INSTITUT CARNOT MICA

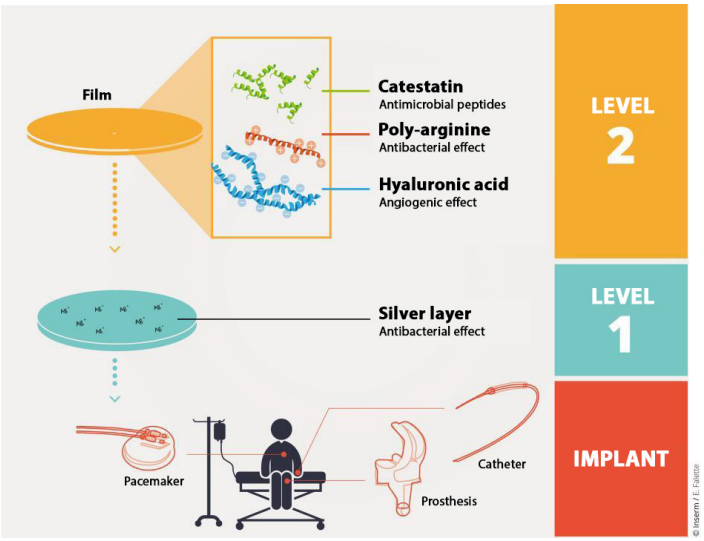
Materials Institute Carnot Alsace

A key player in Innovative Materials

The first antimicrobial film for the implants of tomorrow!

Implantable medical devices (orthopaedic prostheses, pacemakers, heart valves, dental implants, etc.) are an ideal interface for micro-organisms that can easily colonise their surface. The bacterial infection then causes an acute inflammatory reaction and leads to the rejection of the implant. These infections are mainly due to fungi and bacteria, such as *Staphylococcus aureus* hosted by the body. The issue related to the implantation of medical devices in the body is to prevent the occurrence of these infections and immune reactions that jeopardize the success of the implantation. With the emergence of multi-resistant bacteria, the antibiotics currently used have an increasingly reduced action, which justifies the development of new strategies.

A bio-film invisible to the naked eye...



It is in this context that researchers from Unit 1121 "Biomaterials and Bioengineering" (Inserm/University of Strasbourg), members of the Institut Carnot MICA, in collaboration with two other members of MICA, a German laboratory and the company Protip Medical, have developed a revolutionary bio-film with antimicrobial and anti-inflammatory properties. Scientists used the combination of two substances: poly(arginine) (PAR) and hyaluronic acid (HA) in order to produce a film invisible to the naked eye (between 400 and 600 nm thick) consisting of several layers. Arginine, which is metabolised by immune cells to fight pathogens, is used to communicate with the immune system in order to obtain the anti-inflammatory effect desired. Hyaluronic acid, a natural component of the body, was chosen for its bio-compatibility and its inhibitory effect on bacterial growth.

...with embedded antimicrobial peptides,

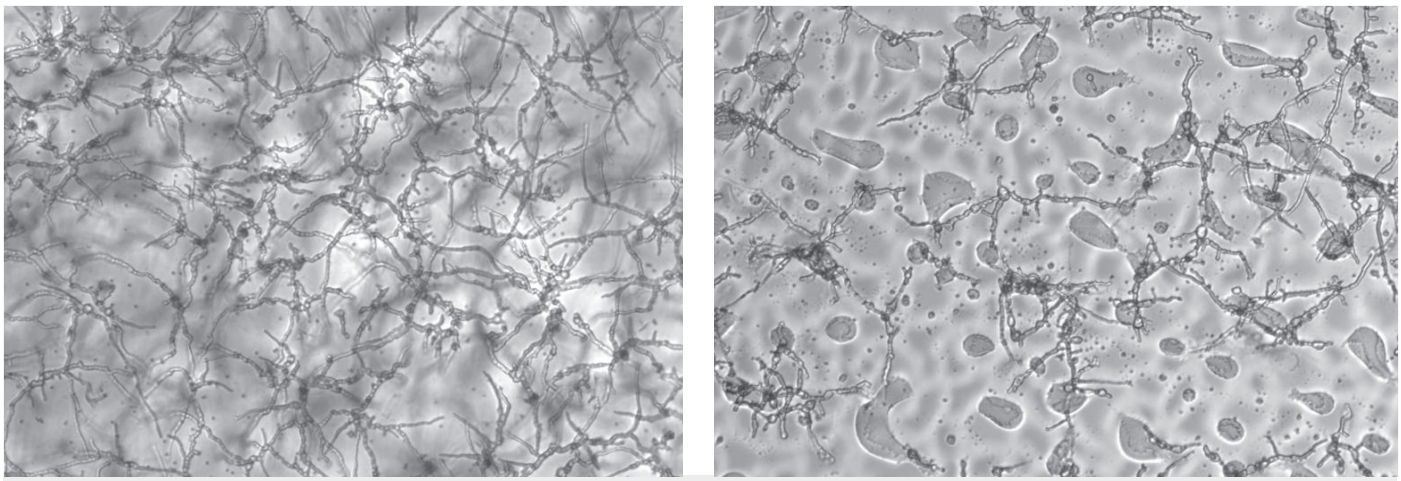
This completely new composition of the bio-film is complemented by the addition of natural antimicrobial peptides, in particular catestatin which prevents possible infections around the implant, thereby providing an alternative to the antibiotics currently used. These peptides are able to kill bacteria by creating holes in their cell walls while preventing a counter-attack from them. Naturally secreted by the body, their final advantage is that they are not toxic.

...deposited on a thin layer of silver,

the poly(arginine) combined with the hyaluronic acid has antimicrobial activity against Staphylococcus aureus for more than 24 hours. " *To extend this activity, we deposited a silver-based precursor on the titanium implant before affixing the film. Silver is an anti-infectious substance currently used for catheters and dressings. This strategy enabled us to obtain a long-term antimicrobial activity*" explains Philippe Lavalle, Inserm research director.

... Effective in limiting inflammation, preventing and controlling infections.

The results of many tests performed on this new film reveal that it reduces inflammation and prevents the most common bacterial and fungal infections. In contact with human blood, the presence of the film on the implant suppresses the activation of inflammatory markers produced normally by cells of the immune system in response to the implantation. " *This film is also capable of inhibiting the growth and proliferation of a yeast strain (Candida albicans) or fungus (Aspegillus fumigatus) causing frequent infections associated with the implant.*" explained Philippe Lavalle.



Behaviour of the fungus *Aspergillus fumigatus* on an untreated surface (on the left) and on a surface treated with the antimicrobial film (on the right). The interconnected filaments observed on the left are typical of these fungi in full growth while the right-hand image shows a complete destruction of this network due to the presence of the film. Within a few years, this new film could be used clinically to control the complex micro-environment around implants and medical devices and protect the body from infection.

This work, in which MICA's three partners were involved, received financial support from the Institut Carnot MICA within the scope of the "Microsurf" Resourcing Project, and the European Commission within the scope of the European project "Immodgel". They have also been published in the journal Advanced Healthcare Materials*.

Harnessing the Multifunctionality in Nature: A Bioactive Agent Release System with Self-Antimicrobial and Immunomodulatory Properties

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