

Chondrocyte Invasion is a Mechanism for Persistent Staphylococcus Aureus Infection

Jerry Chang, David Kerr, Thorsten M Seyler

INTRODUCTION: *Staphylococcus aureus* is a leading cause of bone and joint infections. Even with extensive antibiotic treatment, there is a high rate of recurrent or chronic infection. *S. aureus* has been shown to invade osteoblasts and fibroblasts, but little is known about its ability to invade and persist within chondrocytes.

METHODS: Human chondrocyte (C20A4), human osteoblast (MG63), and mouse fibroblast (NIH-3T3) cell lines were cultured *in vitro* and infected with *S. aureus*. Cells were then washed and treated with high dose antibiotic containing media with adequate extracellular killing, then replaced with maintenance dose antibiotic media. Each day, antibiotic media and washed cell lysate from each cell line were collected and individually plated on tryptic soy agar (TSA) plates and assessed for colony forming units (CFU). Maintenance antibiotic media was refreshed daily.

RESULTS: Initial high dose antibiotic media yielded 0 CFU. C20A4 lysates yielded 1.4×10^3 CFU/mL up to 6 days post infection. MG63 lysates grew 433 CFU/mL up to 6 days post infection. 3T3 grew 322 CFU/mL up to 3 days post infection. Maintenance antibiotic cell media yielded no CFU each day for all cell lines.

DISCUSSION AND CONCLUSION:

S. aureus readily invaded all tested cell lines as demonstrated by colony growth from cell lysates. No colonies grew from initial high dose or maintenance dose antibiotic media suggesting adequate killing of extracellular *S. aureus*. Even after one week of antibiotic treatment, *S. aureus* continued to grow from lysed C20A4 cells. Our findings showed chondrocytes harbored a higher load of intracellular infection and for a longer duration compared to positive control osteoblast and fibroblast cell lines. This suggests chondrocyte invasion could potentially contribute to the recurrence of bone and joint infections even after thorough treatment with antibiotic therapy.

