

methods can also reduce and/or inhibit metastasis, cancer drug resistance, or combinations thereof. In some cases, the compositions and methods are useful for modulating kinesin-13 expression, and the compositions and methods can reduce chromosomal instability.

5 For example, methods and compositions are described herein that can increase the expression and/or activity of kinesin-13 proteins such as Kif2b, MCAK/Kif2c, or KIF13A in cells. In some cases, the methods and compositions can increase the expression and/or activity of ABCC4, ABCG2. The methods can also include inhibiting STING, cGAS, NF- κ B transcription factor p52, NF- κ B
10 transcription factor RelB, ENPP1, LT β R, BAFFR, CD40, RANK, FN14, NIK (MAP3K14), MST1, or any combination thereof in a mammalian cell. Such compositions and methods are useful for treating and inhibiting the progression of cancer, including the development and progression of metastatic cancer.

Other methods are described herein that include assays for the design
15 and development of new compounds that are useful for treatment of cancer, including metastatic cancer.

In one aspect, the present disclosure refers to a method comprising: (a) mixing a test compound with a metastatic cancer cell sample in a culture medium to produce a test assay; (b) incubating the test assay for a time and under conditions sufficient for the test
20 compound to associate with or penetrate the cells; (c) measuring:

- cGAMP amounts or concentrations in the culture medium, in the cells, or in a combination thereof to produce a test assay value;
- distances between centrosomes within a series of the cells to produce a mean distance result;
- a quantity of RELB translocation into nuclei of the cells; and

(d) selecting a test compound with:

- 25
- a lower test assay cGAMP value than a reference cGAMP value;
 - a lower mean distance result than a reference distance;
 - lower quantity of RELB translocation into nuclei of the cells than a reference quantity;

to thereby produce a test compound effective for treatment of chromosomal instability.

In another aspect, the present disclosure refers to a method comprising: (a) measuring: the amount or concentration of cGAMP produced from a known number or weight of cells or tissues from a cell or tissue sample that has been obtained from a patient, to generate a reference cGAMP value; (b) mixing the same known number or weight of
5 cells or tissues from the sample with a test compound to generate a test assay; (c) measuring the cGAMP amount or concentration in the test assay to generate a test assay cGAMP value; (d) optionally repeating steps (b) and (c); and selecting any test compound with a lower test assay cGAMP value than the reference cGAMP value to thereby identify at least one effective test compound.

10 In another aspect, the present disclosure refers to an effective test compound produced by the method as disclosed herein.

In another aspect, the present disclosure refers to use of a chemotherapeutic agent in a composition in the manufacture of a medicament for administration to a patient with a cell sample or bodily fluid sample:

- a. having at least 10% detectable chromosomal missegregations within one or cells of the cell sample;
- b. having at least 3% detectable micronuclei within one or cells of the cell sample;
- c. having detectable cytosolic double-stranded DNA within one or cells of the cell sample; or
- d. having at least 10% greater concentration or amount of cGAMP in the cell sample or bodily fluid sample.

15 **Brief Description of the Figures**

FIG. 1A-1K illustrates that chromosomal aberrations are prevalent in human metastases. FIG. 1A graphically illustrates the Weighted Genomic Instability Index (wGII) of matched primary tumors (P) and brain metastases (M), where $n = 61$ primary tumors-metastasis matched pairs, boxes span the 25th-75th
20 percentiles, bars span 10th-90th percentile, and significance was tested using Wilcoxon matched-pairs signed rank test. RCC, renal cell carcinoma. FIG. 1B-1 graphically illustrates differences in wGII between metastases and matched primary breast tumors. FIG. 1B-2 graphically illustrates differences in wGII between metastases and matched primary lung tumors. FIG. 1B-3 graphically
25 illustrates differences in wGII between metastases and matched renal cell carcinoma primary tumors. FIG. 1B-4 graphically illustrates differences in wGII between metastases and matched primary tumors. FIG. 1C graphically illustrates the number of clones (based on karyotypes) in primary (P) breast tumors ($n =$

What is claimed is:

1. A method comprising: (a) mixing a test compound with a metastatic cancer cell sample in a culture medium to produce a test assay; (b) incubating the test assay for a time and under conditions sufficient for the test compound to associate with or penetrate the cells; (c) measuring:
 - cGAMP amounts or concentrations in the culture medium, in the cells, or in a combination thereof to produce a test assay value;
 - distances between centrosomes within a series of the cells to produce a mean distance result;
 - a quantity of RELB translocation into nuclei of the cells; and(d) selecting a test compound with:
 - a lower test assay cGAMP value than a reference cGAMP value;
 - a lower mean distance result than a reference distance;
 - lower quantity of RELB translocation into nuclei of the cells than a reference quantity;to thereby produce a test compound effective for treatment of chromosomal instability.
2. The method of claim 1, wherein the reference is
 - a. the amount or concentration of cGAMP in an assay mixture that does not contain a test compound;
 - b. the distance between centromeres in metastatic cancer cells within an assay mixture that does not contain a test compound; or
 - c. the quantity of RELB translocation into nuclei of metastatic cancer cells within an assay mixture that does not contain a test compound.
3. The method of claim 1 or 2, further comprising extracting the sample or culture medium with an alcohol to produce an alcohol extract before measuring the cGAMP.
4. The method of claim 3, further comprising purifying the alcohol extract by Solid Phase Extraction (SPE) using one or more HyperSep aminopropyl solid phase columns to produce a semi-pure test sample before measuring the cGAMP of the semi-pure test sample.
5. The method of any one of claims 1-4, wherein measuring cGAMP amounts or concentrations comprises liquid chromatography and/or mass spectroscopy to measure the level of cGAMP.
6. The method of any one of claims 1-5, wherein the test compound is to be further administered to an animal model to identify a therapeutic agent.

7. The method of claim 6, wherein the therapeutic agent is to be further administered to a patient.
8. A method comprising: (a) measuring: the amount or concentration of cGAMP produced from a known number or weight of cells or tissues from a cell or tissue sample that has been obtained from a patient, to generate a reference cGAMP value; (b) mixing the same known number or weight of cells or tissues from the sample with a test compound to generate a test assay; (c) measuring the cGAMP amount or concentration in the test assay to generate a test assay cGAMP value; (d) optionally repeating steps (b) and (c); and selecting any test compound with a lower test assay cGAMP value than the reference cGAMP value to thereby identify at least one effective test compound.
9. The method of claim 8, wherein the sample comprises metastatic cancer cells or metastatic tissues.
10. The method of 8 or 9, further comprising extracting the cell or tissue sample with an alcohol to produce an alcohol extract before measuring the cGAMP.
11. The method of any one of claims 8-10, further comprising extracting the cell or tissue sample with methanol to produce a methanol extract and measuring the cGAMP in the methanol extract.
12. The method of claim 10 or 11, further comprising purifying the alcohol extract or the methanol extract by Solid Phase Extraction (SPE) using one or more HyperSep aminopropyl solid phase columns to produce a semi-pure test sample before measuring the cGAMP of the semi-pure test sample.
13. The method of any one of claims 8-12, wherein measuring cGAMP amounts or concentrations comprises liquid chromatography and/or mass spectroscopy.
14. The method of any one of claims 8-13, wherein the effective test compound is to be further administered to an animal cancer model.
15. The method of any one of claims 8-14, wherein the effective test compound is to be further administered to a patient or to the patient from whom the cell or tissue sample as obtained.
16. An effective test compound produced by the method of any one of claims 1-15.
17. The method of any one of claims 1-15, wherein the cell sample is from a patient, and the method further comprising measuring:
 - a. detectable chromosomal missegregations within one or cells of the cell sample;
 - b. detectable micronuclei within one or cells of the cell sample; or
 - c. detectable cytosolic double-stranded DNA within one or cells of the cell sample.

18. The method of claim 17, further comprising monitoring samples from the patient over time to quantify chromosomal missegregations, micronuclei, cytosolic double-stranded DNA, or cGAMP within cells or bodily fluids of the patient.
19. The method of claim 17, further comprising (a) quantifying expression levels of the following genes in a test sample from a patient: PELI2, BMP2, SHH, TNS4, RAB3B, ROBO1, ARHGAP28, CHN2, CST1, F13A1, CPVL, SEMA6D, C9orf152, NHSL2, GTF2IP7, DPYSL3, PCDH7, KHDRBS3, TRAC, TMEM156, CST4, CD24, or FGF5, to generate quantified expression levels each of following genes in the test sample: PELI2, BMP2, SHH, TNS4, RAB3B, ROBO1, ARHGAP28, CHN2, CST1, F13A1, CPVL, SEMA6D, C9orf152, NHSL2, GTF2IP7, DPYSL3, PCDH7, KHDRBS3, TRAC, TMEM156, CST4, CD24, or FGF5; and (b) informing the patient of longer metastasis-free survival when each quantified expression level is greater than a median reference expression level for each of these genes.
20. The method of claim 17, wherein the median reference expression level for each of these genes is the median expression of each of these genes in samples from a series of patients with metastatic cancer.
21. The method of claim 17 or 18, wherein the patient has breast cancer.
22. Use of a chemotherapeutic agent in a composition in the manufacture of a medicament for administration to a patient with a cell sample or bodily fluid sample:
 - a. having at least 10% detectable chromosomal missegregations within one or cells of the cell sample;
 - b. having at least 3% detectable micronuclei within one or cells of the cell sample;
 - c. having detectable cytosolic double-stranded DNA within one or cells of the cell sample; or
 - d. having at least 10% greater concentration or amount of cGAMP in the cell sample or bodily fluid sample.
23. The use of claim 22, wherein the cell sample or bodily fluid sample has:
 - a. 15 - 20% of chromosomes exhibiting missegregations in anaphase cells of the cell sample;
 - b. 5 - 8% of cells in the cell sample exhibiting micronuclei;
 - c. 1-fold to 2-fold increase in staining intensity within the cytosol compared to a normal non-cancer tissue; or
 - d. 1-fold to 2-fold greater concentration or amount of cGAMP in the bodily fluid sample than a non-cancerous bodily fluid sample.

24. The use of claim 22, wherein the metastatic chemotherapeutic agent is a composition comprising one or more kinesin-13 protein(s), one or more MCAK protein(s), or a combination thereof.
25. The use of claim 22, wherein the metastatic chemotherapeutic agent is a composition comprising a kinesin-13 nucleic acid or an expression cassette having a promoter operably linked to a nucleic acid segment encoding a kinesin-13 protein.
26. The method of any one of claims 1-15 and 17-21, the effective test compound of claim 16, or the use of claim 22 or 23, wherein the metastatic cancer cell sample, the sample, the cell sample, or the test sample comprises metastatic cancer cells with one or more chromosomal instability.