

**Table S1. GAS strains used in this study.**

Strain	Characteristics	Source/reference
950771 (771)	Encapsulated necrotizing fasciitis isolate	[33]
771SLO-	<i>slo</i> -negative deletion mutant of 771	[27]
771NADase-	<i>nga</i> -negative deletion mutant of 771	[27]
771SLO(Y255A)	Y255A point mutant of <i>slo</i> , deficient in pore formation but competent for NADase translocation by SLO	This study
188	Unencapsulated mutant of 950771	[33]
188SLO-	<i>slo</i> -negative deletion mutant of 188	[47]
188NADase-	<i>nga</i> -negative deletion mutant of 188	[14]
188SLS-	<i>sagA</i> -negative deletion mutant of 188	This study
188SLO-SLS-	<i>slo</i> and <i>sagA</i> -negative deletion mutant of 188	This study
188NADase(G330D)	G330D point mutant of <i>nga</i> , lacking NAD-glycohydrolase activity, in strain 188	This study
188SLO(Y255A)	Y255A point mutant of <i>slo</i> , deficient in pore formation but competent for NADase translocation by SLO, in strain 188	This study
188(pSIV)	188 containing <i>streptococcal</i> IPTG-inducible vector (pSIV). <i>Erm</i> <sup>R</sup>	[15]
188SLO-(pSIV)	188SLO- containing pSIV. <i>Erm</i> <sup>R</sup>	[15]
188SLO-(piSLO)	188SLO- containing IPTG-inducible SLO in pSIV. <i>Erm</i> <sup>R</sup>	[15]
188(pDL278)	188 containing empty pDL278 vector. <i>Spc</i> <sup>R</sup>	This study
188NADase-(pDL278)	188NADase- containing empty pDL278 vector. <i>Spc</i> <sup>R</sup>	This study
188(pSEC-IFS)	188 containing secreted IFS (SEC-IFS) under constitutive control of <i>PguaB</i> in pDL278. <i>Spc</i> <sup>R</sup>	This study
JRS4	Derivative of the M6 strain D471 from the Rockefeller University collection	[44]
JRS4SLO-	<i>slo</i> -negative deletion mutant of JRS4 (SLO1)	[43]
JRS4NADase-	<i>nga</i> -negative deletion mutant of JRS4 (SPN1)	[28]

Abbreviations: *Erm*, erythromycin; *Spc*, spectinomycin.

\* Reference numbers refer to reference list of the article.