The Gram-positive bacterial pathogen, *Staphylococcus aureus*, causes a wide range of invasive diseases, but is most commonly associated with complicated skin and soft tissue infections (SSTIs). The immunometabolic host response to *S. aureus* SSTIs, with particular emphasis on the fate of host arginine, has important implications on disease outcomes. For instance, arginine serves as the substrate for inducible Nitric Oxide Synthase (iNOS) in the production of nitric oxide (NO·) an important innate immune effector. Curiously, *S. aureus* is remarkably resistant to NO·, a trait that distinguishes this species from almost all other bacteria. *S. aureus* NO··resistance hinges on the ability of the bacterium to metabolically adapt to the constraints imposed by this immune radical. The initial stages of a *S. aureus* SSTI involve robust immune cell infiltrate accompanied by vigorous iNOS expression and NO· production. However, given the intrinsic NO··resistance of *S. aureus*, this response is ineffectual at clearing the infection. Rather, as the host response gradually shifts into the post-inflammatory, pro-fibrotic phase, host arginine begins to fuel the production of collagen and polyamines. The latter comprise a series of polycationic biological amines that exert potent ant-staphylococcal properties. Accordingly, the post-inflammatory phase of the host wound healing response is critical to the eventual resolution of a *S. aureus* SSTI. Given the above, a thorough understanding of the coordinated wound healing response might yield insights for improved treatments for non-resolving *S. aureus* SSTIs.