the concept in children with suspected non-tuberculous mycobacterial lymphadenitis and demonstrated that it worked. With this proof of principle, we produced monoclonal antibodies to bovine IFN-gamma, developed a sensitive EIA and proceeded to major field trials in cattle. These trials demonstrated the improved sensitivity of the test over the tuberculin skin test and the BOVIGAM assay was launched by CSL as a commercial product.

Commercial success

While the Australian trials were convincing it took many years running trials in NZ, Ireland, USA, Spain, and Italy before gaining international acceptance and OIE approval.

In parallel with this work in cattle, CSL developed a human version of the assay based on the promising data from our earlier work in children. Eventually CSL exited the diagnostic field and the BOVIGAM technology was sold to Prionics while an Australian start-up Cellestis acquired the rights for use in humans. The human TB assay was approved by the FDA in 2000 and marketed as QuantiFERON-TB.

The format of the IFN-gamma which involved a 2-stage process, with incubation of whole blood with antigens followed by detection of IFN-gamma, allowed for a major improvement in TB testing in humans. Vaccination with BCG induced false positive results with the Mantoux test so the introduction of M. tuberculosis -specific antigens allowed for accurate diagnosis of human TB even in vaccinated individuals. QuantiFERON-TB Gold is now the standard of care for the diagnosis of latent TB in humans and marketed globally by Qiagen.

Conclusion.

Robert Koch first described the tuberculin reaction in 1891 and the skin test became the cornerstone of immuno-diagnosis for TB in both animals and humans. It has taken over a century for a new TB test to match and in many circumstances replace skin testing. The IFN-gamma assay has disrupted the field and remains the only invitro based disease diagnostic in regular use in veterinary or human health.