Key Session 1
[O3] INTERACTIONS BETWEEN STAPHYLOCOCCI, OSTEOBLASTS AND OSTEOCLASTS – WHAT DO WE KNOW IN 2016?

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Bone is a mineralized hard tissue that is constantly remodeled under the coordinated action of the bone matrix-forming osteoblasts and the bone matrix-resorbing osteoclasts. This balance is impaired when infection occurred, mostly caused by Staphylococcus aureus that is able to induce chronic forms characterized by inflammation and progressive bone destruction. We investigated the cellular mechanisms of staphylococcal-induced bone destruction and the switching from acute BJI to chronic BJI using ex-vivo infection models of osteoblasts and osteoclasts.

Our most recent results suggest that two complementary mechanisms are involved in bone loss during bone infections: i) staphylococcal invasion of osteoclast precursors induce their diversion from osteoclastogenesis and their differentiation into activated macrophages that actively secrete pro-inflammatory cytokines, which are able to enhance the bone resorption capacity of uninfected, mature osteoclasts and promote the migration as well as osteoclastogenesis of the uninfected precursors to the site of infection; and ii) infection of mature osteoclasts by S. aureus directly enhance their ability to resorb bone by promoting cellular spreading and fusion. In addition, using recombinant staphylococcal toxins, we demonstrated the ability of Panton Valentine leukocidin, a pore-forming toxin, to kill directly mature human osteoclasts while superantigenic toxins, such as TSST-1, are able to enhance bone resorption capacity of these cells.

Moreover, comparing isolates recovered from initial and recurrent BJI episode from the same patient with persisting or relapse of BJI, we showed that recurrent isolates tend to be less cytotoxic, to induce a lower inflammatory response, to persist longer in intracellular compartment of osteobasts and to induce a lower mortality in mice infection model than initial isolates, despite no significant change at genomic level. These findings suggests that S.aureus BJI chronicization is associated with an in vivo bacterial phenotypical adaptation during the course of infection, leading to higher intraosteoblastic persistence, lower virulence as well as host immune escape.
Put together these data demonstrate that some physiopathological traits and clinical signs of BJIs are likely related to the intracellular life, the toxin profiles and the adaptative processes of clinical S. aureus isolates, which may open perspectives for innovative targeted therapeutics and bacteriological predictive tools of clinical outcomes in the setting of BJIs.