MICROBIOLOGIE, INFECTIOLOGIE ET IMMUNOLOGIE

Université de Montréal

CONFÉRENCE

« Conférence prononcée en anglais – Lecture given in English »

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Mechanomicrobiology: how microbes respond to forces versity

During colonization of biomaterials and host tissues, surface-attached bacteria must cope with physical stresses, such as fluid flow and cell-surface interactions. It has become clear that mechanics has a profound influence on bacterial behavior, such as cell adhesion, however we still know little about how exactly cell surface molecules sense and respond to mechanical forces. To withstand mechanical stress, bacterial pathogens use a family of surface proteins (called adhesins) that promote cell adhesion to host extracellular proteins such as fibronectin and fibrinogen, as well as cell–cell adhesion and biofilm formation. Using single-molecule atomic force microscopy, we recently demonstrated that adhesins from the nosocomial pathogens *Staphylococcus epidermidis* and *S. aureus* bind their host proteins with ultrastrong forces, ~2 nN, similar to those of covalent bonds. These adhesin interactions thus represent the strongest receptor-ligand interaction ever measured so far, being much larger than the forces reported for other cell adhesion molecules, and for the mechanically strong biotin-streptavidin and cohesin-dockerin complexes. We also discovered intriguing catch bond phenomena where some staphylococcal adhesins behave as force-sensitive molecular switches that activate bacterial adhesion under physical stress, meaning bacterial adhesion is weak at low tensile force, but dramatically enhanced by mechanical tension. These findings favor a model whereby force induces conformational changes in the adhesin, from a weakly binding state to a strongly binding state. These studies have identified sophisticated mechano-sensitive binding mechanisms in adhesins, which represent promising new targets for anti-adhesion therapy. Overall, our experiments highlight the importance of mechanobiology in regulating pathogen adhesion.

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