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2-hour Oral Session

First identification of genetic element that carries Toll-like receptor homologue and resistance genes in *Staphyloccocus aureus*

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Bacterial strategies for innate immune evasion involve manipulation of the Toll-like receptors by signaling Toll/interleukin-1 receptor (TIR) homologues such as TirS for *Staphylococcus aureus*.

Using a tirS-specific PCR, we studied its prevalence in 230 well-characterized clinical *S. aureus* strains from various genetic backgrounds. We show that tirS gene is present in 5% of tested stains, as well in methicillin resistant *S. aureus* (MRSA) than in methicillin sensitive *S. aureus* (MSSA) strains. Interestingly, we report the presence of tirS in 100% of the tested strains of the ST5/TSST-1 Géraldine MRSA clone. We identified tirS gene on the mobile genetic element SCCmec of this clone. Using an *in vitro* NF-κB-dependent luciferase reporter system, we demonstrated that TirS inhibited TLR2, TLR 4 and TLR 5 and IL-1R signaling suggesting a pleotropic effect of TirS on adaptor protein involved in cell signaling pathways. Moreover, the impact of TirS expression on *S. aureus* virulence was investigated in mice skin infection model using isogenic tirS +/- Géraldine strains. TirS expression was associated with significant reduction of the skin lesion but did not affect the number of bacteria recovered from the skin and bacterial dissemination into the mice, suggesting that TirS impact the inflammatory response associated with the severity of lesion.

This is the first description of bacterial TIR homolog protein carried by genetic element conferring resistance to antibiotics, linking modulation of virulence to antimicrobial resistance.