The rates of infection by community-acquired multi-drug resistant *Staphylococcus aureus* (CA-MRSA) have risen dramatically over the past decade and a half in the United States. CA-MRSA is responsible for rapidly progressive diseases, including necrotizing pneumonia, severe sepsis, and necrotizing fasciitis. Consequently, novel antibacterial strategies are needed to combat the rising antibiotic resistance seen in CA-MRSA strains. The USA300 CA-MRSA strain has been mutagenized using the *Bursa aurealis* transposon to create the Nebraska Transposon Mutant Library (NTML). We have screened the 1920 non-essential, defined transposon insertions in the NTML for strains that are either susceptible or resistant to methanol extracts of *Centaurea nigrescens* leaves and flowers. Of the insertion strains screened, ~2% show marked increased susceptibility to methanol extracts of *C. nigrescens*. Insertions in two different drug efflux transporters, EmrB/QacA and epi-G ABC-like transporter, have been identified. The EmrB/QacA drug resistance transporter subfamily is a multi-drug efflux pump responsible for the export of toxic molecules from bacteria and yeast. The epi-G ABC transporters are involved in lantibiotic (peptide antibiotics containing thioether bridges) export. These results confirm the effectiveness of the screen as a means for identifying drug-resistance genes affected by the *C. nigrescens* methanolic extract and suggest a role for drug efflux proteins in the resistance of *S. aureus* CA-MRSA to antibacterial plant metabolites.