

Potential Probiotic Therapy of Inhibitory Commensal *S. epidermidis* on Decolonization/Treatment of MRSA and *C. acnes* and Their Infections

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Studying human nasal colonization among 250 healthy participants in Shanghai, China, we found the nasal colonization rate of *S. aureus* and *S. epidermidis* was 19% and 97.1% respectively. *S. epidermidis* was confirmed as the predominant nasal commensal. The distribution of nasal colonization was: 18.6% SA+SE+, 78.5% SA-SE+, 2% SA-SE-, and 0.4% SA+SE- (SA=*S. aureus*, SE=*S. epidermidis*). MRSA nasal colonization is an endemic risk factor for many life-threatening diseases. Intriguingly, there are more than 80% of people in our study capable of evading *S. aureus* colonization. The purpose of this study is to elucidate this evasion mechanism and explore its potential application. We observed a strong negative correlation between colonization of inhibitory *S. epidermidis* strains (biofilm inhibitory ability >25%) and co-colonization of *S. aureus*. Absence of inhibitory *S. epi.* significantly increased colonization rate of *S. aureus* ($P < 0.001$, odds ratio = 17.5). Supernatants of inhibitory *S. epi.* were found to not only inhibit the biofilm formation, but also the growth of MRSA. Inhibitory *S. epi.* supernatants inhibited MRSA biofilm formation by 60% in a dose-dependent manner and inhibited the growth of MRSA by 30%. Inhibitory *S. epi.* cells can completely inhibit the growth of MRSA by co-culturing. Both inhibitory *S. epi.* supernatants and cells also showed inhibition effects on *C. acnes* growth. PMSF neutralization tests, PCR, and DNA sequencing confirmed the inhibitory factor was Epidermidis Serine Protease. Our study provided scientific data to support probiotic applications of inhibitory *S. epi.* for decolonization and treatment of MRSA and *C. acnes*.

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