

## PARTIAL RETRACTION

## yadBC of Yersinia pestis, a New Virulence Determinant for Bubonic Plague

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Volume 76, no. 2, p. 578 – 587, 2008. Page 578, Abstract, lines 7 and 8: We retract the last sentence of the Abstract.

Page 578, column 2, lines 13 to 18: We retract the last sentence of the Introduction.

Pages 585, Results, column 1, lines 1 to 8 from the bottom: We retract the last three sentences of the paragraph entitled "Tests for importance of *yadBC* in bubonic plague and pneumonic plague in mice."

Page 585, Discussion, column 2, lines 19 and 20 from the bottom: We retract the phrase "severely compromised."

In recent studies, Tanya Myers-Morales, Annette Uittenbogaard, Amanda A. Gorman, and Susan C. Straley have discovered that the yadBC mutant used for measuring virulence by the intradermal (i.d.) route became corrupted at the last step of its creation (transformation of the Lcr virulence plasmid), with the revised conclusion that yadBC is not a major virulence determinant for the skin infection. The original result, described in the second paragraph under "Tests for importance of yadBC in bubonic plague and pneumonic plague in mice" at the end of the Results section, is therefore retracted. Statements repeating the conclusion drawn from those results therefore also are incorrect: the last sentences of the Abstract and Introduction and the phrase "severely compromised" in the Discussion. The results and conclusions in the rest of the paper are not affected, because the strains used were Lcr or were fully virulent.

The original  $\Delta yadBC$  mutant had been made independently in two backgrounds: Pgm<sup>+</sup> Lcr<sup>-</sup> (avirulent) and Pgm<sup>-</sup> Lcr<sup>+</sup> (conditionally virulent from an intravenous route). Then, working in biosafety level 3 (BSL3) containment with select-agent security, we had reconstituted potential virulence of the Pgm<sup>+</sup> Lcr<sup>-</sup>  $\Delta yadBC$  mutant by restoring the Lcr plasmid. During this last step, that  $\Delta yadBC$  strain evidently acquired a virulence-abolishing mutation that did not show up in our *in-vitro* phenotypic characterization assays. That strain was avirulent by the i.d. route, as described in our published article. Meanwhile, a complemented  $\Delta yadBC/BC^{+}$  strain (with restoration of yadBC in the native location) did not acquire a virulence-abolishing mutation when we restored the Lcr plasmid, and it was virulent by the i.d. route. Hence, we reported that yadBC is required for lethality of bubonic plague. However, when we recently found that the  $Pgm^{-}Lcr^{+}\Delta yadBC$  strain that we had made in parallel at the outset was fully virulent in the systemic plague model, we became concerned that something may have been wrong with the  $\Delta yadBC$  strain that we had reconstituted to virulence in BSL3. It was important to know if yadBC is actually required for virulence in bubonic plague and perhaps not in systemic plague or whether it is not required for virulence in either case. Therefore, we derived a  $\Delta pgm$  derivative of the Pgm<sup>+</sup> Lcr<sup>+</sup>  $\Delta yadBC$  strain that had been avirulent by the i.d. route, tested its virulence in systemic plague, and found that it also was avirulent in that model. We now knew that that strain was corrupted. So we restored the Lcr plasmid again to the Pgm<sup>+</sup> Lcr  $\Delta yadBC$  strain. This time it did not acquire a virulence-abolishing mutation and was only slightly attenuated by the i.d. route (two of six mice given a dose of 71 CFU died and two of two mice given a dose of 524 CFU died). This result shows that the effect of *yadBC* in bubonic plague is subtle or redundant. We feel that the further lethality studies required to determine a true 50% lethal dose value are not justified, because many mice would be required to quantify a relatively small attenuation.

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