CLAIMS

1. A genetically engineered microorganism comprising a gene encoding a surface protein, wherein the surface protein specifically interacts with one or more cell membrane(s) receptor,

wherein the one or more cell membrane receptor(s) are not exposed to the luminal side of epithelial cells of normal gastrointestinal tissue and/or epithelial tissue lining the bile duct, pancreatic duct, or common bile duct, *etc*.; and

wherein the one or more cell membrane receptor(s) are exposed to the luminal side of epithelial cells of diseased gastrointestinal tissue and/or epithelial tissue lining the bile duct, pancreatic duct, or common bile duct, *etc*.,

wherein the surface protein promotes binding and invasion of epithelial cells of diseased gastrointestinal tissue and/or epithelial tissue lining the bile duct, pancreatic duct, or common bile duct, *etc*.,

wherein the microorganism comprises one or more gene(s) encoding at least one detection marker operably linked to a promoter.

2. The genetically engineered microorganism of claim 1, wherein the promoter is a mammalian promoter or a microbial promoter.

3. The genetically engineered microorganism of claim 2, wherein the promoter is a microbial promoter and the gene encoding the detection marker further encodes an internal ribosome entry site (IRES).

4. The genetically engineered microorganism of any one of claims 1-3, wherein the at least one detection marker is selected from a fluorescent protein, a bioluminescent protein, a contrast agent for magnetic resonance imaging (MRI), a Positron Emission Tomography (PET) reporter, an enzyme reporter, a contrast agent for use in computerized tomography (CT), a Single Photon Emission Computed Tomography (SPECT) reporter, a photoacoustic reporter, an X-ray reporter, an ultrasound reporter, and ion channel reporters (*e.g.* cAMP activated cation channel).

5. The genetically engineered microorganism of claim 4, wherein the fluorescent protein is a near-infrared fluorescent protein selected from iRFP670, miRFP670, iRFP682, iRFP702, miRFP703, miRFP709, iRFP713 (iRFP), iRFP720 and iSplit.

6. The genetically engineered microorganism of any one of claims 1 to 5, wherein the one or more gene(s) encoding at least one detection marker comprises at least one intron.

7. The genetically engineered microorganism of any one of claims 1 to 6, wherein the surface protein is an invasin, or a fragment thereof.

8. The genetically engineered microorganism of any one of claims 1 to 7, wherein the microorganism comprises a second exogenous gene encoding a lysin that lyses the endocytotic vacuole, optionally wherein the lysin is listeriolysin O, or a derivative thereof.

9. The genetically engineered microorganism of any one of claims 1 to 8, wherein the microorganism is *Escherichia coli* Nissle 1917 or a derivative thereof.

10. The genetically engineered microorganism of any one of claims 1 to 9, wherein the gene encoding the surface protein is integrated at a genomic site.

11. The genetically engineered microorganism of any one of claims 8-10, wherein the second gene encoding the lysin is integrated at a genomic site.

12. The genetically engineered microorganism of claim 11, wherein the gene encoding the surface protein, the second gene encoding the lysin and the gene(s) encoding at least one detection marker are integrated at a single genomic site genomic site.

13. The genetically engineered microorganism of any one of claims 8 or 9, wherein the gene encoding the surface protein, and /or the second gene encoding the lysin are inserted on a plasmid.

14. The genetically engineered microorganism of claim 13, wherein the one or more gene(s) encoding at least one detection marker is inserted on a plasmid different from a plasmid that harbors the gene encoding the surface protein and/or the gene encoding the lysin.

15. The genetically engineered microorganism of any one of claims 8-14, wherein the microorganism is *Escherichia coli* Nissle 1917 or a derivative thereof and one or more of the genes encoding the surface protein, the lysin, and the detection marker are carried on plasmid pMUT1 or plasmid pMUT2, and/or a derivatives thereof.

16. The genetically engineered microorganism of any one of claims 13 to 15 wherein the plasmid(s) carrying one or more of the gene encoding the surface protein, the lysin, and the detection marker further comprises a selection mechanism.

17. The genetically engineered microorganism of claim 16, wherein the selection mechanism is selected from an antibiotic resistance marker, a toxin-antitoxin system, a marker causing complementation of a mutation in an essential gene, a cis acting genetic element and a combination of any two or more thereof.

18. The genetically engineered microorganism of claim 17, wherein the essential gene is selected from *dapA*, *dapD*, *murA*, *alr*, *dadX*, *murI*, *dapE*, *thyA* and a combination of any two or more thereof, optionally wherein the essential genes are a combination of *alr* and *dadX*, and optionally wherein the plasmid and/ or the second plasmid is selected by complementation of the *alr* and *dadX* mutations by a functional *alr* gene present on the plasmid and/ or the second plasmid.

19. The genetically engineered microorganism of any one of claims 1-18, wherein the microorganism harbors at least one nutritional auxotrophic mutation selected from *dapA*, *dapD*, *dapE*, *murA*, *alr*, *dadX*, *murI*, *thyA*, *aroC*, *ompC*, and *ompF*, optionally wherein the strain harbors a combination of *dapA alr* and *dadX* auxotrophic mutations.

20. Use of the genetically engineered microorganism of any one of claims 1 to 19 in the preparation of a composition for detecting diseased epithelial cells, wherein the composition comprising the genetically engineered microorganism is to be administered to the subject; wherein expression of the detection marker is to be detected for thereby detecting diseased epithelial cells to diagnose a disease in the subject, optionally wherein a treatment is to be administered to the subject.

21. The use of claim 20, wherein the disease is selected from a precancerous lesion, cancer, ulcerative colitis, Crohn's disease, Barrett's esophagus, irritable bowel syndrome and irritable bowel disease.

22. The use of claim 21, wherein the precancerous lesion comprises:

a polyp selected from sessile polyp, serrated polyp (*e.g.* hyperplastic polyps, sessile serrated adenomas/polyps, and traditional serrated adenoma), sessile serrated polyp, flat polyp, sub-pedunculated polyp , pedunculated polyp, and a combination thereof;

a biliary intraepithelial neoplasm (BilIN) selected from BilIN-1, BilIN-2, BilIN-3, and cholangiocarcinoma; and/or

a pancreatic intraepithelial neoplasm (PanIN) selected from PanIN -1, PanIN -2, PanIN -3 and pancreatic ductal adenocarcinoma (PDAC).

23. The use of claim 22, wherein the polyp is a diminutive polyp.

24. The use of claim 21 or 22, wherein the precancerous lesion has a size of less than about 0.1 mm, less than about 0.25 mm, less than about 0.5 mm, less than about 1 mm, less than about 2 mm, less than about 5 mm, less than about 8 mm, less than about 10 mm, less than about 15 mm, less than about 20 mm, less than about 25 mm, or less than about 30 mm.

25. The use of claim 21, wherein the cancer comprises Lynch syndrome, familial adenomatous polyposis, hereditary non-polyposis colon cancer (HNPCC), or a sporadic cancer.

26. The use of claim 21, wherein the cancer is selected from squamous cell carcinoma of anus, low-grade squamous intraepithelial lesions (LSIL) of anus, high-grade squamous intraepithelial lesions (HSIL) of anus, colorectal cancer, colorectal adenocarcinoma, familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, colorectal polyposis (*e.g.* Peutz–Jeghers syndrome, juvenile polyposis syndrome, MUTYH-associated polyposis, familial adenomatous polyposis/Gardner's syndrome, and Cronkhite-Canada syndrome), carcinoid, pseudomyxoma peritonei, duodenal adenocarcinoma, premalignant adenoma of small bowel, distal bile duct carcinomas, biliary intraepithelial neoplasm (BilIN), BilIN-1, BilIN-2, BilIN-3 or cholangiocarcinoma, pancreatic ductal adenocarcinoma (PDAC), pancreatic intraepithelial neoplasm (PanIN), PanIN -1, PanIN -2, PanIN -3, gastric carcinoma, signet ring cell carcinoma (SRCC), gastric lymphoma (MALT lymphoma), linitis plastic (Brinton’s disease), and squamous cell carcinoma of esophagus and adenocarcinoma.

27. Use of claim 20, wherein the disease is cancer and a treatment is to be administered to a subject if the expression of the detection marker is observed.