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A mutant Neisseria meningitidis strain expressing exogenous transferrin binding proteins can be used to evaluate vaccine antigens targeting other transferrin receptor-expressing bacteria

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Background

A subset of bacteria residing in the nasopharynges of vertebrate hosts have evolved to express a common iron scavenging mechanism that targets and removes iron from the host glycoprotein transferrin (Tf). The two components of the bacterial Tf receptor – in particular, the lipoprotein component, Tf binding protein B (TbpB) – are considered viable vaccine candidates for preventing disease caused by these pathogens as they are essential for bacterial survival and proliferation in the host. However, the rodent infection models that have been developed to evaluate vaccines targeting these pathogens have been plagued by either insufficient or excessive virulence of the bacteria in the rodent. By contrast, mouse infection models have been successfully used previously to simulate invasive Neisseria meningitidis infections as well as to evaluate the efficacy of the N. meningitidis Tf receptor as a prospective vaccine for preventing meningococcal disease in humans.

Aim/Methods

To address the shortcomings of small animal infection models for Tf receptor-expressing bacterial pathogens, we established and optimized a mouse sepsis model using a naturally competent serogroup A strain of N. meningitidis. We then inserted the tbpBA operon derived from the porcine pathogen Actinobacillus pleuropneumoniae (App) into the chromosome of the meningococcal strain using natural transformation and

were able to demonstrate that the mutant strain was virulent in C57BL/6 mice when administered alongside porcine Tf. To determine whether this infection model was suitable for evaluating the utility of Tf receptors as vaccine antigens, we then immunized mice with a set of recombinant TbpB antigens and subsequently infected the animals with the mutant N. meningitidis strain.

Results

Immunization with recombinant TbpB antigens derived from App conferred 100% protection against lethal challenge with the App Tf receptor-expressing strain of N. meningitidis.

Conclusions

Using the App Tf receptor as a proof-of-concept, we demonstrated that cloning exogenous tbpBA operons into a N. meningitidis strain for which a robust mouse sepsis model has been established appears to be a viable method for evaluating Tf receptor-based vaccines targeting pathogens for which few suitable small animal infection models have been developed and for which effective vaccines are not yet available.