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Molecular Piracy via Capsid Size Determination by *Staphylococcus aureus* Pathogenicity Island 1

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Bacteriophages are involved in many aspects of the spread and establishment of virulence factors in *Staphylococcus aureus*, including the mobilization of genetic elements known as *S. aureus* pathogenicity islands (SaPIs), which carry genes for superantigen toxins and other virulence factors. *S. aureus* pathogenicity island 1 (SaPI1) is normally stably integrated into the host genome, but can become mobilized by "helper" bacteriophage 80α, leading to the packaging of SaPI1 genomes into phage-like transducing particles that are composed of structural proteins supplied by the helper phage. The resultant SaPI1 transducing particles have capsids that are about one-third the volume of the helper phage, proportional to the smaller SaPI1 genome [1].

We have used cryo-electron microscopy (cryo-EM) and icosahedral reconstruction to determine the structures of the procapsid and the mature capsid for both 80α and SaPI1. 80α and SaPI1 procapsids have diameters of 51 nm and 37 nm, respectively, a rounded shape and an internal scaffolding core. Upon capsid expansion that occurs during DNA packaging, mature capsids measure 63 nm for 80α and 47 nm for SaPI1. Cryo-EM reconstructions display icosahedral T=7 and T=4 symmetry for 80α and SaPI1, respectively [2]. The 80α capsid protein (gp47) has an HK97-like fold and the capsid is organized into pentameric and hexameric clusters that interact via prominent trimeric densities. Unique to the SaPI1 procapsid reconstructions are internal densities that bridge capsid subunits across capsomers, suggesting that an internal SaPI1-encoded scaffolding protein participates in capsid size determination [3].

Two SaPI1-encoded proteins, gp6 and gp7, that were previously implicated genetically in capsid size determination were detected in SaPI1 procapsids by mass spectrometry [4]. Insertion of the genes encoding gp6 and gp7 into the 80α genome led to the formation of packaged, small SaPI1-like particles. Deletion of SaPI1 *orf6* led to the production of both SaPI1- and 80α-sized particles, suggesting that gp6 promotes the efficient formation of small capsids. Remarkably, deletion of *orf7* completely abolished the formation of small capsids, but yielded large procapsids that contain gp6. Cryo-EM reconstructions of these procapsids display densities linking capsid subunits, similar to those in SaPI1 procapsids. The presence of gp6 and gp7 as structural components of SaPI1 procapsids, but not in mature virions, suggests that they may function together as an efficient, size-determination, scaffolding protein system [5].

References

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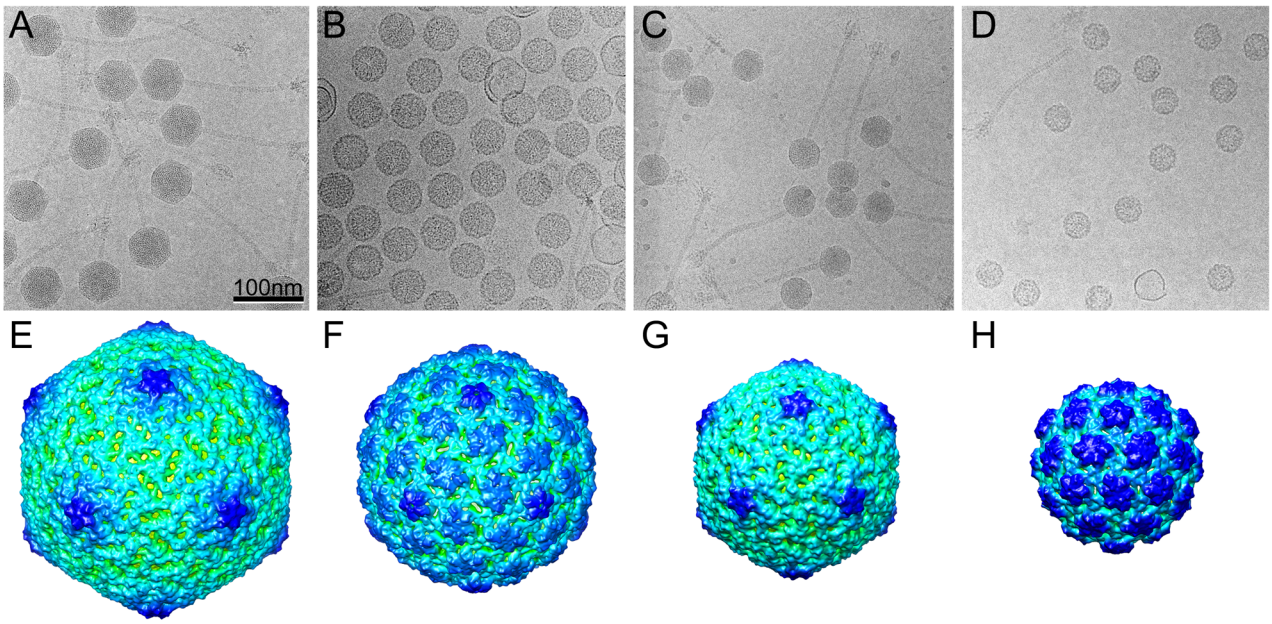

FIG. 1. Cryo-electron micrographs (top) and icosahedral reconstructions (bottom) of 80α virions (A,E), 80α procapsids (B,F), SaPI1 virions (C,G) and SaPI1 procapsids (D,H).

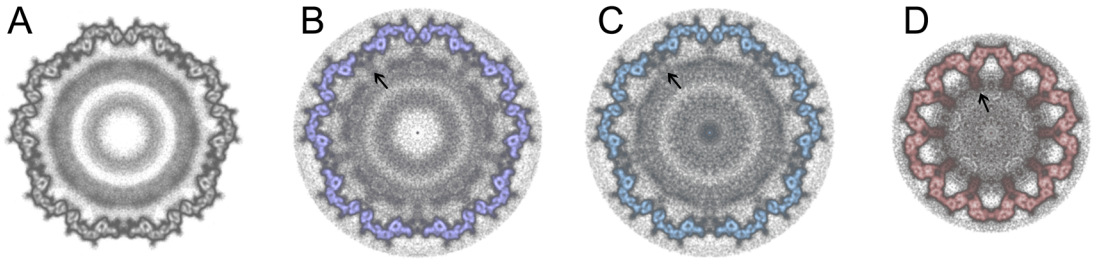

FIG. 2. Central sections through the procapsid reconstructions of 80α (A), 80α with SaPI1 *orf6* and *orf7* inserted (B), SaPI1 Δ*orf7* (C) and SaPI1 (D), viewed down the five-fold axis. Internal density not present in A can be seen in B-D (arrows) suggesting that this density is contributed by SaPI1 gp6.

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