MedicalXpress

MRSA study suggests strategy shift needed to develop effective therapeutics

March 17 2009

USA300--the major epidemic strain of methicillin-resistant *Staphylococcus aureus* (MRSA) causing severe infections in the United States during the past decade--inherits its destructiveness directly from a forefather strain of the bacterium called USA500 rather than randomly acquiring harmful genes from other MRSA strains. This finding comes from a new study led by scientists at the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health.

The study authors suggest that a radical shift may be needed in how scientists should design MRSA therapeutics. Instead of the current focus on neutralizing MRSA by targeting products of mobile genetic elements—DNA molecules that bacteria acquire randomly by interacting with other bacteria—scientists should switch to looking at the permanent DNA backbone (core genome) of USA300 to understand how increased production of certain proteins such as toxins affects its virulence in humans.

NIAID scientist Michael Otto, Ph.D., directed the study, which involved analyzing DNA sequences of the major epidemic forms of S. aureus. The research team found that the lineage of the bacteria fell into three distinct families: (1) USA300 and its forefather, USA500, which are epidemic in U.S. hospital and community settings; (2) MRSA found primarily in hospitals in the United Kingdom and Europe; and (3) MRSA found in hospitals in South America, Europe and Asia.

The researchers then tested the different lineages in mice, observing that

the USA300 and USA500 strains were significantly more destructive than the other strains. Further, when interacting with human immune cells, the USA300 and USA500 strains killed nearly 80 percent of the immune cells, compared with a rate of less than 10 percent for all other strains tested. Finally, when the scientists evaluated what in the bacteria was killing the immune cells, they found that levels of alpha toxin and alpha-type phenol-soluble modulins (PSMs) were significantly higher in USA300 and USA500 compared with the other strains. Earlier NIAID studies determined that alpha toxin and alpha-type PSMs play a crucial role in determining the severity of community-associated MRSA infection.

Another important finding of the study, according to Dr. Otto, is that USA300 and USA500 are nearly identical in virulence, as is their level of virulence gene production. This suggests that the Panton-Valentine leukocidin (PVL) and other mobile genetic elements long believed to play key roles in USA300 virulence have no significant impact, because while USA300 carries the PVL and other mobile genes, USA500 does not.

More information: M Li et al. Evolution of virulence in epidemic community-associated methicillin-resistant Staphylococcus aureus. *Proceedings of the National Academy of Sciences* DOI: 10.1073/pnas.0900743106 (2009).

Source: NIH/National Institute of Allergy and Infectious Diseases (news : web)