New hope for dialysis patients as 'immune-fingerprints' discovered

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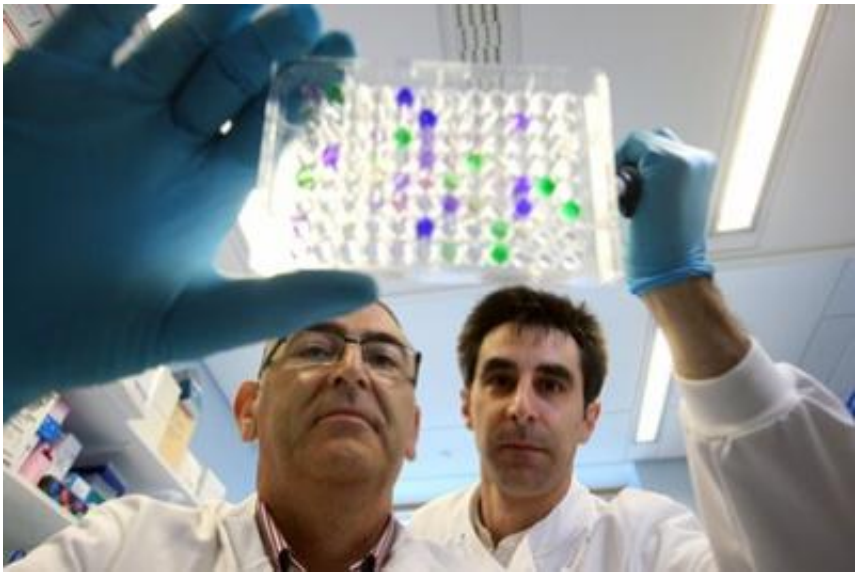

University scientists who are committed to developing improved treatments for patients with chronic kidney disease have discovered a novel way of significantly accelerating the detection of bacterial infection using the patient's own immune system.

Current diagnostic tests are often delayed by days that can lead to treatment failure and sometimes even death. Dialysis patients with chronic kidney disease rely on fast and accurate diagnosis of infection so doctors are able to administer the correct antibiotic treatment to ensure a

fair chance of recovery.

Professor Nicholas Topley and Dr Matthias Eberl from the School of Medicine have shown proof-of-concept that patients' unique immune responses to infection can be used to accurately detect which organism is causing infection within hours. Together with commercial partners, the Cardiff group is using these new insights, which they call 'immune-fingerprints', to inform the development of a point-of-care test.

"Infection is the biggest obstacle for any dialysis patient as it can seriously hamper their treatment and their chances of leading a normal life," said Professor Topley. "Through my own experience as a transplant patient, my research in dialysis patients over the past 25 years and in talking to patient groups, I observed that conventional tests just aren't quick enough and are often inconclusive, which can be a fatal shortcoming.

"We therefore decided that more needed to be done to ensure that patients had every chance of receiving a successful treatment and a healthy future, and from then on committed our research efforts to finding a new approach to identifying and targeting infection, looking to the body's own natural defences for inspiration."

Dr Matthias Eberl from Cardiff's Institute of Infection & Immunity explained "The immune system is capable of rapid, sensitive and specific detection of a broad spectrum of microbes, which has been optimised over millions of years of evolution. A patient's early immune response is therefore likely to provide a far better insight into the true nature and severity of microbial infections than current tests, which are based on the microbiological identification of the potential pathogen (a concept introduced by Robert Koch more than a century ago)."

To test this theory, scientists performed a detailed immunological and

microbiological analysis of samples obtained from peritoneal dialysis patients with acute infection/peritonitis (a condition in which the thin tissue that lines the inner wall of the abdomen becomes inflamed). Laboratory tests revealed that each bacterial infection leaves a distinct immune signature and robustly discriminates between different types of infection.

This is the first time that scientists have attempted – or succeeded - to distinguish soluble and cellular components in defining responses to specific germs in an infected human and to translate the idea of immune fingerprints into a potential diagnostic tool.

The data provide proof-of-concept that using immune fingerprints to inform the design of point-of-care tests will help target antibiotic prescriptions and improve patient management. With the immune fingerprint test, doctors would be able to differentiate rapidly between serious and benign infections and be able to prescribe suitable and accurate treatments.

Elaine Davies, Head of Research Operations for Kidney Research UK, said: "Kidney Research UK welcomes this publication about new evidence on how we might in future tackle this problem earlier thereby reducing the infection risk and complications for patients who are already coping with the life-threatening consequences of kidney failure."

A spokesperson for Welsh Kidney Patients Association said:

"As a renal patient myself I understand the anxiety patients feel waiting for tests results. To have two or more courses of antibiotics to cure an infection is very worrying to patients already taking a lot of different medicines, especially in this age of the superbug. A test that gives a quick, accurate diagnosis of infection, enabling the correct antibiotics to be given as soon as possible, will benefit renal patients immensely. The

fact that this test may help detect other infections including the 'superbugs' present in hospitals today is very exciting and would benefit anyone who has to be admitted to hospital. This research is of great importance and will have enormous benefits for all patients."

A spokesperson for Involving People, part of National Institute for Social Care and Health Research Clinical Research Centre (NISCHR CRC), said: "Professor Topley and his team ensured the research and its potential outputs have meaning and relevance for dialysis patients by consulting with them and involving them in the development of the research."

Dialysis treatment is a daily reality for all patients that can last for many years and incurs a huge annual cost for the NHS of £25,000 per patient. This cost rises significantly if the patient is hospitalised and increases a further £8000-£15,000 if the patient is suffering with an infection.

In primary care, antibiotic over-prescription is a major problem, relating to doctors' inability to diagnose the kind of infection the patient has. This is the main driver behind multi-drug resistance – a major global threat to human health, as identified by the World Health Organisation (WHO).

Bacterial infections remain a leading cause of disease and death worldwide and pose a critical challenge for public health in the 21st century, not least due to the unprecedented spread of antibiotic resistance.

The paper, entitled 'Pathogen-Specific Local Immune Fingerprints Diagnose Bacterial Infection in Peritoneal Dialysis Patients' is published today in the *Journal of the American Society of Nephrology*. An online version can be accessed here.