Blood, Bugs and Medical Devices: In Search of Next-Generation Biomaterials

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Introduction

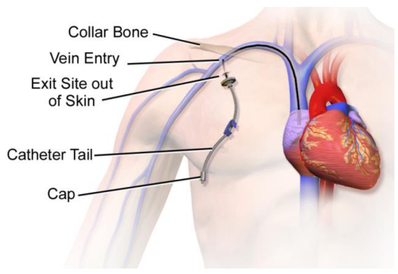
The Problem

- **Venous catheters** are commonly used blood-contacting medical devices in an **intensive care setting** to **administer medication**, **blood sampling**, **feeding** and **dialysis**
- **Bacterial attachment** and **biofilm formation** on these **medical devices** is a **major healthcare problem**
  - **250,000 infections**, **62,000 deaths** costing **$14 billion (USD) annually** in US alone (World Health Organisation[1])
  - A biofilm[2] is a **complex aggregation** of **bacteria on a surface** forming a **slimy coating** in which bacteria are **protected from** the **surrounding environment** and estimated to be up to **1000 times more resistant** to **antibiotics**

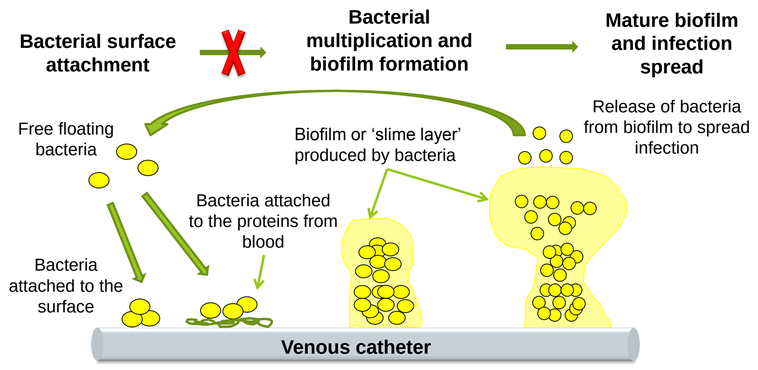
The Solution

- To find **a bacterial resistant material** that **prevents attachment of bacteria at an early stage** (shown by **red cross**) **without killing the bacteria** (**killing** the bacteria = increased chance of **resistance**)
  - Would **reduce antibiotic use** associated with **blood-contacting** medical devices
- The **detailed mechanism** of how **bacteria stick to surfaces** is **poorly understood,** therefore the method we conceived **screens hundreds of novel materials simultaneously for bacterial resistant** and **blood compatibility** properties

Venous Catheter in a Patient



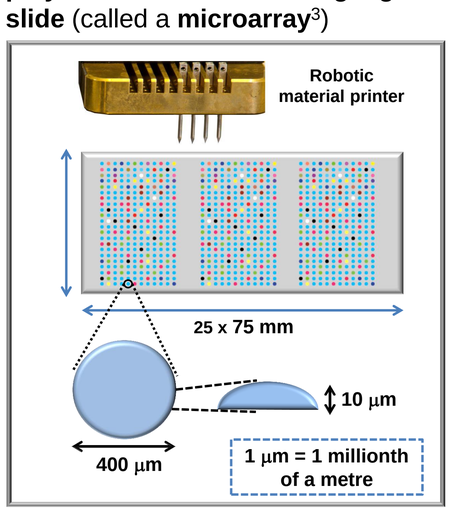
The Process of Bacterial Attachment and Biofilm Formation



Method

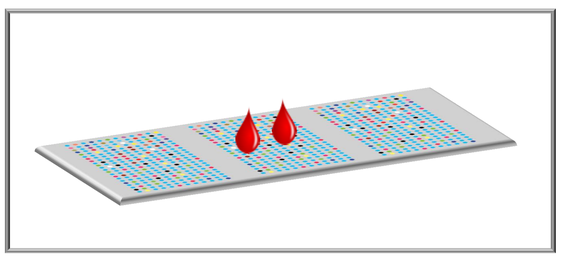
STEP 1

A robotic printer used to **print hundreds of micro spots** of **novel polymer materials** on a **single glass slide** (called a **microarray**[3])



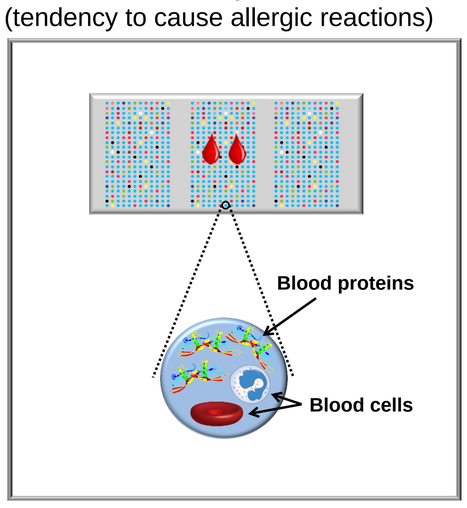
STEP 2

Covered **microarray** with **human blood** for **2 hours** at **37 ºC** to **simulate a blood contacting medical device**



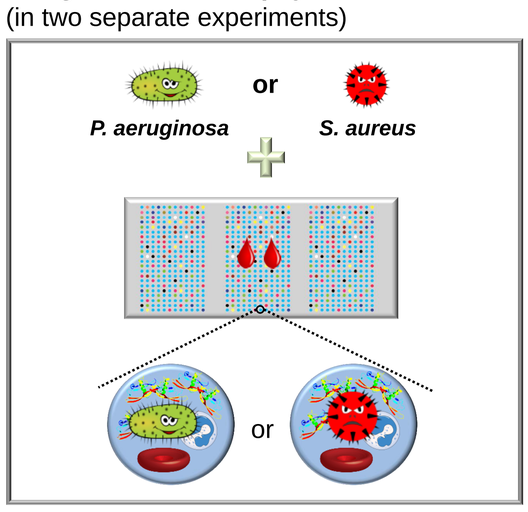
STEP 3

Analysed each material for **blood compatibility** - **toxicity, blood clotting** and **immune system activation** (tendency to cause allergic reactions)



STEP 4

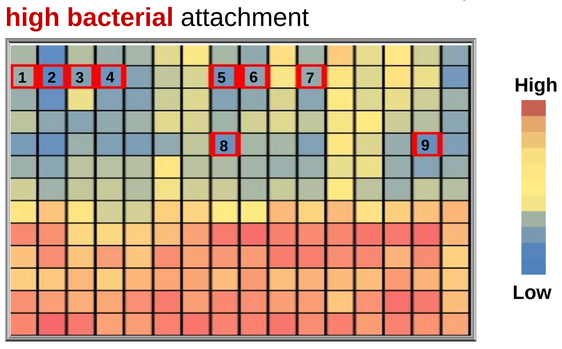
Exposed microarray slide to **two common biofilm forming bacteria:** ***Pseudomonas aeruginosa*** and ***Staphylococcus aureus*** (in two separate experiments)



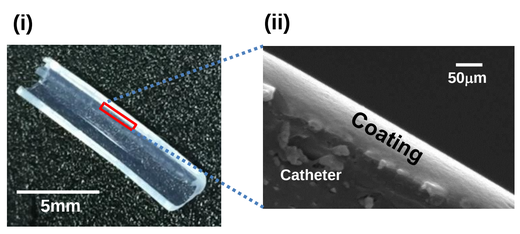
Results

Bacterial Attachment on Microarray Spots

A **colour coded** representation of bacterial attachment on each material: **blue** represents **low bacterial** attachment and **red** represents **high bacterial** attachment

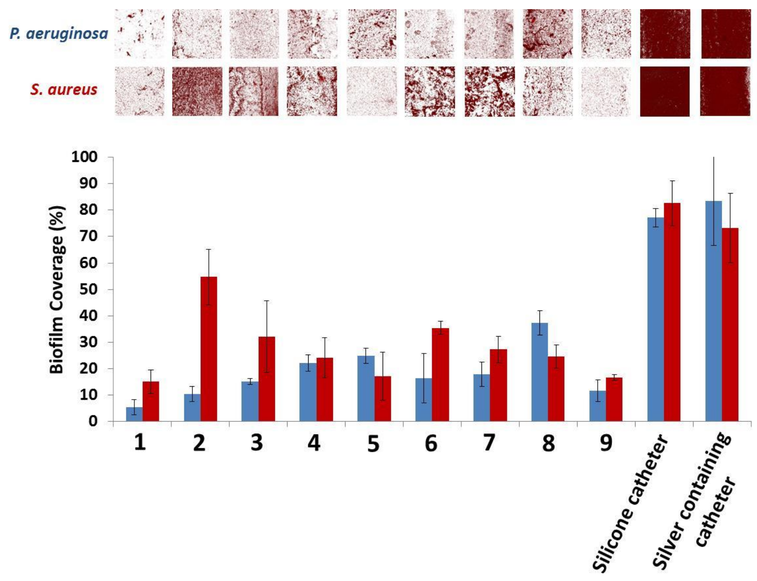


Top 9 materials (red rectangles) were then synthesised in bulk quantities and used to coat commercially available catheter sections (i), confirmed by a scanning electron microscopy (ii)



Bacterial Attachment on Top 9 Materials

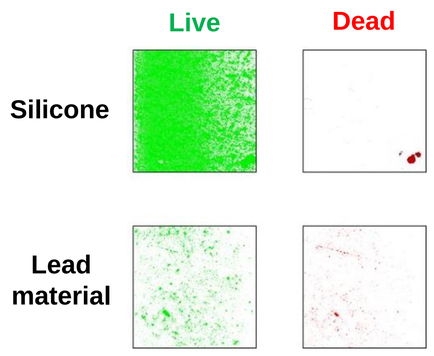
Bacterial resistant blood compatible materials selected from high-throughput microarray screening (red rectangles), were **compared** to **current silicone** and **silver containing venous catheter used clinically**. The confocal microscope images show **surface bacterial coverage** on each material (**bacteria** labelled **red**, surface appears white)



Mechanism of Action

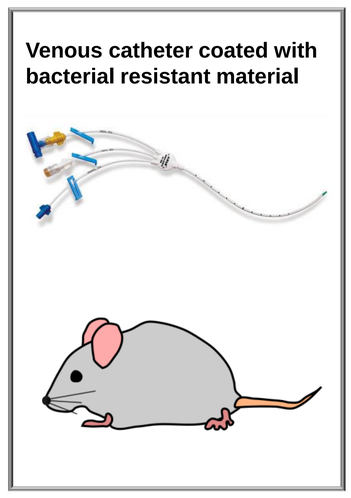
Bacteria dilemma - To stick or **Not to stick?**

- As a bacterial cell approaches a surface, it uses its **numerous sensors** to **sense the surface** and decides **whether to stick** or **not to stick** the surface
- To confirm **anti-attachment** (**rather than killing**) mechanism, bacteria attached on our lead (best) material and silicone catheter were stained with two dyes - the **green** dye represents **live** bacteria and **red** dye shows **dead** bacteria



Next Step

Lead bacterial resistant blood compatible material will be **tested** in a **mouse infection model** for **efficacy**



Conclusions

- ✓ **We have developed and validated a high-throughput method to screen a large library of novel bacterial resistant and blood compatible materials**
- ✓ **Bacterial resistant materials identified from high-throughput screening could not have been identified from the current understanding of the mechanism of attachment of bacteria on the surfaces**
- ✓ **All top 9 materials identified from our screening showed less bacterial attachment on the surface when compared to current clinically used venous catheter devices**

Future Work

- ❖ To test the efficacy of lead material in mice and licence lead material to medical device manufacturers

References

1. World Health Organisation: http://www.who.int/patientsafety/implementation/bsi/en/ (date accessed 05/02/2016)
2. Donlan, R.M., Biofilms and device-associated infections. *Emerging Infectious Diseases,* **2001**, *7*, (2), 277-281.
3. Hook A.L. *et. al.,* Combinatorial discovery of polymers resistant to bacterial attachment, *Nature Biotechnology* **30** (2012), no. 9, 868-875.

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