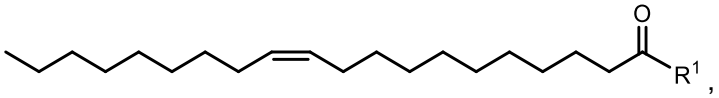
and architectural changes and is the focal neoplastic lesion, which has the highest risk of gastric cancer development. Dysplasia may evolve into adenocarcinoma when oncogenic environments chronically persist, and therefore, it is considered a key transition stage entering adenocarcinoma development in epithelial carcinogenesis. Dysplastic stem cells, a stem cell population which is first present in the dysplastic stage and evolves to gastric adenocarcinoma, was recently identified. However, the molecular and cellular mechanisms of the precancerous metaplasia progression to dysplasia and even to adenocarcinoma still remain poorly understood.

Metabolism includes all the chemical reactions that produce energy or generate biological building blocks of cells. Metabolic reprogramming is essential for supplying energy to meet the increased demands when cells need exponential growth and proliferation, especially in cancer cells. Cells stabilize metabolic pathways to control suitable levels of critical metabolites which are linked to cell signaling pathways and epigenetics. Recent studies have reported that bioactive metabolites are important for regulation of cellular heterogeneity, tumor growth, and immune response. Fatty acid (FA) metabolism in cancer is implicated in tumor progression, metastasis potential, and drug resistance. FAs are critical in cellular homeostasis in a variety of biological processes including energy supply and storage, cell signaling, transcription control, phospholipid synthesis, and membrane fluidity. FAs are synthesized *de novo* or obtained from the diet and modified through metabolic pathways that include desaturation and elongation steps. In particular, FA desaturation generates building blocks of membrane lipids and protects the cells against lipotoxicity of saturated fatty acids which impair membrane fluidity. Stearoyl-CoA desaturase (SCD) is a key enzyme that generates monounsaturated fatty acids (MUFAs) which contribute to lipid homeostasis. Although it is well known that the FA metabolism supports cancer cell proliferation and progression, it remains undefined whether the FA metabolism occurs to fuel dysplastic cells or even any specific metabolic pathway can regulate dysplasia proliferation or progression.

What is needed are conjugated metabolites for cancer and precancer detection and treatment.

SUMMARY

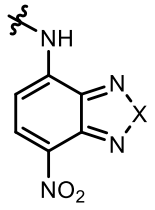
In an aspect, there is provided a compound of formula (I):



,

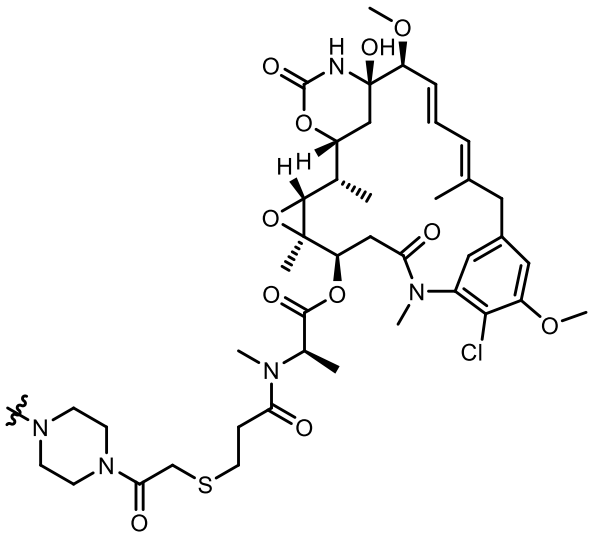
wherein R^1 is:

a fluorophore or a luminescent label selected from 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan), nitrobenzoselenadiazole, fluorescein, rhodamine, aminomethylcoumarin acetate (AMCA), calcein, or cyanine;



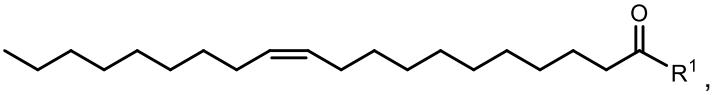
, where X is O or Se;

mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90; or



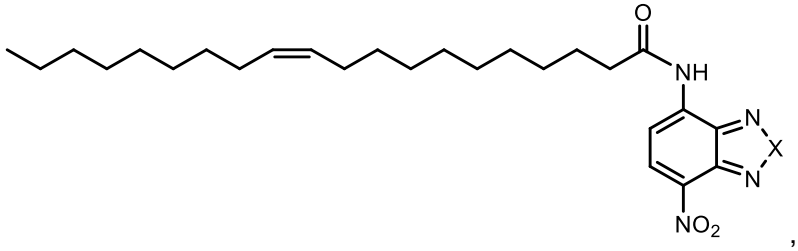
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One example described herein is a compound of formula (I):



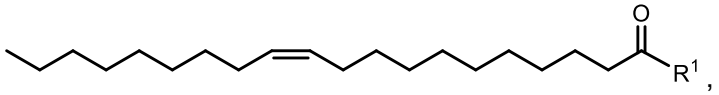
,

wherein R^1 is a fluorophore or a luminescent label selected from 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan), nitrobenzoselenadiazole, fluorescein, rhodamine, aminomethylcoumarin acetate (AMCA), calcein, or cyanine. In one example, the compound is:



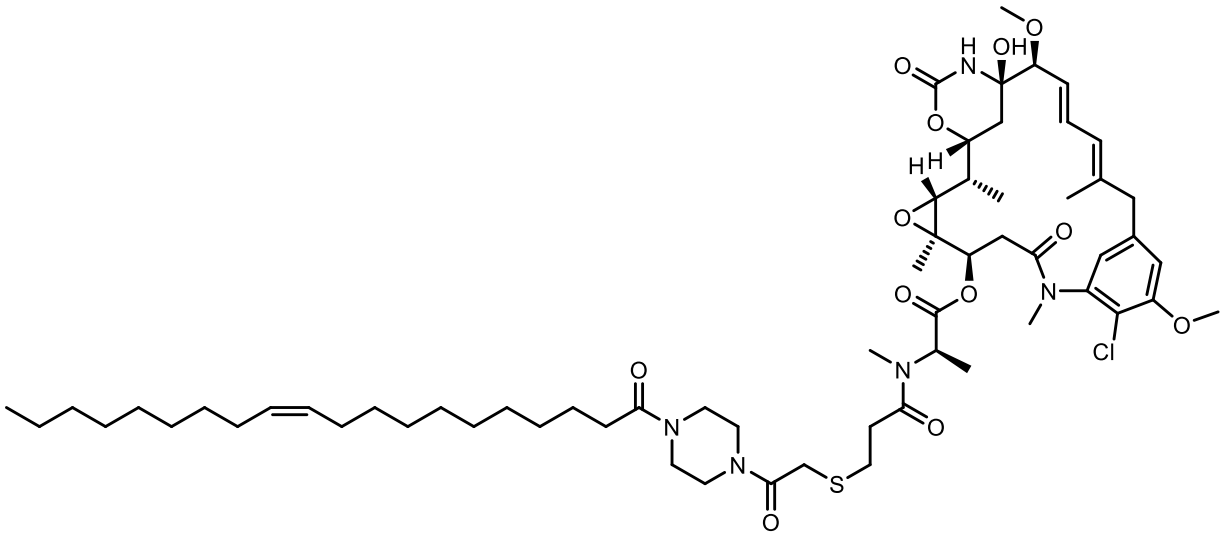
, where X is O or Se.

Another example described herein is a compound of formula (I):



,

wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90. In one example, the compound is:

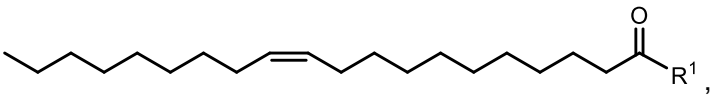


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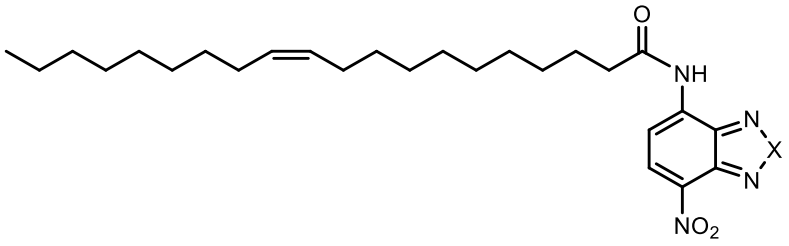
In another aspect, there is provided a method for detecting epithelial cell dysplasia, the method comprising: contacting an epithelial cell with a compound as described herein; incubating for a period of time; irradiating the epithelial cell with ultraviolet light, whereby a dysplastic epithelial cell will fluoresce; and imaging the fluorescent dysplastic epithelial cell. In one example, imaging comprises positron emission tomography (PET) imaging, mass spectrometry imaging, immunofluorescence imaging,

fluorescence molecular endoscopy, or fluorescence-guided intraluminal endoscopy. In another example, the epithelial cell comprises a gastric epithelial cell.

Another example described herein is a research tool for detecting epithelial dysplasia, the research tool comprising a compound of formula (I):

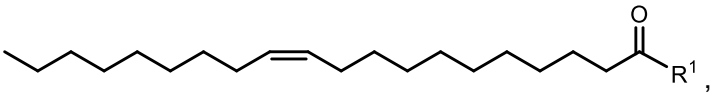


wherein R^1 is a fluorophore or a luminescent label selected from 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan), nitrobenzoselenadiazole, fluorescein, rhodamine, aminomethylcoumarin acetate (AMCA), calcein, or cyanine. In one example, the compound is:

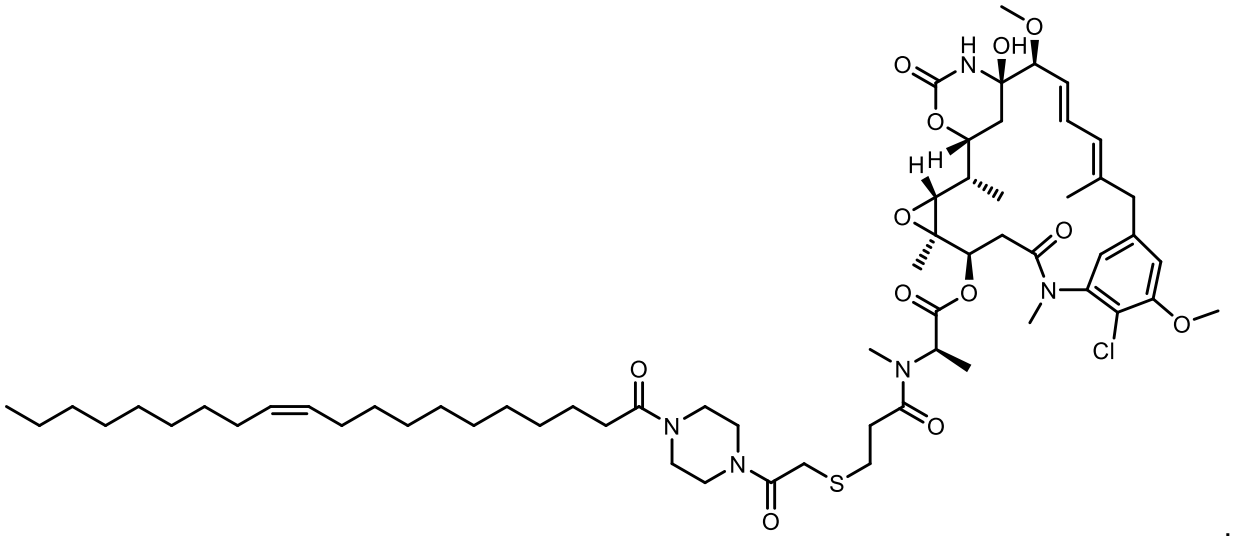


, where X is O or Se.

Another example described herein is a research tool comprising a compound of formula (I):

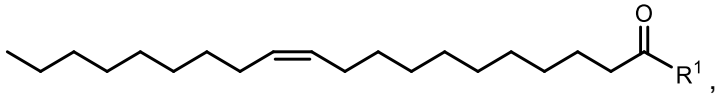


wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90. In one example, the compound is:



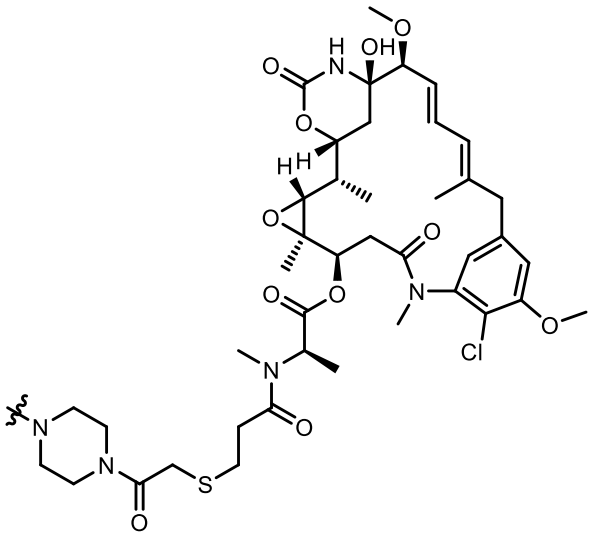
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In another aspect, there is provided a use of a compound of formula (I):



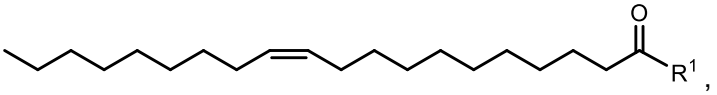
in the manufacture of a medicament for inhibiting cancer or precancer in a cell or a subject in need thereof,

wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90, or

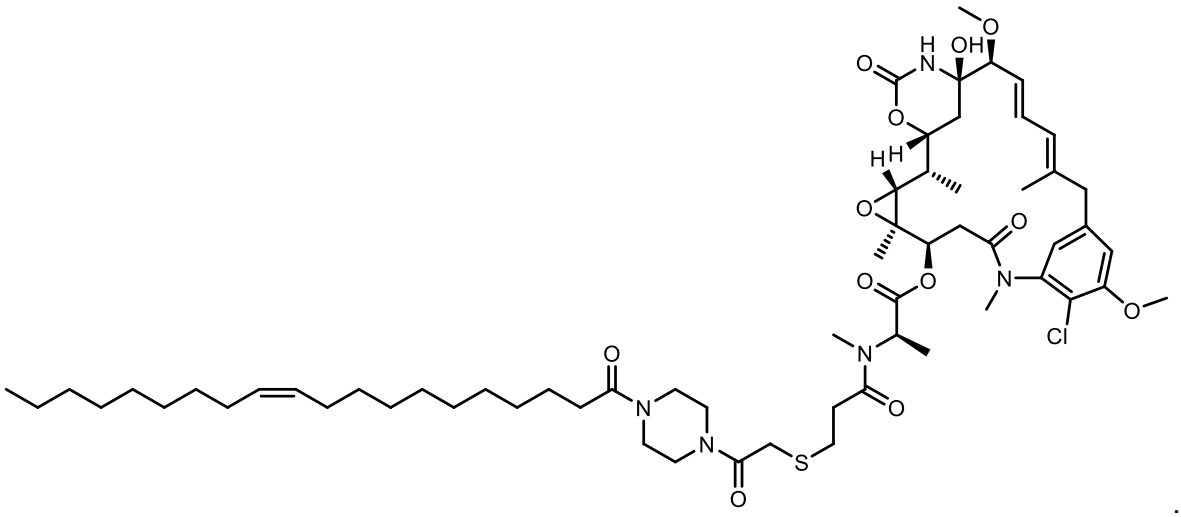


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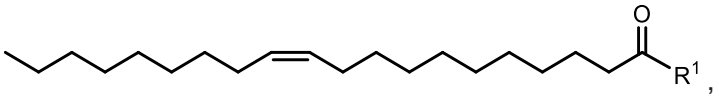
Another example described herein is a method of inhibiting cancer or precancer in a cell or a subject in need thereof, the method comprising administering to the cell or the subject a therapeutically effective amount of a compound of formula (I):



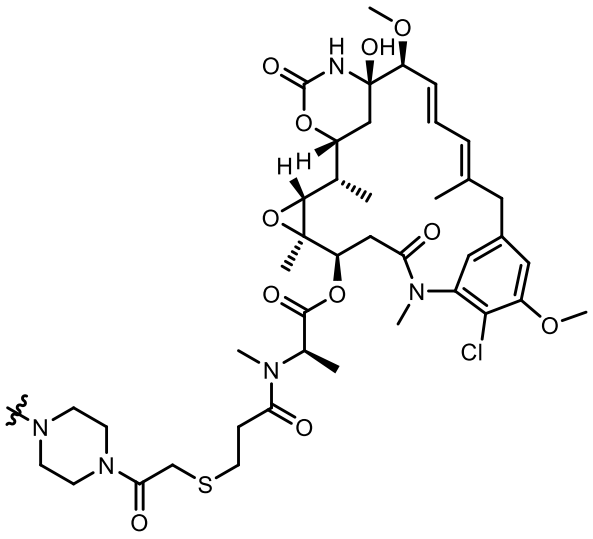
wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90. In one example, the compound is:



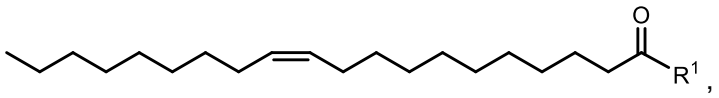
In another aspect, there is provided a use of formula (I):



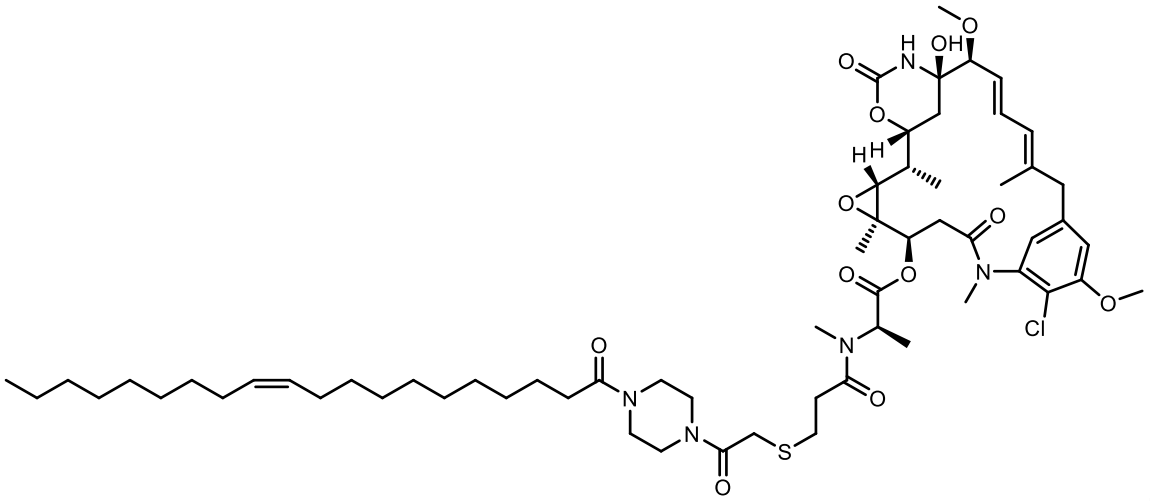
in the manufacture of a medicament for treating a subject having cancer or precancer,
wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, Yttrium-90, or



Another example described herein is a method of treating a subject having cancer or precancer, the method comprising administering to the subject a therapeutically effective amount of a compound of formula (I):



wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90. In one example, the compound is:



. In another example, the subject has gastrointestinal cancer or precancer, or is suspected of developing gastrointestinal cancer or precancer.

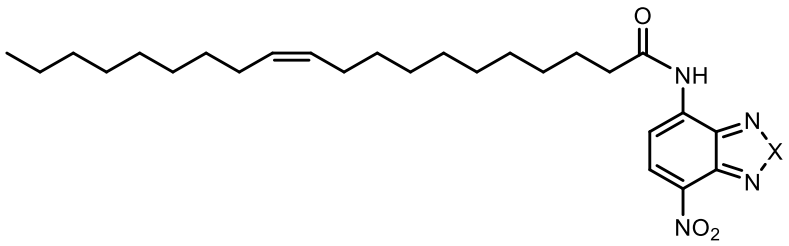
In another aspect, there is provided a use of a therapeutically effective amount of 4-(2-chlorophenoxy)-*N*-(3-(methylcarbamoyl)phenyl)piperidine-1-carboxamide (A939572) in the manufacture of a medicament for inhibiting the transition of a metaplastic cell to a dysplastic cell in a cell or a subject in need thereof.

Another example described herein is a method for inhibiting the transition of a metaplastic cell to a dysplastic cell, the method comprising administering a therapeutically effective amount of 4-(2-chlorophenoxy)-*N*-(3-(methylcarbamoyl)phenyl)piperidine-1-carboxamide (A939572) to a cell or a subject in need thereof. In one example, the therapeutically effective amount of A939572 is from about 5 mg/kg to about 100 mg/kg. In another example, the therapeutically effective amount of A939572 is administered on a daily basis for about 1 day to about 6 months. In another example, the cell comprises a gastric epithelial cell. In another example, the subject has gastrointestinal cancer or precancer, or is suspected of developing gastrointestinal cancer or precancer.

Another example described herein is a method for treating a metaplastic cell to reduce the incidence of carcinoma, the method comprising administering a therapeutically effective amount of 4-(2-chlorophenoxy)-*N*-(3-(methylcarbamoyl)phenyl)piperidine-1-carboxamide (A939572) to a cell or a subject in need thereof. In one example, the method inhibits the transition of the metaplastic cell to a dysplastic cell, thereby reducing the incidence of carcinoma in the cell or the subject in need thereof. In another example, the therapeutically effective amount of A939572 is from about 5 mg/kg to about 100 mg/kg. In another example, the therapeutically effective amount of A939572 is administered on a daily basis

for about 1 day to about 6 months. In another example, the cell comprises a gastric epithelial cell. In another example, the subject has gastrointestinal cancer or precancer, or is suspected of developing gastrointestinal cancer or precancer.

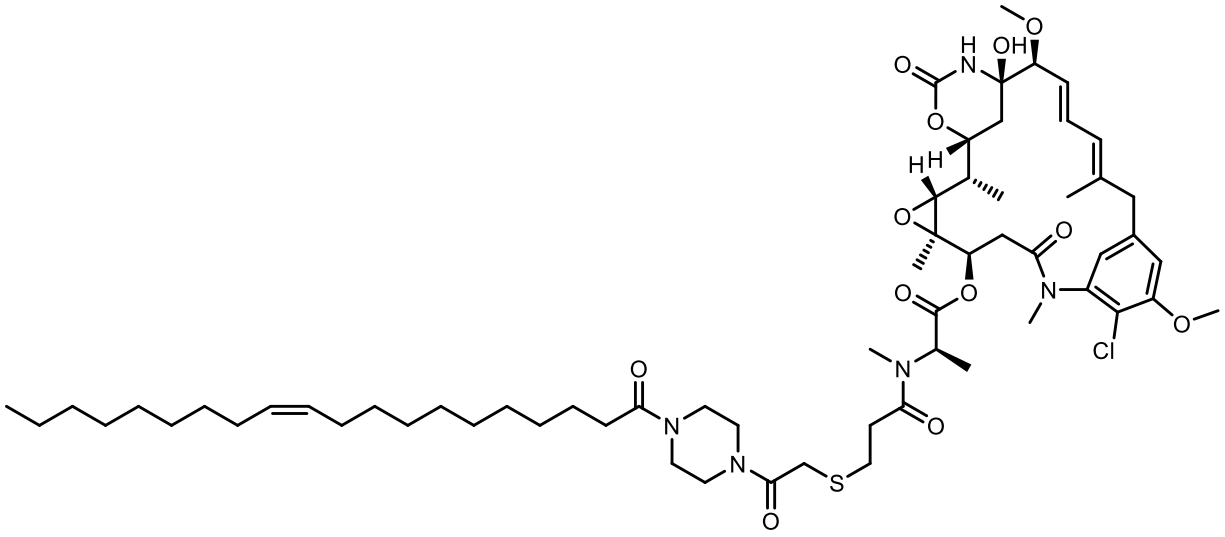
In another aspect, there is provided a method of making a compound comprising *cis*-11-eicosenoic acid conjugated to 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan) or nitrobenzoselenadiazole:



, where X is O or Se;

the method comprising: (a) combining *cis*-11-eicosenoic acid with dimethylformamide (DMF) solvent to create a solution; (b) adding *N*,*N*-diisopropylethylamine (DIPEA) to the solution; (c) adding 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) to the solution to create a reaction mixture; (d) mixing the reaction mixture; (e) adding nitrobenzofurazan or nitrobenzoselenadiazole to the reaction mixture to create a conjugate mixture; (f) mixing the conjugate mixture; and (g) one or more of diluting, washing, drying, or filtering the conjugate mixture to generate the compound. In one example, steps (a)–(e) are performed at about 0 °C and steps (f)–(g) are performed at room temperature. In another example, the conjugate mixture is diluted with ethyl acetate and washed with aqueous citric acid. In another example, the conjugate mixture is dried over $MgSO_4$. In another example, the method further comprises purifying the compound using column chromatography.

In another aspect, there is provided a method of making a compound comprising *cis*-11-eicosenoic acid conjugated to mertansine:



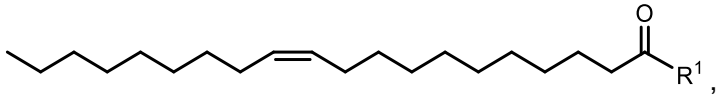
,

the method comprising: (a) combining mertansine carboxylic acid with dimethylformamide (DMF) solvent to create a solution; (b) adding hexafluorophosphate azabenzotriazole tetramethyl uranium (HATU) and *N*-methylmorpholine (NMM) to the solution to create a reaction mixture; (c) mixing the reaction mixture; (d) adding piperazine-conjugated *cis*-11-eicosenoic acid to the

CLAIMS

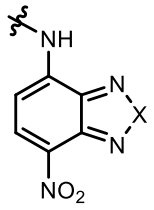
What is claimed:

1. A compound of formula (I):



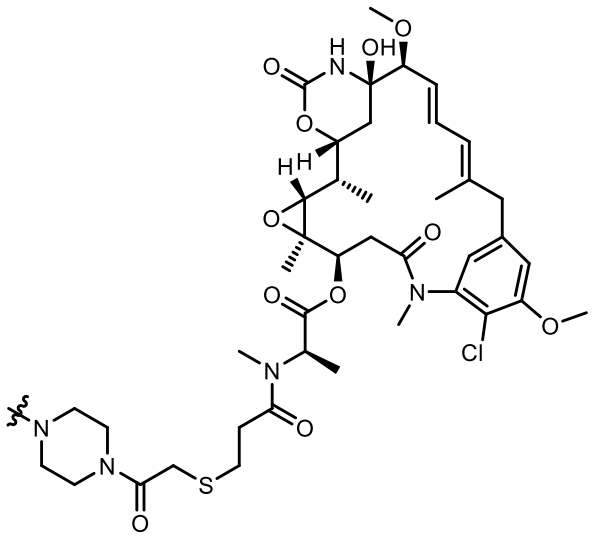
wherein R^1 is:

a fluorophore or a luminescent label selected from 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan), nitrobenzoselenadiazole, fluorescein, rhodamine, aminomethylcoumarin acetate (AMCA), calcein, or cyanine;



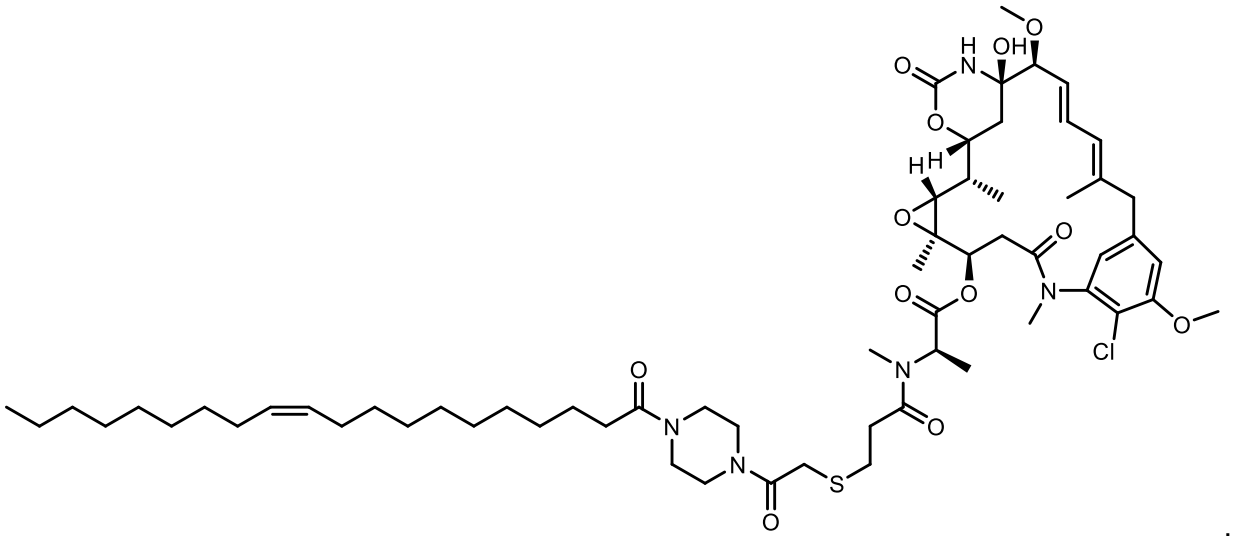
, where X is O or Se;

mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or Yttrium-90; or



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2. The compound of claim 1, wherein the compound is:

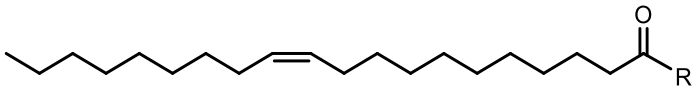


3. A method for detecting epithelial cell dysplasia, the method comprising:
contacting an epithelial cell with the compound of claim 1;
incubating for a period of time;
irradiating the epithelial cell with ultraviolet light, whereby a dysplastic epithelial cell will fluoresce; and
imaging the fluorescent dysplastic epithelial cell.

4. The method of claim 3, wherein imaging comprises positron emission tomography (PET) imaging, mass spectrometry imaging, immunofluorescence imaging, fluorescence molecular endoscopy, or fluorescence-guided intraluminal endoscopy.

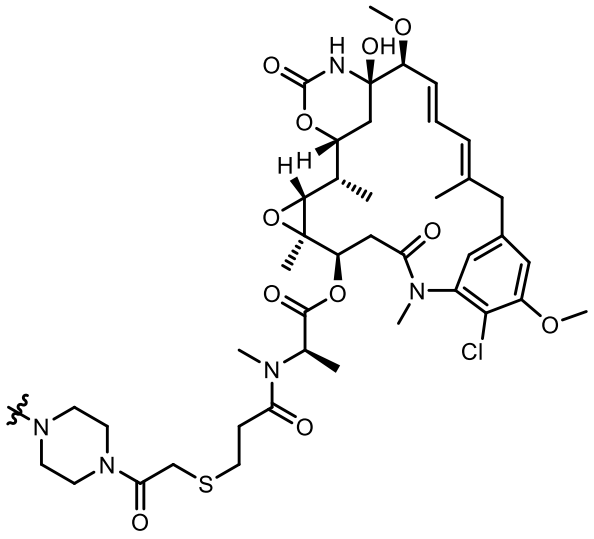
5. The method of claim 3, wherein the epithelial cell comprises a gastric epithelial cell.

6. Use of a compound of formula (I):



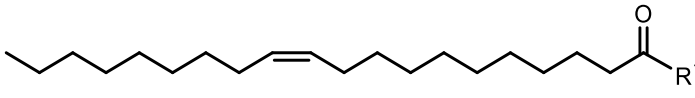
, in the manufacture of a medicament for inhibiting cancer or precancer in a cell or a subject in need thereof,

wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin, or



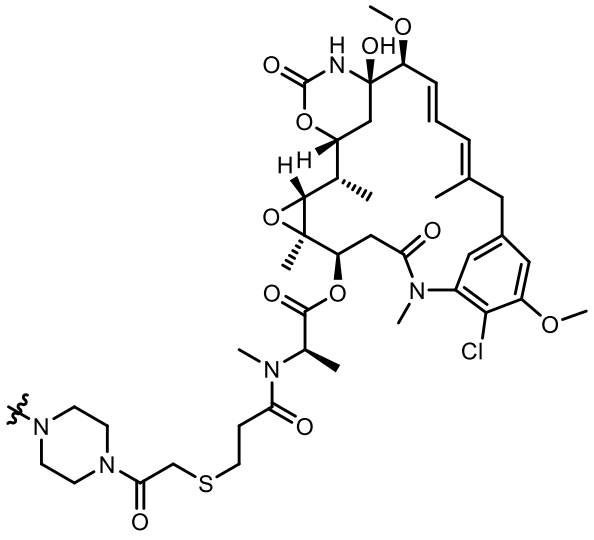
Yttrium-90, or .

7. Use of formula (I):



, in the manufacture of a medicament for treating a subject having cancer or precancer,

wherein R^1 is selected from mertansine (DM1), taxol, calicheamicin, monomethyl auristatin E (MMAE), deruxtecan, SN-38, Pseudomonas exotoxin, diphtheria toxin,



Yttrium-90, or .

8. The use of claim 7, wherein the subject has gastrointestinal cancer or precancer, or is suspected of developing gastrointestinal cancer or precancer.

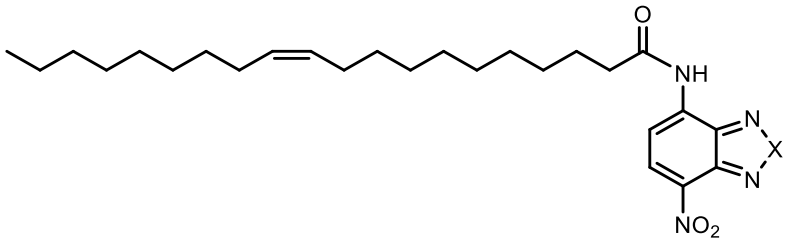
9. Use of a therapeutically effective amount of 4-(2-chlorophenoxy)-*N*-(3-(methylcarbamoyl)phenyl)piperidine-1-carboxamide (A939572) in the manufacture of a medicament for inhibiting the transition of a metaplastic cell to a dysplastic cell in a cell or a subject in need thereof.

10. The use of claim 9, wherein the therapeutically effective amount of A939572 is from about 5 mg/kg to about 100 mg/kg.

11. The use of claim 9, wherein the therapeutically effective amount of A939572 is administered on a daily basis for about 1 day to about 6 months.

12. The use of claim 9, wherein the cell comprises a gastric epithelial cell.

13. A method of making a compound comprising *cis*-11-eicosenoic acid conjugated to 7-nitrobenzo[c][1,2,5]oxadiazol-4-amine (nitrobenzofurazan) or nitrobenzoselenadiazole:



, where X is O or Se;

the method comprising:

(a) combining *cis*-11-eicosenoic acid with dimethylformamide (DMF) solvent to create a solution;

(b) adding *N*,*N*-diisopropylethylamine (DIPEA) to the solution;

(c) adding 2-(1H-benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HBTU) to the solution to create a reaction mixture;

(d) mixing the reaction mixture;

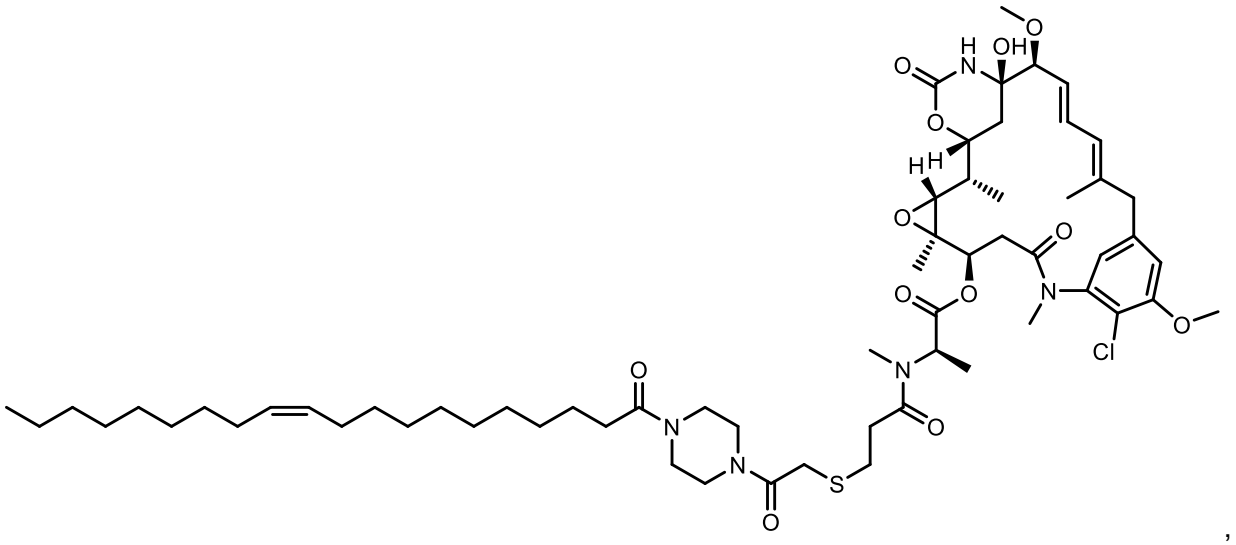
(e) adding nitrobenzofurazan or nitrobenzoselenadiazole to the reaction mixture to create a conjugate mixture;

(f) mixing the conjugate mixture; and

(g) one or more of diluting, washing, drying, or filtering the conjugate mixture to generate the compound.

14. The method of claim 13, wherein steps (a)–(e) are performed at about 0 °C and steps (f)–(g) are performed at room temperature.

15. A method of making a compound comprising *cis*-11-eicosenoic acid conjugated to mertansine:



,

the method comprising:

(a) combining mertansine carboxylic acid with dimethylformamide (DMF) solvent to create a solution;

(b) adding hexafluorophosphate azabenzotriazole tetramethyl uranium (HATU) and *N*-methylmorpholine (NMM) to the solution to create a reaction mixture;

(c) mixing the reaction mixture;

(d) adding piperazine-conjugated *cis*-11-eicosenoic acid to the reaction mixture to create a conjugate mixture;

(e) mixing the conjugate mixture; and

(f) one or more of diluting, washing, drying, or filtering the conjugate mixture to generate the compound.