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P1258 Staphylococcus aureus-osteoblasts interaction: in vitro activity of novel anti-staphylococcal molecules

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Background: *Staphylococcus aureus* (SA) bone and joint infections (BJI) infections are a major public health problem as despite the combination of surgical management and prolonged antibiotic treatment, the therapeutic failure rate remains high. BJI have a huge cost for the society, both at the human and economical levels. The interaction between SA and osteoblasts (OB, responsible for bone formation) is a decisive step in this type of infection. SA can be internalized by and persist In OBs, hiding from antibiotic treatments. In this context, two new molecules have been developed to specifically target intracellular SA. The objective of this preliminary study was to evaluate in vitro the effect of these 2 molecules in an SA/OB interaction model.

Materials/methods: Our previously published infection model has been implemented for the interaction between SA HG001 and human OB MG-63. The 2 molecules to be tested were added after 3h of infection and elimination of all extracellular bacteria. At 24 and 48h post-infection, the number of intracellular SA was assessed by plating counts and lactate deshydrogenase was quantified in the supernatant to monitor cytotoxicity. Both molecules were tested at 3 concentrations using rifampin (known to have a good intracellular killing effect) as control.

Results: Molecules 1 and 2 at 3.2mg/mL were able to significantly decrease by 50% the number of intracellular SA after 24h of treatment compared to untreated infected OB ($p<0.05$ and $p<0.001$ respectively). These effects are similar to what is observed for rifampin, molecule 2 being even more effective ($p<0.001$). This molecule is also active on bacteria already persisting for 24h, i.e. when the treatment is initiated 24h post-infection. Both molecules did not show any cytotoxic effect on OB.

Conclusions: The preliminary results are very promising for these 2 new anti-staphylococcal molecules in the eradication of intracellular SA, with an even higher efficacy than rifampin for molecule 2. These molecules, in combination with standard antibiotics, could be a valuable innovative therapeutic option for the treatment of BJI.