

Panobacumab is a fully human IgM/ κ mAb directed against *P. aeruginosa* O11 (O-polysaccharide lipopolysaccharide [LPS] portion). This drug, not released yet for use, is in the study phase and is being investigated for its efficacy. The serotype O11 LPS mAb panobacumab was tested in a clinically relevant cyclophosphamide-induced neutropenia murine model and in combination with meropenem in susceptible and meropenem-resistant *P. aeruginosa*-induced pneumonia. Observations showed that *P. aeruginosa*-induced pneumonia was dramatically increased in neutropenic mice compared with immunocompetent mice. First, panobacumab reduced significantly lung inflammation and improved bacterial clearance in the neutropenic host lung. Second, the combination of panobacumab and meropenem had an additive effect. Third, panobacumab retained activity in a meropenem-resistant *P. aeruginosa* strain. In conclusion, panobacumab contributes to clear *P. aeruginosa* in neutropenic hosts, as well as in combination with antibiotics in immunocompetent hosts. This suggests beneficial effects from concurrent treatment, even in immunocompromised subjects, who suffer most of morbidity and mortality of *P. aeruginosa* infections.

19.2.4 LC10 Versus *Staphylococcus aureus*

Staphylococcus aureus is one of the main causes of pneumonia in inpatients and in healthy subjects in the community. *S. aureus* pneumonia is a fatal disease, with mortality rates of 60%. Treatment of these infections is complicated by the fact that 50% of *S. aureus* isolates from pneumonia patients are methicillin-resistant *S. aureus* (MRSA), thus reducing safe and effective treatment options. To overcome this public health issue, several approaches have been developed; among these approaches is the use of mAbs directed against *S. aureus* and its virulence determinants, which can be used in prophylaxis and as an adjuvant therapy with antibiotics.

Alpha-toxin (AT) is an important virulence factor in the disease pathogenesis of *S. aureus*. Passive immunization with LC10 has increased survival and decreased the number of bacteria in lungs and kidneys of infected mice and showed protection against various clinical *S. aureus* isolates. The lungs of mice infected with *S. aureus* exhibited bacterial pneumonia, including generalized inflammation, while the lungs of mice given LC10 showed minimum inflammation and retained a healthy architecture.

The reduction in inflammation and damages in animals treated with LC10 resulted in reduced vascular protein leak and blood CO₂ levels. LC10 was also assessed for its therapeutic activity combined with vancomycin or linezolid, and the treatment resulted in a significant increase ($P < 0.05$) in survival over monotherapies. The lungs of animals treated with antibiotic plus LC10 showed less inflammatory tissue damage than those given monotherapy. This data