NOVEL TOXIN-DERIVED DELIVERY CONSTRUCTS FOR ORAL DELIVERY

CROSS-REFERENCE

[0001] This application claims the benefit of U.S. Provisional Application Nos. 62/640,168 filed March 8, 2018; 62/640,188 filed March 8, 2018; and 62/640,194 filed March 8, which applications are incorporated herein by reference in their entirety for all purposes.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing in the form of a "paper copy" (PDF File) and a file containing the referenced sequences (SEQ ID NO: 1 – SEQ ID NO: 221) in computer readable form (ST25 format text file) which is submitted herein. The Sequence Listing is shown using standard three letter code for amino acids, as defined in 37 C.F.R. 1.822. Said ASCII copy, created on March 8, 2019, is named 40566-711_601_SL.txt and is 350,816 bytes in size.

BACKGROUND

[0003] The gut epithelium has thwarted efforts to orally administer large molecule biologics because proteins cannot diffuse across the barrier or sneak through the tight junctions. When they are taken up by endocytosis — the only route left to them — they are typically degraded in lysosomes rather than being transported into the body. This inability to be readily absorbed across the intestinal epithelium continues to be a limiting factor in developing commercially viable oral formulations of these agents. The most common solution is to use systemic administration, but that can often create considerable side effects and reduce patient convenience that negatively affects compliance.

INCORPORATION BY REFERENCE

[0004] All references disclosed herein are hereby incorporated by reference in their entirety for all purposes.

SUMMARY

[0005] The present disclosure provides methods and composition for transport and/or delivery of a cargo molecule to certain location(s) within a cell (e.g., a supranuclear location) or across a cell (e.g., epithelial cell), either in vitro or in vivo (e.g., in a rodent or a human). Such cargo can be directed to a set of location(s) by coupling it to a carrier molecule. Such carrier molecule can interact with unique receptors both on the cell surface and intracellularly for the targeted delivery of the cargo. Various such carrier, cargos, and uses thereof are described herein.