
Michael Kaleko1, Christian Furlan-Freguia1, Brian Fanelli1, Nur A. Hasan1, Rita R. Colwell2, Sheila Connelly1
1Synthetic Biologics, Inc., Rockville, MD, USA, 2CosmosID, Inc., Rockville, MD, USA

ABSTRACT

Distal release ribaxamase formulations, engineered to secrete beta-lactamase distal to the site of oral antibiotic administration, were designed to prevent the emergence of antibiotic resistant enterococci and vancomycin-resistant enterococci. Formulations, engineered to contain distal release ribaxamase, were engineered for dissolution in the lower small intestine distal to the site of oral antibiotic absorption. SYN-007 Protects the Gut Microbiome from Amoxicillin

SYN-007 formulations, 30 mg/kg PO, were collected before and after the last antibiotic +/- SYN-007 doses (16 doses of each total). Real-time qPCR was used to determine relative abundance of key markers of the intestinal microbial community in each sample. A heatmap displays beta-lactamase gene frequency.

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

In enteric enterococci, ribaxamase significantly reduced the frequency after antibiotic exposure. Change in relative frequency (mean of the indicated antibiotic) compared to vehicle control was determined.

RESULTS

Three distal-release formulations of ribaxamase, SYN-007, were produced. Formulations 1 and 3 were composed of enteric-coated enzyme pellets within enteric-coated capsules. Formulation 2 was composed of enteric-coated pellets in uncoated capsules. Dissolution testing verified that enzyme was released at low pH (conditions in the stomach), was not released after 2 hrs at pH 5.5, conditions of the upper small intestine, and was released at pH 7.4, conditions of the lower small intestine/colon. In contrast, SYN-007 formulation 3 was released at pH 7.4.

SYN-007 Formulation 3 Does Not Affect Amoxicillin Systemic Absorption

Amoxicillin serum levels were measured the first and last amoxicillin doses to determine if SYN-007 interfered with amoxicillin systemic absorption. Amoxicillin Serum Pharmacokinetics

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

The microbiome composition was significantly changed after amoxicillin exposure. Microbiome expansion was reflected by increased frequency of antibiotic resistance genes in each sample. This heatmap displays beta-lactamase gene frequency.

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

In enteric enterococci, ribaxamase significantly reduced the frequency after antibiotic exposure. Change in relative frequency (mean of the indicated antibiotic) compared to vehicle control was determined.

SYN-007 Protects the Gut Microbiome from Amoxicillin

SYN-007 formulations, 30 mg/kg PO, were collected before and after the last antibiotic +/- SYN-007 doses (16 doses of each total). Real-time qPCR was used to determine relative abundance of key markers of the intestinal microbial community in each sample. A heatmap displays beta-lactamase gene frequency.

SYN-007 Formulation 3 Does Not Affect Amoxicillin Systemic Absorption

Amoxicillin serum levels were measured the first and last amoxicillin doses to determine if SYN-007 interfered with amoxicillin systemic absorption. Amoxicillin Serum Pharmacokinetics

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

The microbiome composition was significantly changed after amoxicillin exposure. Microbiome expansion was reflected by increased frequency of antibiotic resistance genes in each sample. This heatmap displays beta-lactamase gene frequency.

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

In enteric enterococci, ribaxamase significantly reduced the frequency after antibiotic exposure. Change in relative frequency (mean of the indicated antibiotic) compared to vehicle control was determined.

SYN-007 Protects the Gut Microbiome from Amoxicillin

SYN-007 formulations, 30 mg/kg PO, were collected before and after the last antibiotic +/- SYN-007 doses (16 doses of each total). Real-time qPCR was used to determine relative abundance of key markers of the intestinal microbial community in each sample. A heatmap displays beta-lactamase gene frequency.

SYN-007 Reduces Emergence of Antibiotic Resistance Genes

In enteric enterococci, ribaxamase significantly reduced the frequency after antibiotic exposure. Change in relative frequency (mean of the indicated antibiotic) compared to vehicle control was determined.

SYN-007 Protects the Gut Microbiome from Amoxicillin

SYN-007 formulations, 30 mg/kg PO, were collected before and after the last antibiotic +/- SYN-007 doses (16 doses of each total). Real-time qPCR was used to determine relative abundance of key markers of the intestinal microbial community in each sample. A heatmap displays beta-lactamase gene frequency.