

Title – Novel Shigellosis Therapy: Treating a Bad Gut Feeling

Program of Study – Biomedical Science

Presentation Type – PowerPoint

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Background

Shigellosis is an acute intestinal disease caused by infection by bacteria of the species *Shigella* or enterohemorrhagic *Escherichia coli* (EHEC), which contains a potent toxin called Shiga-toxin. Shigellosis affects over 150 million individuals world-wide each year, over one million of which result in death. The most severely affected subset of the population is children in developing countries. This disease is transmitted via a fecal-oral route. Clinical manifestations include mild to severe diarrhea, abdominal cramping, and fever, often leading to malnutrition and dehydration. *Shigella* and Shiga toxin-containing bacteria have developed multiple drug resistance, leaving the condition without treatment options. *Citrobacter rodentium* (CR), a bacterium that is genotypically and phenotypically similar to EHEC, is used to model Shigellosis in mice to study this disease.

Materials

Mice were infected with CR containing Shiga-toxin and either did or did not receive treatment with (1) streptomycin or (2) valproic acid, manganese, and glycine. Treatment efficacy was assessed by gastrointestinal transit, mouse weight, and colonic inflammation.

Results

Conventional mice showed significant weight loss, colonic inflammation, and decreased cecum weight in relation to mice receiving continual strep treatment. Additionally, treatment with VPA and Mn reduced the inflammatory response of CR infection.

Conclusion

The increased diseased response of mice receiving no antibiotic treatment in relation to those receiving strep treatment shows that bacterial competition drives pathogenesis. We propose that VPA and Mn treatment mitigate this EHEC virulence by acting as a histone deacetylase inhibitor to induce transcriptional repression of Gb3 receptors and suppressing expression of stx carrier protein GPP130, thus providing the first available treatment to EHEC-induced Shigellosis.