By screening many candidate host genes related to immunocompetence, wound healing, and apoptosis, as well as bacterial genes related to exotoxin and biofilm formation, the authors discovered the combination of genes for discriminating the infected wound from a colonised wound, which was not possible by counting the bacterial number from biopsy samples.

From the host genes, the expression of *Foxp3*, encoding regulatory T-cell (Treg)-specific forkhead box transcription factor Foxp3, was only expressed in the colonisation group. On the other hand, from the bacterial genes, the expression of *toxA*, encoding virulence factor exotoxin A, which is regulated by quorum sensing system, was only detected in the infection group[3] *[Fig 3]*. By exploring these specific marker genes, the authors shed light on the establishment of appropriate diagnosis of wound infection and they believe the clinical application of this concept could be put into practise in the near future.

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1. *European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel. Prevention and treatment of pressure ulcers: clinical practice guideline. 2009; National Pressure Ulcer Advisory Panel, Washington DC.*
2. *Asada M, Nakagami G, Minematsu T, et al. Novel models for bacterial colonisation and infection of full-thickness wounds in rats.* Wound Repair Regen. *2012; in press.*
3. *Asada M, Nakagami G, Minematsu T, et al (2012) Novel biomarkers for the detection of wound infection by wound fluid RT-PCR in rats.* Exp Dermatol *21(2):118-22.*

Expert Commentary

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Of the thousands of microorganisms in existence, there are only a limited number that colonise the human host. Some can cause disease (pathogens) and the remainder (non-pathogens) cannot because they do not have the mechanisms to do so. This is not always consistent and we now know that a microorganism can lose and acquire pathogenic (virulence) genes. We know these virulence genes can be switched on and off by environmental factors and more recently, we have come to accept that microorganisms do not grow as single species (as we see in the laboratory), but as a community or biofilm in the host. In addition, we know that there can be an interaction of a pathogen and a non-pathogen and the combined effect on the host can be different to the effect of the two individual microorganisms.

Current diagnostic microbiology is still based on the postulates introduced by Robert Koch (1843-1910) over a century ago and rely on the isolation of a pathogen from an infected site. Following isolation, a potential pathogen is identified and reported along with an antimicrobial susceptibility to assist in the treatment of the patient. These cultural methods have been the mainstay of traditional diagnostic microbiology and have helped our understanding and ability to control many bacterial diseases, such as typhoid, meningitis, tuberculosis and cholera. Development of non-culture techniques (molecular and immunological) and a fuller understanding of exactly how microorganisms cause disease has raised a large number of questions and has also led to numerous research projects in all aspects of infectious disease. The introduction of molecular techniques has allowed the study of the epidemiology and potential treatment of a wide range of microorganisms without ever having to culture them.

The techniques outlined in the two articles featured here have been applied successfully to difficulties with accurate diagnosis of wound infection and critical colonisation. The data captured in the first article by Wolcott and colleagues show that there is a greater diversity of bacterial species present in chronic wounds within a biofilm than previously reported using traditional methods. The relevance of these findings suggest that it is not always the presence of an individual microorganism (or pathogen) that causes problems with wound healing, but the interactive effect of the polymicrobial community contained in a biofilm. Whether the comprehensive identification and diversity of all the different species of microorganism in a wound will make a significant impact on diagnosis and treatment has yet to be determined.

The quantitative detection of extracellular biological molecules (biomarkers) released into the wound by the microorganism and/or in combination with host molecules, highlighted by Nakagami and colleagues, shows great promise as an alternative diagnostic culture tool. If detection of certain biomarkers in a wound is shown to differentiate between microbial colonisation and infection then this would help the practitioner make urgent treatment choices when necessary. Molecular techniques are slowly moving into the hospital pathology laboratory, but are still too costly and time consuming for diagnosis of many infections, and traditional methods continue to be used. Where the causative microorganism is a communicable threat or a life-threatening disease (eg tuberculosis, meningitis) molecular techniques have been introduced , but often at large university hospitals or the Health Protection Agency Reference Centre in the UK, rather than in routine hospital laboratories. Their future introduction into hospital laboratories is dependent upon cost, usability and applicability to treatment.

The application of these non-cultural techniques to chronic wounds and wound care in the research setting has helped with the understanding of why some wounds do not heal, especially in a patient where they should. The understanding that a biofilm exists on many surfaces in chronic wounds has shown that accurate sampling can be difficult and full identification of microorganisms within a wound by conventional techniques is almost impossible. The reporting of potential pathogens with antibiotic sensitivities will continue to be the normal practice of routine diagnostic laboratories until other techniques have been proven to have more patient benefit and are cost effective.

Further development of non-cultural methods that detect biological markers can certainly help the clinician move towards more understanding and accurate diagnosis of wound infection or wound colonisation, especially if these assays can be used near the patient at the point of care. This would give the clinician more confidence to administer antibiotics and/or effect a change of treatment in the form of debridement, topical antisepsis or perhaps radical surgery.