WHAT IS CLAIMED IS:

1. An isolated delivery construct comprising:

a carrier, wherein the carrier consists of an amino acid sequence having at least 80% sequence identity to the amino acid sequences of SEQ ID NO: 4 or SEQ ID NO: 5; and

a biologically active cargo coupled to the carrier, wherein the isolated delivery construct is capable of transcytosing across a polarized epithelial cell.

2. The isolated delivery construct of claim 1, wherein the carrier consists of an amino acid sequence having at least 90%~~, 99% or 100%~~ sequence identity to the amino acid sequence of SEQ ID NO: 4 or SEQ ID NO: 5~~; or wherein the carrier consists of SEQ ID NO: 4 or SEQ ID NO: 5~~.

3. The isolated delivery construct of claim 1, wherein the carrier consists of an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 4 or SEQ ID NO: 5.

4. The isolated delivery construct of claim 1, wherein the carrier consists of an amino acid sequence having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 4 or SEQ ID NO: 5.

5. The isolated delivery construct of claim 1, wherein the carrier consists of the amino acid sequence of SEQ ID NO: 4 or SEQ ID NO: 5.

~~3~~6. An isolated delivery construct comprising:

a cholix carrier having at most 265 amino acids, wherein the cholix carrier comprises a domain I of an exotoxin, or a truncated and/or modified version thereof, and

a biologically active cargo coupled to the carrier,

wherein the cholix carrier is capable of delivering the biologically active cargo across a polarized epithelial cell via transcytosis.

~~4. The isolated delivery construct of claim 3, wherein the cholix carrier has a C-terminus at position 206, 245, 251, or 265.~~

~~5. The isolated delivery construct of claims 1-3, wherein the carrier does not have a C-terminus at position 265.~~

~~6~~7. The isolated delivery construct of any one of claims ~~1-5~~1-6, wherein:

(a) the carrier consists of domain I of a cholix toxin; and/or

(b) the biologically active cargo is coupled to the carrier via a spacer~~, optionally wherein the spacer comprises GGGGSGGGGSGGGGS (SEQ ID NO: 210)~~.

8. The isolated delivery construct of claim 7, wherein the spacer comprises GGGGSGGGGSGGGGS (SEQ ID NO: 210).

~~7~~9. The isolated delivery construct of any preceding claim, wherein the carrier is configured to deliver the biologically active cargo to the basal side of the epithelial cell.

~~8~~10. The isolated delivery construct of any preceding claim, wherein the carrier interacts with one or more of ribophilin 1, SEC24, CK-8, TMEM132, GRP75, ERGIC-53, or perlecan, and does not display interaction with one or more of a clathrin or GPR78, or a combination thereof~~, optionally wherein the interaction is a selective interaction or the interaction is a pH-dependent interaction~~.

11. The isolated delivery construct of claim 10, wherein the interaction is a selective interaction or the interaction is a pH-dependent interaction.

~~9~~12. The isolated delivery construct of any preceding claim, wherein:

(a) the delivery of the heterologous cargo across an epithelial cell occurs in vitro from the apical surface of the epithelial cell to a basolateral compartment; and/or

(b) the polarized epithelial cell is from a human.

~~10~~13. The isolated delivery construct of claim ~~9~~12, wherein the human polarized epithelial cell is a human polarized gut epithelial cell~~, optionally wherein the human polarized gut epithelial cell is a Caco-2 cell~~.

14. The isolated delivery construct of claim 13, wherein the human polarized gut epithelial cell is a Caco-2 cell.

~~11~~15. The isolated delivery construct of any preceding claim, wherein the biologically active cargo:

(a) is a macromolecule, small molecule, peptide, polypeptide, nucleic acid, mRNA, miRNA, shRNA, siRNA, antisense molecule, antibody, DNA, plasmid, vaccine, polymer nanoparticle, or catalytically-active material; and/or

(b) is a hormone, a cytokine, a therapeutic antibody, a functional fragment thereof, or any combination thereof.

~~12~~16. A pharmaceutical composition comprising an isolated delivery construct according to any one of claims ~~1-11~~1-15, for use in therapy in a subject.

~~13~~17. ~~The composition for use~~ Use of the isolated delivery construct according to any one of claims ~~12~~1-15 in the manufacture of a pharmaceutical composition for treating an inflammatory disease in a subject, wherein:

(a) the subject to be treated is a human; and/or

(b) the composition is formulated for oral administration, topical administration, pulmonary administration, intra-nasal administration, buccal administration, sublingual administration, or ocular administration.

~~14~~18. The ~~composition for~~ use according to claim ~~12-~~17~~and claim 13~~, ~~wherein the composition is for use in treating an inflammatory disease, an autoimmune disease, a cancer, a metabolic disease, a fatty liver disease, or a growth hormone deficient growth disorder, optionally~~ wherein the inflammatory disease is selected from an inflammatory bowel disease, psoriasis or bacterial sepsis.

~~15~~19. The ~~composition for~~ use according to ~~claims 12-14~~claim 17 or 18, wherein:

(a) the inflammatory ~~bowel~~ disease is Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischemic colitis, diversion colitis, Behcet's syndrome or indeterminate colitis~~; or~~

~~(b) the autoimmune disease is systemic lupus erythematosus (SLE), pemphigus vulgaris, myasthenia gravis, hemolytic anemia, thrombocytopenia purpura, Grave's disease, Sjogren's disease, dermatomyositis, Hashimoto's disease, polymyositis, inflammatory bowel disease, multiple sclerosis (MS), diabetes mellitus, rheumatoid arthritis, or scleroderma; or~~

~~(c) the cancer is a non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia, hairy cell leukemia, acute lymphoblastic leukemia, multiple myeloma, carcinomas of the bladder, kidney ovary, cervix, breast, lung, nasopharynx, malignant melanoma, rituximab resistant NHL, or leukemia; or~~

~~(d) the metabolic disease is diabetes, obesity, diabetes as a consequence of obesity, hyperglycemia, dyslipidemia, hypertriglyceridemia, syndrome X, insulin resistance, impaired glucose tolerance (IGT), diabetic dyslipidemia, or hyperlipidemia~~.

~~16. A composition for use for treating a condition in a subject in need thereof, the composition comprising a carrier comprising a domain I of a pseudomonas exotoxin (PE), lacking a domain II of the PE, lacking a domain Ib of the PE and lacking a domain III of the PE, wherein the carrier is coupled to a heterologous cargo.~~

~~17. The composition for use of claim 16, wherein the carrier consists of an amino acid sequence having at least 80%, 90%, 99% or 100% sequence identity to the amino acid sequence of SEQ ID NO: 137; or wherein the carrier consists of SEQ ID NO: 137.~~

~~18. The composition for use of claim 16 or 17, wherein the carrier further comprises at least one N-terminal methionine residue.~~

~~19. The composition for use of any one of claims 16-18, wherein the composition is formulated for pulmonary administration.~~

20. Use of the isolated delivery construct according to any one of claims ~~1-11~~1-15 in the manufacture of a medicament for the treatment of an inflammatory disease, an autoimmune disease, a cancer, a metabolic disease, a fatty liver disease, or a growth hormone deficient growth disorder~~, optionally wherein the inflammatory disease is an inflammatory bowel disease, psoriasis or bacterial sepsis~~.

21. The use according to claim 20, wherein the medicament is for treatment of an inflammatory disease selected from an inflammatory bowel disease, psoriasis or bacterial sepsis.

~~21~~22. The use according to claim 20 or 21, wherein:

(a) the inflammatory ~~bowel~~ disease is Crohn's disease, ulcerative colitis, collagenous colitis, lymphocytic colitis, ischemic colitis, diversion colitis, Behcet's syndrome or indeterminate colitis; or

(b) the autoimmune disease is systemic lupus erythematosus (SLE), pemphigus vulgaris, myasthenia gravis, hemolytic anemia, thrombocytopenia purpura, Grave's disease, Sjogren's disease, dermatomyositis, Hashimoto's disease, polymyositis, inflammatory bowel disease, multiple sclerosis (MS), diabetes mellitus, rheumatoid arthritis, or scleroderma; or

(c) the cancer is a non-Hodgkin's lymphoma, Hodgkin's lymphoma, chronic lymphocytic leukemia, hairy cell leukemia, acute lymphoblastic leukemia, multiple myeloma, carcinomas of the bladder, kidney ovary, cervix, breast, lung, nasopharynx, malignant melanoma, rituximab resistant NHL, or leukemia; or

(d) the metabolic disease is diabetes, obesity, diabetes as a consequence of obesity, hyperglycemia, dyslipidemia, hypertriglyceridemia, syndrome X, insulin resistance, impaired glucose tolerance (IGT), diabetic dyslipidemia, or hyperlipidemia.