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NOVEL DEVELOPMENTS AND METHODOLOGIES FOR PRESERVING CHILD WELLBEING FROM SERIOUS INFECTION

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Bacterial meningitis continues to be an important cause of mortality and morbidity in infants and children through the world, and a major contributing factor is our incomplete understanding of the pathogenesis of this disease. A highdegree of bacteraemia and bacterial invasion of the bloodbrain barrier represent the key steps in the development of bacterial meningitis, but the underlying mechanisms remain incompletely understood. Using trancriptome analysis of bacteria derived from a high-degree of bacteraemia and meningitis, we showed that a high-degree of bacteraemia exploits oxidative stress within bacterial cell and reducing oxidative stress inhibits the development of bacterial meningitis. Using proteomic arrays, RNA-Seq analysis and CRISPR/Cas9 approaches, we showed that bacterial invasion of the blood-brain barrier exploits specific host factors and counteracting such exploited host factors inhibits bacterial penetration of the blood-brain barrier as well as reduces the

mortality and morbidity associated with bacterial meningitis. These findings demonstrate that elucidation of the microbial and host factors contributing to bacterial penetration of the blood-brain barrier provides an innovative approach for the development of prevention and therapy of bacterial meningitis. This is the first demonstration of utilizing state of the art methodolgies for discovery of targets for bacterial meningitis for protecting infants and children from serious infections

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