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Genetic Analysis of Mechanisms Required for Chicken Colonization by *Campylobacter jejuni*

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Campylobacter jejuni is an important foodborne pathogen of humans. Its virulence mechanisms are less well understood than are those of other foodborne pathogens such as *Salmonella* and *Listeria*. This is due, in part because of limited genetic methods available for its study, as well as a lack of good animal models. We developed a *mariner*-based system of transposon mutagenesis, combining *in vitro* transposition with natural competence to carry out chromosome mutagenesis of *C. jejuni*. With this method, and applying other genetic approaches we developed for making allele-directed mutants in *C. jejuni*, we have begun to dissect the biology and pathogenicity of this important pathogen. For an animal model, we are focusing on a natural host, the chicken, which is responsible for the majority of human infections. Chickens are colonized to high titers in the gastrointestinal tracts of chickens but, unlike humans, chickens colonized by *C. jejuni* remain healthy. We carried out signature-tagged mutagenesis of *C. jejuni* to identify traits required for cecal colonization of day-of-hatch chicks. Among the traits we identified in this screen, genes encoding enzymes for *N*-linked protein glycosylation (*pgl*) arose several times, suggesting the importance of this phenotype in chick colonization. Several proteins are predicted to be modified by the Pgl system; most are periplasmic or surface proteins. Mutagenesis of several of these revealed that not all *N*-linked glycoproteins are required for chick colonization. Furthermore, despite the extensive enzymology required to glycosylate proteins, glycosylation is not a requirement of all glycoproteins. These observations raise questions as to the role of *N*-linked protein glycosylation in *C. jejuni*. Finally, we are carrying out an analysis of chick colonization by *C. jejuni*, taking advantage of mutants isolated through signature-tagged mutagenesis to better understand the host innate response to colonization with wild type and colonization-deficient strains. Our data suggest that the chicken responds immunologically to infection by *C. jejuni* but that this response is ultimately unable to clear the microbes.