**Scientific Abstract:**

Zinc (Zn) is sometimes supplemented at elevated concentrations (2,000-3,000 ppm) in swine diets, ostensibly to prevent enteric infections and promote growth. Studies from Denmark have suggested a genetic linkage and a phenotypic association among Zn resistance, encoded by the czrC gene, methicillin-resistance, encoded by the mecA gene, and tetracycline resistance (encoded by the tetM gene in S. aureus). We have previously shown that nasal carriage of mecA-positive MRSA exhibits a dose-response to zinc supplementation in pigs. A longitudinal study was performed to evaluate the association of in-feed Zn and chlortetracycline (CTC) supplementation (at two levels) with the prevalence of MRSA in pigs. The study consisted of 240 weaned piglets, housed in 48 pens (5 piglets/pen), randomly assigned to six treatments in a 2×3 complete factorial design. Treatment factors included diets with normal (30 mg/kg) or high (2,500 mg/kg of feed) concentrations of Zn, with or without CTC at low (5 mg/kg) or high (22 mg/kg BW) levels, and the interaction terms for Zn with low or high CTC. Nasal, skin, and tonsillar swabs were collected from all piglets on Days 0, 21, and 42. The samples were inoculated onto MRSA CHROMagar and presumptive MRSA colonies were confirmed by genus (Staph) and species (nuc) specific PCR. The presumptive MRSA isolates were tested for mecA and czrC by PCR. Zinc susceptibility was determined by the agar gel dilution method. Statistical analyses were carried out using STATA (v.12.1). Overall treatments and days, the prevalence of mecA-positive MRSA was 42.8% (308/720), 37.2% (268/720), and 42.6% (307/720) in nasal, skin, and tonsillar samples, respectively. The prevalence of czrC-positive MRSA was 20% (144/720), 21.1% (152/720), and 14.3% (103/720) in nasal, skin, and tonsillar swabs, respectively. The Zn, sampling day (period) and treatment interactions had a significant effect on the prevalence of mecA and czrC-positive MRSA in all three collection sites (P < 0.001). The occurrence of czrC gene was strongly associated with mecA-positive MRSA isolates (P < 0.0001). The median MICs of Zn for zinc resistant and susceptible isolates were 8 and 4 mM, respectively (P < 0.001). The prevalence of mecA- and czrC-positive MRSA was affected by Zn (P < 0.05) but not CTC supplementation (P > 0.05). The observed association between czrC and mecA genes points to the importance of elevated Zn supplementation in selection and propagation of antibiotic resistant bacteria such as MRSA in swine production.