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Medical Education

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**The use of molecular "genomic" techniques and how they may help better understand wound infections**

Dr. Matthew Malone

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**ZERO ZERO**  
ZERO ZERO  
PRESSURE VENOUS  
ULCER RECURRENCE  
INCIDENCE ZERO  
WASTE OF  
HEALTHCARE  
RESOURCES  
ZERO  
DELAY  
IN WOUND  
HEALING  
ZERO  
DIABETIC  
AMPUTATIONS  
ZERO  
DELAY  
SURGICAL SITE  
COMPLICATIONS  
ZERO  
PRESSURE IN WOUND  
ULCER HEALING  
INCIDENCE  
ZERO ZERO

**CLOSER TO ZERO®**  
We're dedicated to helping reduce the human and economic consequence of wounds, helping you get CLOSER TO ZERO

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**Resources available for download**

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# The use of molecular "genomic" techniques and how they may help better understand wound infections.

Dr Matthew Malone PhD, FFPM RCPS (Glasg)  
Director of Research, South Western Sydney Limb Preservation and Wound Research  
Conjoint Senior Lecturer, School of Medicine, Western Sydney University



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# History of microbiology and bacterial culture

As proposed by Robert Koch, a pure culture is the foundation of all research in infectious diseases. In 1877, Koch began his studies of wound infections in animals. With his new techniques for identifying bacteria, he distinguished various disease states – septicemia, gangrene, abscess – at the microscopic level.



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# The current methods for how we view wound infections from clinical perspective.



1. A patient attends with a wound and clinical features of infection



Infection in acute wounds (including surgical/traumatic wounds and burns) in otherwise healthy individuals is usually obvious to an experienced clinician. Individuals present with classic (over) signs and symptoms of a clinical wound infection.



In immunocompromised individuals or in cases of chronic biofilm infection – classic signs of infection may not present themselves and early detection-identification may require the clinician to be more aware of subtle or covert signs of infection.

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### Molecular approaches

- 16S rDNA sequencing
- Whole genome sequencing (Shotgun sequencing)
- RNA Transcriptome
- Nanopore sequencing

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16S sequence work flow

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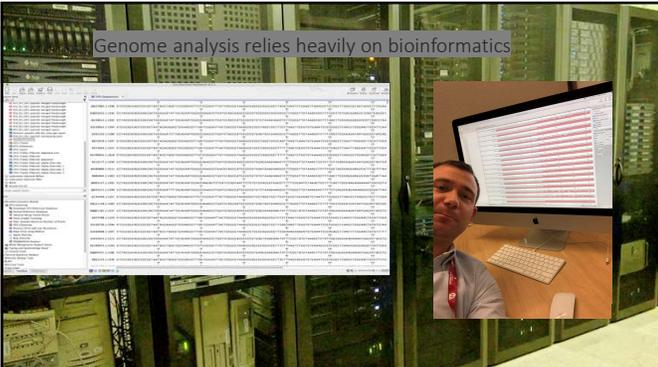
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Genome analysis relies heavily on bioinformatics



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UNDERSTANDING WHAT THIS ALL MEANS?

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The future

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How have molecular studies been employed for wound infection ?

Year	Author	Title
2019	Malone et al	Analysis of proximal bone margins in diabetic foot osteomyelitis by conventional culture, DNA sequencing and microscopy.
2018	Ishani et al	Understanding the microbiome of diabetic foot osteomyelitis: Insights from molecular and microscopic approaches
2017	Malone et al	Next Generation DNA Sequencing of Tissues from Infected Diabetic Foot Ulcers
2017	Shurko et al	Identification of Pathogens Directly From Diabetic Foot Infections by Shotgun Metagenomic Sequencing
2015	van Asten	The microbiome of diabetic foot osteomyelitis
2018	Crisologo	Are We Misdiagnosing Diabetic Foot Osteomyelitis?

Number of studies employing molecular sequencing

Year	Diabetic Foot Infection	Diabetic Wound Microbiome
2008-2012	2	0
2013-2016	3	1
2017-2019	9	2

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So why do some wounds develop infection and others don't? Why do some wounds have greater infection severity?

**Microbial**

- Type of bacteria – species or strain?
- Virulence and pathogenicity ?
- Colonizers vs known pathogens?
- Antibiotic resistance?

**The HOST**

- Primary Immunodeficiencies?
- Acquired Immunodeficiencies?
- Diabetes
- Arterial Disease
- Nutrition

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Michael Radzieta<sup>1,3</sup>, Fatemeh Sadeghpour-Heravi<sup>4</sup>, Honghua Hu<sup>4</sup>, Karen Vickery<sup>4</sup>, Timothy J Peters<sup>5</sup>, Thomas Jeffries<sup>6</sup>, Hugh Dickson<sup>1</sup>, Saskia Schwarzer<sup>1,3</sup>, Slade O. Jensen<sup>1,3</sup>, Matthew Malone<sup>1,3</sup>

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2. Infectious Diseases and Microbiology, School of Medicine, Western Sydney University, Sydney, Australia.
3. Antibiotic Resistance and Mobile Elements Group, Ingham Institute of Applied Medical Research, Sydney, Australia.
4. Surgical Infection Research Group, Faculty of Medicine and Health Sciences, Macquarie University, Sydney, Australia
5. Immunogenomics Laboratory, Immunology Division, Garvan Institute of Medical Research, Darlinghurst, NSW, Australia
6. School of Science and Health, Western Sydney University, Sydney, Australia

**Key Words:** Diabetic Foot Infection, Diabetic Foot Ulcer, Metagenomic Shotgun Sequencing.

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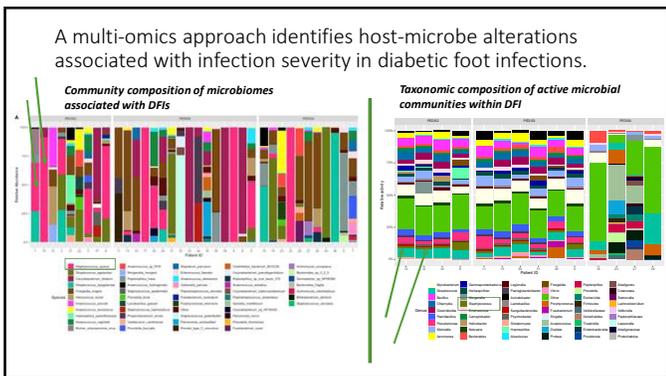
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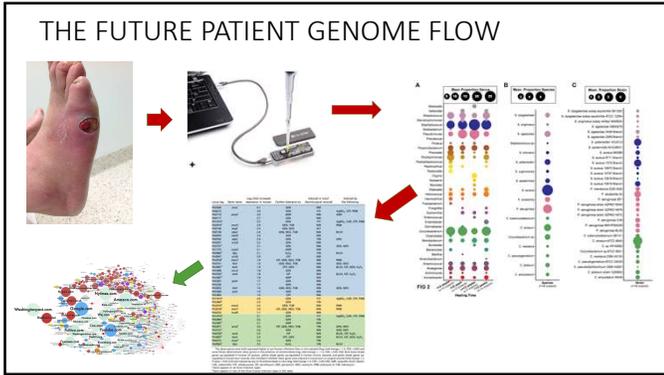
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**a Precision medicine system**

**b Precision medicine goals**

Nature Reviews | Cardiology

Review Article | Open Access | Published: 21 November 2019

#### Artificial intelligence for precision medicine in neurodevelopmental disorders

Mohammed Uddin<sup>1,2</sup>, Yujang Wang<sup>3</sup> & Marc Woodbury-Smith<sup>1,2</sup>

*npj Digital Medicine* 2, Article number: 112 (2019) | Cite this article  
6091 Accesses | 1 Citations | 26 Altmetrics | Metrics

**Abstract**

The ambition of precision medicine is to design and optimize the pathway for diagnosis, therapeutic intervention, and prognosis by using large multidimensional biological datasets that capture individual variability in genes, function and environment. This offers clinicians the opportunity to more carefully tailor early interventions—whether treatment or preventative in nature—to each individual patient. Taking advantage of high performance computer capabilities, artificial intelligence (AI) algorithms can now achieve reasonable success in predicting risk in certain cancers and cardiovascular disease from available multidimensional clinical and biological data. In contrast, less

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### Future Pharmacological Targets?

Enriched Microbial BGIs			
FolDase PsaA	PsaA is a foldase for secreted proteins and pathogenicity factors on the cell surface, namely of Gram-positive bacteria.	14.8	0.00
Two-component system sensor histidine kinase K6D0	Bacterial capability of responding to external stimuli is conferred by a specialized signal transduction mechanism, which relies on the two-component systems. Environmental signal used for control of virulence and resistance factors.	13.0	0.02

**Antimicrobial Agents and Chemotherapy**

Antimicrob. Agents Chemother. 2019 Mar; 63(3): 1486–1495.  
Published online 2019 Feb 28 | DOI: 10.1128/AAC.02332-19

**The *Staphylococcus aureus* Chaperone PsaA Is a New Auxiliary Factor of Oxacillin Resistance Affecting Penicillin-Binding Protein 2A**

Arora, Jasmeet<sup>1</sup>\*; Caputo, Massimo<sup>2</sup>; Riccardi, Anna<sup>3</sup>; Ferraro, Maria<sup>4</sup>; Ferraro, G. Paolo<sup>5</sup>; Abramo, E. Elisabetta<sup>6</sup>; Wilson, L. Kelly<sup>7</sup>; and Johnson, Richard<sup>8</sup>\*

\* Author information · Article notes · Copyright and License information (Disclaimer)

**Journal of Bacteriology**

Volume 191, Number 10, October 2019

**A Two-Component Signal Transduction System Essential for Growth of *Bacillus subtilis*: Implications for Anti-Infective Therapy**

DOI: 10.1128/JB.01100-19

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# Thank you

“Before I came to this lecture, I was confused.  
After hearing it I am still confused, but on a higher level”



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## Resources available for download



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- You will receive your participation certificate upon survey completion via email.



Stay tuned for S+N Closer to Zero Podcast !

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If you have any questions contact us at [ProfEd.ANZ@smith-nephew.com](mailto:ProfEd.ANZ@smith-nephew.com)



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