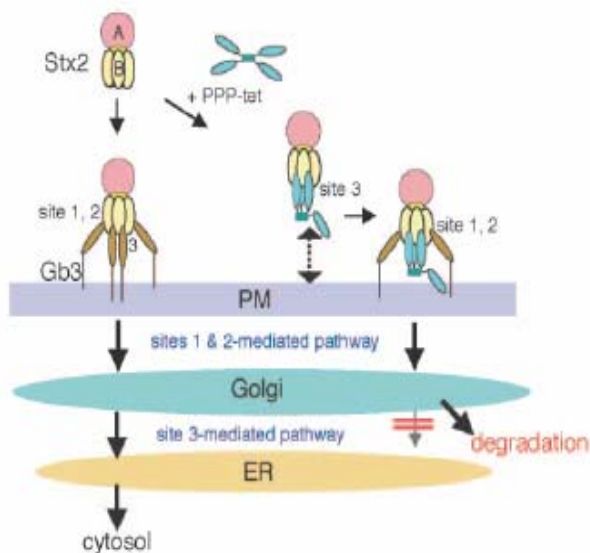


# Inhibition of the Shiga toxin: Synthesizing a Gb3 Receptor Analogue

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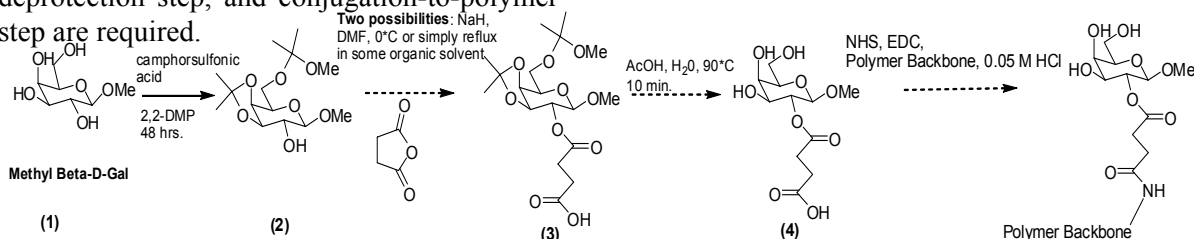
**Background.** Food poisoning as a result of ingestion of contaminated produce containing shiga toxin, produced by the bacteria *Shigella dysenteriae*, can cause significant gastrointestinal distress and in severe cases lead to death. This pathogen binds to a trisaccharide receptor (Gb3) expressed on intestinal cell surfaces. Previous work by Nishikawa et al. has shown that a linked tetrapeptide (PPP-tet) is able to bind to the B subunit of shiga toxin, preventing infection (**Figure 1**). Mindful of this work, and the natural Gb3 shiga toxin target, we endeavor to create a sugar derived Gb3 mimic bound to a polymer backbone that will prevent shiga toxin infection.



**Figure 1. Mechanism of inhibitory action by PPP-tet**

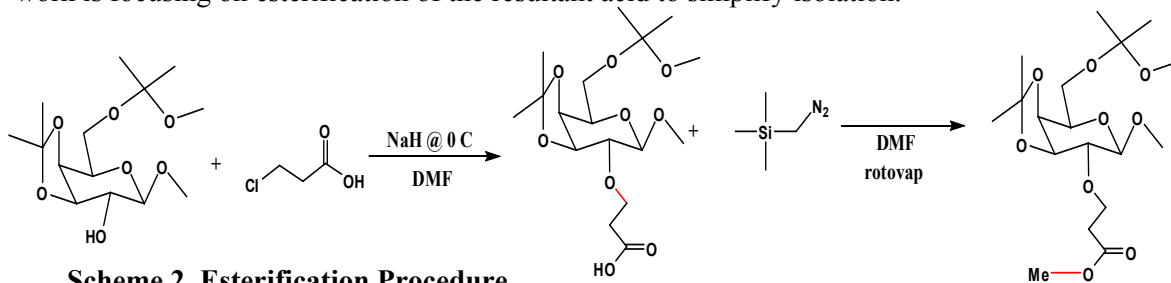
Image: Nishikawa, K. et. al. *The FASEB Journal* Dec 2006 v20 E2077

**Approach.** Gb3 contains a galactose as the terminal sugar in the trisaccharide. Our initial attempt will be to tether galactose to a biopolymer to determine its ability to inhibit shiga toxin infection. The synthetic approach being investigated requires 4 steps (**Scheme 1**). A selective protection step, tethering step, a deprotection step, and conjugation-to-polymer step are required.



**Scheme 1. Synthetic map**

**Results.** As verified by NMR, alcohol protection proceeded smoothly to yield (2). Unfortunately, isolation of the acid product (3) from the tethering reaction has been problematic. As a result, current work is focusing on esterification of the resultant acid to simplify isolation.



**Scheme 2. Esterification Procedure**

**Future Work.** After isolating the the acid product (3), this molecule will then deprotected and appended to a biocompatible polymer. Biological assays of this material will indicate if shiga toxin infection can be abrogated by a galactose bound polymer.

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