The central role of human hemostatic system in formation of Staphylococcus aureus biofilms

Lay audience summary

Introduction & goal of the project

Staphylococcus aureus ("golden staph", "MRSA") is a bacteria that is one of the leading causes of potentially lethal infections worldwide. It is proficient in causing chronic infections, which are often associated with bacteria forming "biofilms" – a slimy layer, with elaborate three-dimensional structure on a microscopic scale, attached to medical implants and human tissues, in which bacteria hide from attacks of antibiotics and immune cells. Understanding of how these biofilms works is the necessary step for designing of novel therapies.

Large part of research efforts on *S. aureus* biofilms concentrated on understanding how the bacteria themselves can construct biofilms. However, it is increasingly clear that *S. aureus* uses human components as building blocks for its biofilms as well. A unique feature of *S. aureus* is its ability to hijack human hemostatic system (that is, the coagulation, system responsible for formation of blood clots composed mainly of large protein polymer fibrin, and the fibrinolysis, responsible for dissolving of these clots). It became recently apparent, that *S. aureus* uses these human systems do deposit fibrin which acts as a scaffold for constructing the biofilm. However, the exact consequences of inclusion of host protein as part of *S. aureus* biofilm remain unstudied.

Planned research activity

This project will study how presence of fibrin scaffold changes properties of S. aureus biofilm. It will focus on changes to biofilm shape, strength, exact composition, and even on biofilm's ability to resist attacks of human cells or to interact with platelets (another type of cells involved in blood coagulation), all caused by presence of fibrin inside the biofilm. To do this, the project will investigate biofilms grown in laboratory in presence of human plasma and/or fibrin, with or without addition of human cells, and it will rely on three-dimensional microscopy, specific immunological staining of different biofilm components, and on biophysical analysis of biofilm viscoelastic properties. Similar analyses will be performed on real biofilms collected from *S. aureus* infections *in vivo* – for example on samples from humans with biofilm-related infections, and on *in vivo* models.

Expected results

This project will generate new knowledge that will help us better understand how staphylococci form biofilms inside human bodies, and will move us a step closer towards new therapies. These novel insights will be potentially applicable also to other bacterial species, as many microorganisms can interact, to a certain degree, with human plasma and fibrin.