

## A type III-like restriction endonuclease functions as a major barrier to horizontal gene transfer in clinical *Staphylococcus aureus* strains

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### Abstract

*Staphylococcus aureus* is an versatile pathogen that can cause life-threatening infections. Depending on the clinical setting, up to 50% of *S. aureus* infections are caused by methicillin-resistant strains (MRSA) that in most cases are resistant to many other antibiotics, making treatment difficult. The emergence of community-acquired MRSA drastically changed the picture by increasing the risk of MRSA infections. Horizontal transfer of genes encoding for antibiotic resistance or virulence factors is a major concern of multidrug-resistant *S. aureus* infections and epidemiology. We identified and characterized a type III-like restriction system present in clinical *S. aureus* strains that prevents transformation with DNA from other bacterial species. Interestingly, our analysis revealed that some clinical MRSA strains are deficient in this restriction system, and thus are hypersusceptible to the horizontal transfer of DNA from other species, such as *Escherichia coli*, and could easily acquire a vancomycin-resistance gene from enterococci. Inactivation of this restriction system dramatically increases the transformation efficiency of clinical *S. aureus* strains, opening the field of molecular genetic manipulation of these strains using DNA of exogenous origin.

**antibiotic resistance; transformation; targetron**

### Footnotes

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