

Aguzzi *et al.*, *Trends Cell Biol*, 26(7), 2016, 547-558). However, in addition to the lack of understanding of the mechanisms governing condensate partitioning of compounds, there is little or nothing known regarding how to identify test compounds that interact with condensates, how to design compounds to improve interactions with condensates, and how such information can be used to improve treatment of diseases.

[0005] All references cited herein, including patent applications and publications, are incorporated by reference in their entirety.

SUMMARY

[0006] In some examples, provided herein are methods of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution; (b) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate. In some examples, the methods further comprise causing the formation of the target condensate prior to step (a).

[0006a] In one aspect, the present disclosure refers to a method of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution; (b) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate.

[0007] In some examples, provided herein are methods of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) adding the test compound to a composition comprising a target condensate and an extra-condensate solution; and (b) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate. In some examples, the methods further comprise causing the formation of the target condensate prior to step (a).

[0008] In some examples, provided herein are methods of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) causing the formation of the target condensate in the presence of the test compound to obtain a composition comprising the target condensate and an extra-condensate solution; and (b) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate.

[0009] In some examples, provided herein are methods of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) adding the test compound to a composition comprising precursor molecules; (b) causing the formation of the target condensate to obtain a composition comprising the target condensate and an extra-condensate

solution; and (c) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate. In some examples, the methods further comprise combining the test compound and a precursor composition comprising precursor molecules prior to step (a). In some examples, the methods further comprise adding the test compound to a precursor composition comprising precursor molecules prior to step (a).

[0010] In some examples, the methods further comprise determining the amount of the test compound in the extra-condensate solution. In some examples, the amount of the test compound in the target condensate is determined prior to, simultaneously with, or after the amount of the test compound in the extra-condensate solution is determined. In some examples, the methods further comprise determining the ratio of the amount of test compound in the target condensate and the amount of test compound in the extra-condensate solution. In some examples, the methods further comprise separating the target condensate from the extra-condensate solution. In some examples, the methods further comprise identifying the target condensate prior to determining the amount of test compound in the target condensate.

[0011] In some examples, dysregulation of the target condensate is associated with a disease. In some examples, the methods further comprise characterizing the target condensate by identifying one or more macromolecules comprised therein. In some examples, the identifying comprises determining the amount of the one or more macromolecules in the target condensate. In some examples, the methods further comprise determining the ratio of the amount of test compound in the target condensate and the amount of the one or more macromolecules in the target condensate. In some examples, the target condensate comprises a protein comprising an intrinsically disordered sequence. In some examples, the methods further comprise labeling the target condensate in order to visualize the target condensate. In some examples, the target condensate is labeled with a radioactive label, a colorimetric label, a chemically-reactive label, or a fluorescent label.

[0012] In some examples, the composition comprises a cell. In some examples, the cell is a microorganism or an animal cell. In some examples, the cell comprises a condensate that is determined to be dysregulated. In some examples, the cell has one or more features of a neurodegenerative or proliferative disease.

[0013] In some examples, the target condensate is a cellular condensate. In some examples, cellular condensate is a cleavage body, a P-granule, a histone locus body, a multivesicular body, a neuronal RNA granule, a nuclear gem, a nuclear pore, a nuclear speckle, a nuclear stress body, a nucleolus, a Oct1/PTF/transcription (OPT) domain, a paraspeckle, a perinucleolar compartment, a PML nuclear body, a PML oncogenic domain, a polycomb body, a processing body, a signaling cluster, a Sam68 nuclear body, a stress granule, or a splicing speckle. In some examples, the target condensate is in a cell. In some examples, the cell is a microorganism or an animal cell. In some examples, the cell has one or more features of a neurodegenerative or proliferative disease. In some examples, the extra-condensate solution is intracellular fluid. In some examples, the intracellular fluid is cytosol or nucleosol.

[0014] In some examples, the target condensate is not in a cell. In some examples, the target condensate is an extracellular condensate. In some examples, the extra-condensate solution is extracellular fluid. In some examples, the extracellular fluid is interstitial fluid.

[0015] In some examples, the method is a cell free assay method. In some examples, the composition does not comprise a cell. In some examples, the composition comprises one or more of: a macromolecule, a salt, and a buffer.

[0016] In some examples, the composition comprises two or more target condensates. In some examples, the methods further comprise repeating the steps of the method for one or more additional condensates.

[0017] In some examples, the test compound is small molecule, a polypeptide, or a nucleic acid. In some examples, the test compound comprises a test compound label. In some examples, the test compound label is a radioactive label, a colorimetric label, a chemically-reactive label, or a fluorescent label. In some examples, the test compound label is a fluorescent label. In some examples, the amount of the test compound is determined by detecting the test compound label. In some examples, the amount of the test compound is determined by mass spectrometry, liquid chromatography, quantitative fluorescent microscopy and spectroscopy, nuclear magnetic resonance spectroscopy, Raman spectroscopy, and/or ultraviolet-visible spectrophotometry.

[0018] In some examples, provided herein are methods of determining the partition characteristics of a plurality of test compounds in a target condensate, the method comprising performing a method of determining the partition characteristic described herein with a plurality

of test compounds. In some examples, the methods further comprise comparing the partition characteristics of a subset or all of the plurality of test compounds in the target condensate. In some examples, the methods further comprise identifying test compounds that have the same or similar partition characteristics in a target condensate. In some examples, the methods further comprise identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics. In some examples, the methods further comprise determining the partition characteristic in a target condensate for one or more additional test compounds that comprise the identified characteristic. In some examples, the methods further comprise determining the partition characteristic in a target condensate for one or more additional test compounds that do not comprise the identified characteristic.

[0019] In some examples, provided herein are methods of determining a relative partition characteristic of a test compound in a target condensate, the method comprising: (i) determining the partition characteristic of the test compound by performing a method of determining a partition characteristic described herein with the test compound; (ii) determining the partition characteristic of a reference compound by performing a method of determining a partition characteristic described herein with the reference compound; and (iii) calculating the ratio of the partition characteristics determined in (i) and (ii), thereby determining the relative partition characteristic of the test compound in the target condensate. In some examples, the test compound comprises a test compound label. In some examples, the reference compound is the test compound label.

[0020] In some examples, provided herein are methods of determining relative partition characteristics of a plurality of test compounds in a target condensate, the method comprising: (1) performing a method of determining a relative partition characteristic of a test compound in a target condensate; and (2) repeating steps (i) and (iii) with a plurality of test compounds. In some examples, the methods further comprise comparing the relative partition characteristics in the target condensate of a subset or all of the plurality of test compounds. In some examples, the methods further comprise identifying test compounds that have the same or similar relative partition characteristics in the target condensate. In some examples, the methods further comprise identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar relative partition characteristics. In some examples, the methods further comprise determining the relative partition

characteristic in the target condensate for one or more additional test compounds that comprise the identified characteristic. In some examples, the methods further comprise determining the relative partition characteristic in the target condensate for one or more additional test compounds that do not comprise the identified characteristic.

[0021] In some examples, provided herein are methods of determining a condensate preference profile of a test compound, the method comprising: (a) determining the partition characteristic of the test compound in a first target condensate according to a method disclosed herein; (b) determining the partition characteristic of the test compound in a second target condensate according to a method disclosed herein; and (c) calculating a ratio of the partition characteristic of the test compound determined in the first target condensate and the second target condensate, thereby determining the condensate preference profile of the test compound. In some examples, the first target condensate and the second target condensate are in the same composition. In some examples, the first target condensate and the second target condensate are in different compositions. In some examples, the partition characteristic of the test compound in the first target condensate is determined prior to, simultaneously with, or after the partition characteristic of the test compound in the second target condensate is determined.

[0022] In some examples, provided herein are methods of determining a condensate preference profile of a test compound, the method comprising: (a) determining the relative partition characteristic of the test compound in a first target condensate according to a method disclosed herein; (b) determining the relative partition characteristic of the test compound in a second target condensate according to a method disclosed herein; and (c) calculating a ratio of the partition characteristic of the test compound determined in the first target condensate and the second target condensate, thereby determining the condensate preference profile of the test compound. In some examples, the first target condensate and the second target condensate are in the same composition. In some examples, the first target condensate and the second target condensate are in different compositions. In some examples, the relative partition characteristic of the test compound in the first target condensate is determined prior to, simultaneously with, or after the relative partition characteristic of the test compound in the second target condensate is determined.

[0023] In some examples, provided herein are methods of determining a condensate preference profile of a test compound, the method comprising: (a) adding the test compound to a composition comprising a first target condensate and a second target condensate; (b)

determining the amount of the test compound in the first target condensate; (c) determining the amount of the test compound in the second target condensate; and (d) calculating a ratio of the amount of the test compound determined in the first target condensate and the second target condensate, thereby determining the condensate preference profile of the test compound. In some examples, the methods further comprise causing the formation of the first target condensate and/or the second target condensate prior to step (a).

[0024] In some examples, provided herein are methods of determining a condensate preference profile of a test compound, the method comprising: (a) adding the test compound to a composition comprising precursor molecules; (b) causing the formation of a first target condensate and a second target condensate in the composition; (c) determining the amount of the test compound in the first target condensate; (d) determining the amount of the test compound in the second target condensate; and (e) calculating a ratio of the amount the test compounds determined in the first target condensate and the second target condensate, thereby determining the condensate preference profile of the test compound. In some examples, the amount of the test compound in the first target condensate is determined prior to, simultaneously with, or after the amount of the test compound in the second target condensate is determined.

[0025] In some examples, the methods further comprise separating the first target condensate and the second target condensate from the composition. In some examples, the methods further comprise identifying the first target condensate and/or the second target condensate prior to determining the amount of test compound in the first condensate and/or the second condensate.

[0026] In some examples, dysregulation of the first target condensate and/or the second target condensate is associated with a disease. In some examples, the methods further comprise characterizing the first target condensate and/or the second target condensate by identifying one or more macromolecules comprised therein. In some examples, the methods further comprise labeling the first target condensate and/or the second target condensate in order to visualize the first target condensate and/or the second target condensate. In some examples, the methods further comprise labeling the first target condensate and the second target condensate in order to visualize the first condensate target condensate and the second target condensate. In some examples, the first target condensate and the second target condensate are labeled with different labels. In some examples, the first target condensate

and/or the second target condensate are labeled with a radioactive label, a colorimetric label, a chemically-reactive label, or a fluorescent label.

[0027] In some examples, the composition comprises a cell. In some examples, the cell is a microorganism or an animal cell. In some examples, the cell comprises a condensate that is determined to be dysregulated. In some examples, the cell has one or more features of a neurodegenerative or proliferative disease.

[0028] In some examples, the first target condensate and/or the second target condensate are cellular condensates. In some examples, the first target condensate is a cleavage body, a P-granule, a histone locus body, a multivesicular body, a neuronal RNA granule, a nuclear gem, a nuclear pore, a nuclear speckle, a nuclear stress body, a nucleolus, a Oct1/PTF/transcription (OPT) domain, a paraspeckle, a perinucleolar compartment, a PML nuclear body, a PML oncogenic domain, a polycomb body, a processing body, a signaling cluster, a viral condensate, a Sam68 nuclear body, a stress granule, or a splicing speckle. In some examples, the second target condensate is a cleavage body, a P-granule, a histone locus body, a multivesicular body, a neuronal RNA granule, a nuclear gem, a nuclear pore, a nuclear speckle, a nuclear stress body, a nucleolus, a Oct1/PTF/transcription (OPT) domain, a paraspeckle, a perinucleolar compartment, a PML nuclear body, a PML oncogenic domain, a polycomb body, a processing body, a signaling cluster, a viral condensate, a Sam68 nuclear body, a stress granule, or a splicing speckle. In some examples, the first target condensate and/or the second target condensate are in a cell.

[0029] In some examples, the first target condensate and/or the second target condensate are extracellular condensates.

[0030] In some examples, the composition does not comprise a cell. In some examples, the composition comprises one or more of: a macromolecule, a salt, and a buffer.

[0031] In some examples, the composition comprises one or more additional target condensates. In some examples, the methods further comprise repeating the steps of the method for one or more additional target condensates.

[0032] In some examples, provided herein are methods of determining condensate preference profiles of a plurality of test compounds, the method comprising performing a method of determining a condensate preference profile described herein with a plurality of test compounds. In some examples, the methods further comprise comparing condensate preference profiles of a subset or all of the plurality of test compounds. In some examples, the methods further

comprise identifying test compounds that have the same or similar condensate preference profiles. In some examples, the methods further comprise identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar condensate preference profiles. In some examples, the methods further comprise determining the relative partition characteristic for one or more additional test compounds that comprise the identified characteristic. In some examples, the methods further comprise determining the relative partition characteristic for one or more additional test compounds that do not comprise the identified characteristic.

[0033] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into or out of a condensate, the method comprising: (a) determining partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the partition characteristics of a subset or all of the plurality of test compounds in the target compound; (c) identifying test compounds that have the same or similar partition characteristics in the target condensate; and (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics.

[0034] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into a condensate, the method comprising: (a) determining partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the partition characteristics of a subset or all of the plurality of test compounds in the target compound; (c) identifying test compounds that have the same or similar partition characteristics in the target condensate; and (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics.

[0035] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into or out of a condensate, the method comprising: (a) determining relative partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the relative partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds that have the same or similar relative partition characteristics in the target condensate; and (d) identifying a characteristic that a subset or all of

the identified test compounds have in common in addition to the same or similar relative partition characteristics.

[0036] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into a condensate, the method comprising: (a) determining relative partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the relative partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds that have the same or similar relative partition characteristics in the target condensate; and (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar relative partition characteristics.

[0037] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into or out of a condensate, the method comprising: (a) determining condensate preference profiles of a plurality of test compounds according to a method described herein; (b) comparing the condensate preference profiles of a subset or all of the plurality of test compounds; (c) identifying test compounds that have the same or similar condensate preference profiles; and (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar condensate preference profiles.

[0038] In some examples, provided herein are methods of identifying a compound characteristic associated with partitioning a compound into a condensate, the method comprising: (a) determining condensate preference profiles of a plurality of test compounds according to a method described herein; (b) comparing the condensate preference profiles of a subset or all of the plurality of test compounds; (c) identifying test compounds that have the same or similar condensate preference profiles; and (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar condensate preference profiles.

[0039] In some examples, provided herein are methods of designing a compound with a desired partition characteristic into or out of a target condensate, the method comprising: (a) determining partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds

that have the same or similar partition characteristics in the target condensate; (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics; and (e)(i) designing a compound that comprises the identified characteristic; or (ii) designing a compound that does not comprise the identified characteristic, thereby designing a compound with the desired partition characteristic into or out of the target condensate. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, designing the compound comprises removing a moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, designing the compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique.

[0039a] In one aspect, the present disclosure refers to a method of designing a compound with a desired partition characteristic into or out of a target condensate, the method comprising: (i) designing a compound that comprises the identified characteristic disclosed herein; or (ii) designing a compound that does not comprise the identified characteristic from claim 17, thereby designing a compound with the desired partition characteristic into or out of the target condensate; optionally wherein the method comprises modifying a precursor of the compound by attaching a moiety to or removing a moiety from the precursor compound, wherein the moiety comprises the identified characteristic corresponding to the desired partition characteristic.

[0040] In some examples, provided herein are methods of designing a compound with a desired partition characteristic to a target condensate, the method comprising: (a) determining partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds that have the same or similar partition characteristics in the target condensate; (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics; and (e) designing a compound that comprises the identified characteristic. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, designing the compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique.

[0041] In some examples, provided herein are methods of designing a compound with a desired relative partition characteristic into or out of a target condensate, the method comprising: (a) determining relative partition characteristics of a plurality of test compounds in the target condensate according to a method disclosed herein; (b) comparing the relative partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds that have the same or similar relative partition characteristics in the target condensate; (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar relative partition characteristics; and (e)(i) designing a compound that comprises the identified characteristic; or (ii) designing a compound that does not comprise the identified characteristic, thereby designing a compound with the desired relative partition characteristic into or out of the target condensate. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired relative partition characteristic to the compound. In some examples, designing the compound comprises removing a moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, designing the compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique.

[0042] In some examples, provided herein are methods of designing a compound with a desired relative partition characteristic, the method comprising: (a) determining relative partition characteristics of a plurality of test compounds in the target condensate according to a method described herein; (b) comparing the relative partition characteristics of a subset or all of the plurality of test compounds in the target condensate; (c) identifying test compounds that have the same or similar relative partition characteristics in the target condensate; (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar relative partition characteristics; and (e) designing a compound that comprises the identified characteristic. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired relative partition characteristic to the compound. In some examples, designing the

compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique.

[0043] In some examples, provided herein are methods of designing a compound with a desired condensate preference profile, the method comprising: (a) determining condensate preference profiles of a plurality of test compounds according to a method disclosed herein; (b) comparing the condensate preference profiles of a subset or all of the plurality of test compounds; (c) identifying test compounds that have the same or similar condensate preference profiles; (d) identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar condensate preference profiles; and (e)(i) designing a compound that comprises the identified characteristic; or (ii) designing a compound that does not comprise the identified characteristic, thereby designing a compound with the desired condensate preference profile. In some examples, the methods further comprise making the compound. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired condensate preference profile to the compound. In some examples, designing the compound comprises removing a moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, designing the compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique.

[0044] In some examples, provided herein are methods of designing a compound with a desired condensate preference profile, the method comprising: (a) determining condensate preference profiles of a plurality of test compounds according to a method described herein; (b) comparing the condensate preference profiles of a subset or all of the plurality of test compounds; (c) identifying test compounds that have the same or similar condensate preference profiles; (d) identifying a characteristic, such as a chemical moiety or motif, that a subset or all of the identified test compounds have in common in addition to the same or similar condensate

preference profiles; and (e) designing a compound that comprises the identified characteristic. In some examples, designing the compound comprises attaching a moiety that comprises the identified characteristic, thereby conferring the desired condensate preference profile to the compound. In some examples, designing the compound comprises changing a first moiety to a second moiety that comprises the identified characteristic, thereby conferring the desired partition characteristic to the compound. In some examples, there is provided a plurality of compounds designed by the methods described herein. In some examples, the compound is designed, in whole or in part, using an approach comprising a modeling, computer, and/or calculation-based technique, *e.g.*, a bioinformatic, cheminformatic, and/or artificial intelligence (AI)-based technique. In some examples, the methods further comprise making the compound.

[0045] In some examples, provided herein are methods of screening a test compound for a desired partition characteristic from a group of candidate compounds, the method comprising: (a) determining a partition characteristic of each of the group of candidate compounds; and (b) identifying the test compound having the desired partition characteristic. In some examples, the partition characteristic of each of the group of candidate compounds is determined *in vitro*. In some examples, the test compound has a suitable partition characteristic for being useful for treating a disease in an individual.

[0046] In some examples, provided herein are methods of identifying a test compound useful for treating a disease in an individual in need thereof, the method comprising: (a) identifying a target condensate associated with the disease; and (b) determining a partition characteristic of a candidate compound in the target condensate, and (c) identifying the test compound having a suitable partition characteristic for being useful for treating the disease.

[0047] In some examples, provided herein are methods of determining a partition characteristic of a test compound in a target condensate, the methods comprising: (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution; (b) obtaining a reference control; (c) measuring a MS signal of the test compound in the extra-condensate solution, or a portion thereof, using a mass spectrometry technique; (d) measuring a MS signal of the test compound in the reference control, or a portion thereof, using a mass spectrometry technique; and (e) comparing the MS signal of the test compound from the extra-condensate solution and the MS signal of the test compound from the reference control, thereby determining the partition characteristic of the test compound in the target condensate. In

some examples, the amount of the test compound combined with the composition is 100 nM or less, and the amount of a precursor molecule in the composition, including in the target condensate, is about 5 μ M.

[0047a] In one aspect, the present disclosure refers to a method of determining a partition characteristic of a test compound in a target condensate, the method comprising: (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution; (b) obtaining a reference control; (c) measuring a MS signal of the test compound in the extra-condensate solution, or a portion thereof, using an MS technique; (d) measuring a MS signal of the test compound in the reference control, or a portion thereof, using an MS technique; and (e) comparing the MS signal of the test compound from the extra-condensate solution and the MS signal of the test compound from the reference control, thereby determining the partition characteristic of the test compound in the target condensate.

[0048] In some examples, provided herein is a library comprising a plurality of compounds, wherein each compound of the plurality of compounds comprises the same moiety comprising a characteristic having a desired partition characteristic.

[0048a] In one aspect, the present disclosure refers to a library comprising a plurality of compounds, wherein each compound of the plurality of compounds is obtained by the method disclosed herein.

[0049] In some examples, provided herein is a method of designing a test compound having a desired partition characteristic, the method comprising modifying a precursor of the test compound by attaching a moiety to the compound, wherein the moiety comprises a characteristic having a desired partition characteristic.

[0050] It will also be understood by those skilled in the art that changes in the form and details of the implementations described herein may be made without departing from the scope of this disclosure. In addition, although various advantages, examples, and objects have been described with reference to various implementations, the scope of this disclosure should not be limited by reference to such advantages, examples, and objects.

BRIEF DESCRIPTION OF THE DRAWINGS

[0051] **FIG. 1** shows exemplary fluorescent images of dyes partitioning in condensates. Dye #10 is not enriched in the condensate, while other dyes are enriched in the condensate.

[0052] **FIGS. 2A** and **2B** depict the regions inside and outside exemplary condensates that were chosen to measure intensities in the presence (**FIG. 2A**) and absence of dye (**FIG. 2B**).

[0053] **FIG. 3** shows the average intensity-in to intensity-out (I-in:I-out) ratios determined for each dye in FUS-SNAP condensates from two different days of experiments. Error bars show standard deviation of the two independent experiments.

[0054] **FIG. 4** shows the average intensity-in to intensity-out (I-in:I-out) ratios determined for each dye in PGL-3 condensates from two different days of experiments. Error bars show standard deviation of the two independent experiments.

[0055] **FIG. 5** shows the ratios of the average I-in:I-out ratio for each dye in FUS-SNAP condensates to the ratios of the average I-in:I-out ratio for each dye in PGL-3 condensates (FUS-SNAP:PGL-3 ratio).

CLAIMS

What is claimed is:

1. A method of determining a partition characteristic of a test compound in a target condensate, the method comprising:
 - (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution;
 - (b) determining the amount of the test compound in the target condensate, thereby determining the partition characteristic of the test compound in the target condensate.
2. The method of claim 1, further comprising causing the formation of the target condensate prior to step (a).
3. The method of claim 1 or 2, wherein
 - (i) the target condensate is formed in the presence of the test compound, optionally wherein the method further comprises combining the test compound and a precursor composition comprising one or more precursor molecules prior to or with formation of the target condensate; or
 - (ii) the target condensate is formed in the absence of the test compound.
4. The method of any one of claims 1-3, wherein determining the amount of the test compound in the target condensate is based on the amount of the test compound in the extra-condensate solution.
5. The method of any one of claims 1-4, further comprising:
 - (i) determining the amount of the test compound in the extra-condensate solution, optionally wherein the method further comprises determining the ratio of the amount of the test compound in the target condensate and the amount of the test compound in the extra-condensate solution; and/or
 - (ii) separating the target condensate from the extra-condensate solution.
6. The method of any one of claims 1-5, further comprising characterizing the target condensate by identifying one or more macromolecules comprised therein, optionally

wherein the method further comprises determining the amount of the one or more macromolecules in the target condensate.

7. The method of any one of claims 1-6, wherein:
 - (i) the target condensate is labeled with a radioactive label, a colorimetric label, or a fluorescent label; and/or
 - (ii) the test compound comprises a test compound label; optionally wherein the test compound label is a radioactive label, a colorimetric label, or a fluorescent label; optionally wherein the amount of the test compound is determined based on the test compound label.
8. The method of any one of claims 1-7, wherein:
 - (i) the method is a cell-based assay, and the composition comprises a cell;
 - (ii) the target condensate is a cellular condensate that is determined to be dysregulated; and/or
 - (iii) the target condensate is in a cell, optionally wherein the cell has one or more features of a neurodegenerative or proliferative disease; optionally wherein the target condensate is a cleavage body, a P-granule, a histone locus body, a multivesicular body, a neuronal RNA granule, a nuclear gem, a nuclear pore, a nuclear speckle, a nuclear stress body, a nucleolus, an Oct1/PTF/transcription (OPT) domain, a paraspeckle, a perinucleolar compartment, a PML nuclear body, a PML oncogenic domain, a polycomb body, a processing body, a Sam68 nuclear body, a stress granule, or a splicing speckle.
9. The method of any one of claims 1-7, wherein the method is a cell-free assay method.
10. The method of any one of claims 1-9, wherein the test compound is a small molecule, a polypeptide, or a nucleic acid.
11. The method of any one of claims 1-10, wherein the amount of the test compound is determined by one or more of mass spectrometry (MS), liquid chromatography, fluorescent microscopy, and ultraviolet-visible spectrophotometry.
12. The method of any one of claims 1-11, further comprising:

- (i) determining a relative partition characteristic of the test compound, wherein the relative partition characteristic of the test compound is determined by comparing the partition characteristic of the test compound in the target condensate and a partition characteristic of a reference compound in the target condensate; and/or
 - (ii) determining a condensate preference profile of the test compound, wherein the condensate preference profile is determined by comparing the partition characteristic of the test compound in the target condensate and a partition characteristic of the test compound in a reference condensate.
13. A method of determining a partition characteristic of a test compound in a target condensate, the method comprising:
- (a) combining the test compound and a composition comprising the target condensate and an extra-condensate solution;
 - (b) obtaining a reference control;
 - (c) measuring a MS signal of the test compound in the extra-condensate solution, or a portion thereof, using an MS technique;
 - (d) measuring a MS signal of the test compound in the reference control, or a portion thereof, using an MS technique; and
 - (e) comparing the MS signal of the test compound from the extra-condensate solution and the MS signal of the test compound from the reference control, thereby determining the partition characteristic of the test compound in the target condensate.
14. The method of any one of claims 1-13, further comprising determining the partition characteristics of a plurality of test compounds in the target condensate, the method comprising performing the method of any one of claims 1-13 for each of the plurality of test compounds.
15. The method of claim 14, further comprising comparing the partition characteristics of a subset or all of the plurality of test compounds in the target condensate.
16. The method of claim 15, further comprising identifying test compounds that have the same or similar partition characteristics in the target condensate.

17. The method of claim 16, further comprising identifying a characteristic that a subset or all of the identified test compounds have in common in addition to the same or similar partition characteristics, optionally wherein the characteristic is a chemical structure or motif.
18. The method of any one of claims 1-17, wherein the target condensate comprises a precursor molecule, and the method further comprises determining an amount of the test compound that associates with the precursor molecule.
19. A method of designing a compound with a desired partition characteristic into or out of a target condensate, the method comprising:
 - (i) designing a compound that comprises the identified characteristic from claim 17; or
 - (ii) designing a compound that does not comprise the identified characteristic from claim 17,thereby designing a compound with the desired partition characteristic into or out of the target condensate;
optionally wherein the method comprises modifying a precursor of the compound by attaching a moiety to or removing a moiety from the precursor compound, wherein the moiety comprises the identified characteristic corresponding to the desired partition characteristic.
20. A library comprising a plurality of compounds, wherein each compound of the plurality of compounds is obtained by the method of claim 19.