(Naumann *et al.*, 2018, *Nat Commun*, 9(1):335; Wegmann *et al.*, 2018, *EMBO J*, 37(7): e98049; and Aguzzi *et al.*, 2016, 26(7): 547-558). However, there is a lack of understanding of the mechanisms governing partitioning of a single macromolecule into or out of a condensate, and there is little or nothing known regarding whether a compound can selectively alter the partitioning of a single macromolecule into or out of a condensate.

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

SUMMARY

[0006] Provided herein are methods of identifying a compound that preferentially affects a level of association of a first macromolecule with one or more target condensates, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; and (b) determining the level of association of the first macromolecule with the one or more target condensates and a level of association of at least one additional macromolecule with the one or more target condensates, wherein the compound preferentially affects the level of association of the first macromolecule with the one or more target condensates if the compound alters the level of the first macromolecule as compared to a first reference level more than the compound alters the level of each additional macromolecule as compared to a reference level for each additional macromolecule. In some examples, the compound does not measurably alter the level of each additional macromolecule compared to the reference level for each additional macromolecule.

[0006a] In one aspect, the present disclosure refers to a method of identifying a compound that preferentially affects a level of association of a first macromolecule with one or more target condensates as compared to another macromolecule associated with the one or more target condensates, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; (b) measuring, after contacting the cellular composition with the

compound, co-localization of the first macromolecule and the other macromolecule via the level of association of the first macromolecule with the one or more target condensates and a level of association of the other macromolecule with the one or more target condensates, wherein the one or more target condensates are the same class of condensate; and (c) determining whether the compound preferentially affects the level of association of the first macromolecule with the one or more target condensates, wherein the determining is by comparing the level of association of the first macromolecule as compared to a reference level for the first macromolecule and the level of association of the other macromolecule as compared to a reference level for the other macromolecule, wherein the compound preferentially affects the level of association of the first macromolecule with the one or more target condensates when the compound alters the level of the first macromolecule as compared to the reference level for the first macromolecule more than the compound alters the level of the other macromolecule as compared to the reference level for the other macromolecule, and wherein the reference level for the first macromolecule is the level of association of the first macromolecule with the one or more target condensates in the absence of the compound, and the reference level for the other macromolecule is the level of association of the other macromolecule with the one or more target condensates in the absence of the compound.

[0007] Also provided herein are methods of identifying a compound that preferentially increases a level of association of a first macromolecule with one or more target condensates, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; and (b) determining the level of association of the first macromolecule with the one or more target condensates and a level of association of at least one additional macromolecule with the

one or more target condensates, wherein the compound preferentially increases the level of association of the first macromolecule with the one or more target condensates if the compound increases the level of the first macromolecule as compared to a first reference level more than the compound increases the level of each additional macromolecule as compared to a reference level for each additional macromolecule. In some examples, the compound does not measurably increase the level of each additional macromolecule compared to the reference level for each additional macromolecule.

[0008] Also provided herein are methods of identifying a compound that preferentially decreases a level of association with one or more target condensates of a first macromolecule, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; and (b) determining the level of association of the first macromolecule with the one or more target condensates and a level of association of at least one additional macromolecule with the one or more target condensates, wherein the compound preferentially decreases the level of association of the first macromolecule with the one or more target condensates if the compound alters the level of the first macromolecule as compared to a first reference level more than the compound decreases the level of each additional macromolecule as compared to a reference level for each additional macromolecule. In some examples, the compound does not measurably decrease the level of each additional macromolecule compared to the reference level for each additional macromolecule.

[0009] In some examples, the first reference level is a level of association of the first macromolecule with one or more reference condensates determined in the absence of the compound. In some examples, the reference level for each additional macromolecule is a level of association for each additional macromolecule with one or more reference condensates determined in the absence of the compound.

[0010] Also provided herein are methods of identifying a compound that preferentially causes a first macromolecule to associate with one or more target condensates, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises

the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; and (b) determining if a first macromolecule and at least one additional macromolecule are associated with the one or more target condensates, wherein the compound preferentially causes the first macromolecule to associate with the one or more target condensates if: (1) the compound causes the first macromolecule to associate with the one or more target condensates; (2) the compound does not cause each additional macromolecule to associate with the one or more target condensates; and (3) the first macromolecule would not be associated with the one or more target condensates in the absence of the compound.

[0011] In some examples, the compound preferentially causes the first macromolecule to associate with the one or more target condensates if (4) one or more of the at least one additional macromolecule would not be associated with the one or more target condensates in the absence of the compound. In some examples, the compound preferentially causes the first macromolecule to associate with the one or more target condensates if (4) each of the at least one additional macromolecule would not be associated with the one or more target condensates in the absence of the compound.

[0012] Also provided herein are methods of identifying a compound that preferentially causes a first macromolecule to disassociate with one or more target condensates, the method comprising: (a) contacting a cellular composition with a compound, wherein (i) the cellular composition comprises the one or more target condensates; and/or (ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound; and (b) determining if a first macromolecule and at least one additional macromolecule are associated with the one or more target condensates, wherein the compound preferentially causes the first macromolecule to disassociate with the one or more target condensates if: (1) the compound causes the first macromolecule not to associate with the one or more target condensates; (2) the compound does not cause each additional macromolecule not to associate with the one or more target condensates; and (3) the first macromolecule would be associated with the one or more target condensates in the absence of the compound.

[0013] In some examples, the compound preferentially causes the first macromolecule to associate with the one or more target condensates if (4) one or more of the at least one additional macromolecule would be associated with the one or more target condensates in the absence of the compound. In some examples, the compound preferentially causes the first macromolecule to associate with the one or more target condensates if (4) each of the at least one additional macromolecule would be associated with the one or more target condensates in the absence of the compound.

[0014] In some examples, step (a) comprises contacting a cellular composition with a compound, wherein the cellular composition comprises the one or more target condensates, and the method further comprises causing the formation of the one or more target condensates prior to step (a). In some examples, step (a) comprises contacting a cellular composition with a compound, wherein the one or more target condensates form after contacting the cellular composition with the compound, and the method further comprises causing the formation of the one or more target condensates.

[0015] In some examples, the at least one additional macromolecule is 2 or more, 3 or more, 4 or more, or 5 or more macromolecules. In some examples, the at least one additional macromolecule is 1-10 macromolecules.

[0016] In some examples, the first macromolecule is aberrantly expressed in a disease state. In some examples, a disease state level of association of the first macromolecule with the one or more target condensates is altered compared to a normal state level of association of the first macromolecule with the one or more target condensates. In some examples, one or more of the at least one additional macromolecule is aberrantly expressed in a disease state.

[0017] In some examples, the first macromolecule is DNA or RNA. In some examples, the first macromolecule is a protein. In some examples, the first macromolecule comprises a mutation that alters the level of association of the first macromolecule with the one or more target condensates compared to a related protein that does not comprise the mutation. In some examples, the first macromolecule is FUS or eIF3.

[0018] In some examples, one or more of the at least one additional macromolecule is DNA or RNA. In some examples, one or more of the at least one additional macromolecule is a

protein. In some examples, one or more of the at least one additional macromolecule comprise a mutation that alters its corresponding level of association with the one or more target condensates compared to a related protein that does not comprise the mutation. In some examples, one or more of the at least one additional macromolecule is FUS, eIF3, G3BP1, FUS and G3BP1, or eIF3 and G3BP1.

[0019] In some examples, the first macromolecule and/or one or more of the at least one additional macromolecule is a fusion protein. In some examples, the first macromolecule and/or one or more of the at least one additional macromolecule comprises a label. In some examples, the method further comprises labeling the first macromolecule and/or one or more of the at least one additional macromolecule. In some examples, the labeling comprises contacting the cellular composition with an antibody or antigen-binding fragment thereof comprising a label. In some examples, the label is a radioactive label, a colorimetric label, or a fluorescent label.

[0020] In some examples, the cellular composition comprises a microorganism or an animal cell. In some examples, the cellular composition comprises an animal cell. In some examples, the animal cell that has one or more features of a neurodegenerative, proliferative, immunological, cardiac, or metabolic disease. In some examples, the animal cell is a HeLa cell, a HEK293 cell, an induced pluripotent stem cell (iPSC cell), a cardiomyocyte, a myocyte, a stem cell-derived cell, a neuron, a cancer cell, an immune cell, or an adipocyte.

[0021] In some examples, the one or more target condensates is a cellular condensate. In some examples, the one or more target condensates is a nuclear condensate or a cytoplasmic condensate. In some examples, the 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 Sam68 nuclear body, a stress granule, or a splicing speckle.

[0022] In some examples, the one or more target condensates is a single target condensate. In some examples, the compound does not measurably alter one or more of: size of the target condensate, location of the target condensate, surface area of the target condensate, and dissolution of the target condensate.

[0023] In some examples, the one or more target condensates is a plurality of target condensates. In some examples, the compound does not measurably alter one or more of: total number of the plurality of target condensates; size of the plurality of target condensates, location of the plurality of target condensates, surface area of the plurality of target condensates, and dissolution of the plurality of target condensates.

[0024] In some examples, the one or more target condensates is a plurality of target condensates. In some examples, the plurality of target condensates is all or a subset of a class of condensates in a portion of the cellular composition. In some examples, the plurality of target condensates is all or a subset of a class of condensates in a cell in the cellular composition. In some examples, the plurality of target condensates is all or a subset of a class of condensates in a portion of a cell in the cellular composition. In some examples, the portion of the cell is the cytoplasm, the nucleus, or an organelle.

[0025] In some examples, the class of condensates comprises condensates which comprise a specific macromolecule. In some examples, the class of condensates comprises condensates which are cleavage bodies; wherein the class of condensates comprises condensates which are p-granules; wherein the class of condensates comprises condensates which are histone locus bodies; wherein the class of condensates comprises condensates which are multivesicular bodies; wherein the class of condensates comprises condensates which are neuronal RNA granules; wherein the class of condensates comprises condensates which are nuclear gems; wherein the class of condensates comprises condensates which are nuclear pores; wherein the class of condensates comprises condensates which are nuclear speckles; wherein the class of condensates comprises condensates which are nuclear stress bodies; wherein the class of condensates comprises condensates which are nucleoli; wherein the class of condensates comprises condensates which are Oct1/PTF/transcription (OPT) domains; wherein the class of condensates comprises condensates which are paraspeckles; wherein the class of condensates comprises condensates which are perinucleolar compartments; wherein the class of condensates comprises condensates which are PML nuclear bodies; wherein the class of condensates comprises condensates which are PML oncogenic domains; wherein the class of condensates comprises condensates which are polycomb bodies; wherein the class of condensates comprises condensates which are processing bodies; wherein the class of condensates comprises

condensates which are Sam68 nuclear bodies; wherein the class of condensates comprises condensates which are stress granules; or wherein the class of condensates comprises condensates which are splicing speckles.

[0026] Also provided herein are methods of identifying a plurality of compounds that preferentially affect the level, decrease the level, or increase the level of association of a first macromolecule with one or more target condensates, or that preferentially cause the first macromolecule to associate or disassociate with one or more target condensates, the method comprising performing a method of identifying a compound disclosed herein with a plurality of compounds.

[0027] In some examples, the method further comprises identifying a characteristic that a subset or all of the identified compounds have in common in addition to ability to preferentially affect the level, decrease the level, or increase the level of association of the first macromolecule with the one or more target condensates, or the ability to preferentially cause the first macromolecule to associate or disassociate with one or more target condensates. In some examples, the method further comprises performing a method of identifying a compound disclosed herein for one or more additional test compounds that comprise the identified characteristic. In some examples, the method further comprises performing a method of identifying a compound disclosed herein for one or more additional test compounds that do not comprise the identified characteristic.

[0028] Also provided herein are methods of identifying a compound characteristic associated with preferentially affecting the level, decreasing the level, or increasing the level of association of a first macromolecule with one or more target condensates, or with preferentially causing the first macromolecule to associate or disassociate with one or more target condensates, the method comprising: (a) performing a method of identifying a plurality of compounds disclosed herein; and (b) identifying a characteristic that a subset or all of the identified compounds have in common in addition to the ability to preferentially affect the level, decrease the level, or increase the level of association of the first macromolecule with one or more target condensates, or the ability to preferentially cause the first macromolecule to associate or disassociate with one or more target condensates.

[0029] Also provided herein are methods of designing a compound that preferentially affects the level, decreases the level, or increases the level of association of a first macromolecule with one or more target condensates, or that preferentially causes the first macromolecule to associate or disassociate with one or more target condensates, the method comprising: (a) performing a method of identifying a plurality of compounds disclosed herein; (b) identifying a characteristic that a subset or all of the identified compounds have in common in addition to the ability to preferentially affect the level, decrease the level, or increase the level of association of the first macromolecule with one or more target condensates, or the ability to preferentially cause the first macromolecule to associate or disassociate with one or more target condensates; and (c) designing a compound that comprises the identified characteristic, thereby designing a compound that preferentially affects the level, decreases the level, or increases the level of association of the first macromolecule with one or more target condensates or preferentially causes the first macromolecule to associate or disassociate with one or more target condensates.

[0030] Also provided herein are methods of identifying a compound useful for treating a disease in an individual in need thereof, the method comprising: performing a method of identifying a compound disclosed herein, wherein the one or more target condensates is associated with the disease, and identifying the compound that preferentially affects the level, decreases the level, or increases the level of association of the first macromolecule with the one or more target condensates or that that preferentially causes the first macromolecule to associate or disassociate with one or more target condensates for being useful for treating the disease. In some examples, the disease is a neurodegenerative, proliferative, immunological, cardiac, or metabolic disease.

[0031] Also provided herein are methods of identifying a compound that preferentially affects a level of association of a first macromolecule with a first set of one or more target condensates, the method comprising: performing a method of identifying a compound disclosed herein with the first set of one or more target condensates; and performing a method of identifying a compound disclosed herein with a second set of one or more target condensates wherein the compound preferentially affects the level of association of the first macromolecule with the first set of one or more target condensates if the compound preferentially affects the level of association of the first macromolecule with the first set of one or more target condensates more than the compound

preferentially affects the level of association of the first macromolecule with the second set of one or more target condensates. In some examples, the compound does not affect the level of association of the first macromolecule with the second set of one or more target condensates.

[0032] Also provided herein are methods of identifying a compound that preferentially increases a level of association of a first macromolecule with a first set of one or more target condensates, the method comprising: performing a method of identifying a compound disclosed herein with the first set of one or more target condensates; and performing a method of identifying a compound disclosed herein with a second set of one or more target condensates wherein the compound preferentially increases the level of association of the first macromolecule with the first set of one or more target condensates if the compound preferentially increases the level of association of the first macromolecule with the first set of one or more target condensates more than the compound preferentially increases the level of association of the first macromolecule with the second set of one or more target condensates. In some examples, the compound does not increase the level of association of the first macromolecule with the second set of one or more target condensates.

[0033] Also provided herein are methods of identifying a compound that preferentially decreases a level of association of a first macromolecule with a first set of one or more target condensates, the method comprising: performing a method of identifying a compound disclosed herein with the first set of one or more target condensates; and performing a method of identifying a compound disclosed herein with a second set of one or more target condensates wherein the compound preferentially decreases the level of association of the first macromolecule with the first set of one or more target condensates if the compound preferentially decreases the level of association of the first macromolecule with the first set of one or more target condensates more than the compound preferentially decreases the level of association of the first macromolecule with the second set of one or more target condensates. In some examples, the compound does not decrease the level of association of the first macromolecule with the second set of one or more target condensates.

[0034] Also provided herein are methods of identifying a compound that preferentially causes a first macromolecule to associate with a first set of one or more target condensates, the method comprising: performing a method of identifying a compound disclosed herein with the first set of

one or more target condensates; and performing a method of identifying a compound disclosed herein with a second set of one or more target condensates wherein the compound preferentially causes the first macromolecule to associate with the first set of one or more target condensates if the compound preferentially causes the first macromolecule to associate with the first set of one or more target condensates more than the compound preferentially causes the first macromolecule to associate with the second set of one or more target condensates.

[0035] Also provided herein are methods of identifying a compound that preferentially causes a first macromolecule to disassociate with a first set of one or more target condensates, the method comprising: performing a method of identifying a compound disclosed herein with the first set of one or more target condensates; and performing a method of identifying a compound disclosed herein with a second set of one or more target condensates wherein the compound preferentially causes the first macromolecule to disassociate with the first set of one or more target condensates if the compound preferentially causes the first macromolecule to associate with the first set of one or more target condensates more than the compound preferentially causes the first macromolecule to associate with the second set of one or more target condensates.

[0036] In some examples, the first and/or second set of one or more target condensates is a cellular condensate. In some examples, the first and/or second set of one or more target condensates is a nuclear condensate or a cytoplasmic condensate.

[0037] In some examples, the first and/or second set of one or more target condensates 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 Sam68 nuclear body, a stress granule, or a splicing speckle.

[0038] In some examples, the first and/or second set of one or more target condensates is a single target condensate.

[0039] In some examples, the first and/or second set of one or more target condensates is a plurality of target condensates. In some examples, the first and/or second set of one or more target condensates is all or a subset of a class of condensates in a portion of the cellular composition.

In some examples, the first and/or second set of one or more target condensates is all or a subset of a class of condensates in a cell in the cellular composition. In some examples, the first and/or second set of one or more target condensates is all or a subset of a class of condensates in a portion of a cell in the cellular composition. In some examples, the portion of the cell is the cytoplasm, the nucleus, or an organelle.

[0040] In some examples, the class of condensates comprises condensates which comprise a specific macromolecule. In some examples, the class of condensates comprises condensates which are cleavage bodies; wherein the class of condensates comprises condensates which are p-granules; wherein the class of condensates comprises condensates which are histone locus bodies; wherein the class of condensates comprises condensates which are multivesicular bodies; wherein the class of condensates comprises condensates which are neuronal RNA granules; wherein the class of condensates comprises condensates which are nuclear gems; wherein the class of condensates comprises condensates which are nuclear pores; wherein the class of condensates comprises condensates which are nuclear speckles; wherein the class of condensates comprises condensates which are nuclear stress bodies; wherein the class of condensates comprises condensates which are nucleoli; wherein the class of condensates comprises condensates which are Oct1/PTF/transcription (OPT) domains; wherein the class of condensates comprises condensates which are paraspeckles; wherein the class of condensates comprises condensates which are perinucleolar compartments; wherein the class of condensates comprises condensates which are PML nuclear bodies; wherein the class of condensates comprises condensates which are PML oncogenic domains; wherein the class of condensates comprises condensates which are polycomb bodies; wherein the class of condensates comprises condensates which are processing bodies; wherein the class of condensates comprises condensates which are Sam68 nuclear bodies; wherein the class of condensates comprises condensates which are stress granules; or wherein the class of condensates comprises condensates which are splicing speckles.

[0041] In some examples, the class of the first set of one or more target condensates is the same as the class of second set of one or more target condensates. In some examples, the class of the first set of one or more target condensates is different than the class of second set of one or more target condensates.

[0042] In some examples, the first set of one or more target condensates is in the same cellular composition as the second set of one or more target condensates. In some examples, the cellular composition comprises a cell comprising the first set of condensate of one or more target condensates and the second set of one or more target condensates. In some examples, the first set of condensate of one or more target condensates is in a first cellular composition, and the second set of one or more target condensates is in a second cellular composition.

[0043] In some examples, the first set of condensate of one or more target condensates are in a cell in the cellular composition, and the cell has one or more features of a disease. In some examples, the disease is a neurodegenerative, proliferative, immunological, cardiac, or metabolic disease.

[0044] Also provided herein are methods of identifying a plurality of compounds that preferentially affect the level, decrease the level, or increase the level of association of a first macromolecule with a first set of one or more target condensates, or that preferentially cause the first macromolecule to associate or disassociate with the first set of one or more target condensates, the method comprising performing a method of identifying a compound disclosed herein with a plurality of compounds.

[0045] In some examples, the method further comprises identifying a characteristic that a subset or all of the identified compounds have in common in addition to ability to preferentially affect the level, decrease the level, or increase the level of association of the first macromolecule with the first set of one or more target condensates, or the ability to preferentially cause the first macromolecule to associate or disassociate with the first set of one or more target condensates.

[0046] In some examples, the method further comprises performing a method of identifying a compound disclosed herein for one or more additional test compounds that comprise the identified characteristic. In some examples, the method further comprises performing a method of identifying a compound disclosed herein for one or more additional test compounds that do not comprise the identified characteristic.

[0047] Also provided herein are methods of identifying a compound characteristic associated with preferentially affecting the level, decreasing the level, or increasing the level of association of a first macromolecule with a first set of one or more target condensates, or with preferentially causing

disease. In some examples, the disease is a neurodegenerative, proliferative, immunological, cardiac, or metabolic disease.

BRIEF DESCRIPTION OF THE DRAWINGS

[0050] **FIG. 1** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with lipoamide.

[0051] **FIG. 2** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with AZD4547, Omipalisib, and TG101209.

[0052] **FIG. 3** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with GW9508, Brefeldin A, AZD3463 and Ketanserin.

[0053] **FIG. 4** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with AZD8931, YM155 and Beta-Lapachone.

[0054] **FIG. 5** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with lipoamide.

[0055] **FIG. 6** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with P121, PF-04691502, and TG101209.

[0056] **FIG. 7** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with Coriphosphine O.

[0057] **FIG. 8** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with YM155, Beta-Lapachone, and Bisindolylmaleimide IX.

[0058] **FIG. 9** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed cells with or without treatment with Cediranib.

[0059] **FIG. 10** is fluorescent micrographs showing the levels of FUS, eIF3, and G3BP1 in stressed HeLa cells carrying BAC FUS-GFP and stressed human iPSC cells with or without treatment with Matisinib.

[0060] **FIG. 11** is a plot of dose-response curves for FUS, eIF3, and G3BP1 in stress granules of stressed HeLa cells carrying BAC FUS-GFP treated with YM155.

CLAIMS

What is claimed is:

1. A method of identifying a compound that preferentially affects a level of association of a first macromolecule with one or more target condensates as compared to another macromolecule associated with the one or more target condensates, the method comprising:

(a) contacting a cellular composition with a compound, wherein

(i) the cellular composition comprises the one or more target condensates; and/or

(ii) the one or more target condensates form simultaneously with and/or after contacting the cellular composition with the compound;

(b) measuring, after contacting the cellular composition with the compound, co-localization of the first macromolecule and the other macromolecule via the level of association of the first macromolecule with the one or more target condensates and a level of association of the other macromolecule with the one or more target condensates,

wherein the one or more target condensates are the same class of condensate; and

(c) determining whether the compound preferentially affects the level of association of the first macromolecule with the one or more target condensates,

wherein the determining is by comparing the level of association of the first macromolecule as compared to a reference level for the first macromolecule and the level of association of the other macromolecule as compared to a reference level for the other macromolecule,

wherein the compound preferentially affects the level of association of the first macromolecule with the one or more target condensates when the compound alters the level of the first macromolecule as compared to the reference level for the first macromolecule more than the compound alters the level of the other macromolecule as compared to the reference level for the other macromolecule, and

wherein the reference level for the first macromolecule is the level of association of the first macromolecule with the one or more target condensates in the absence of the compound, and the reference level for the other macromolecule is the level of association of the

other macromolecule with the one or more target condensates in the absence of the compound.

2. The method of claim 1, wherein the one or more target condensates are in the same cell type.

3. The method of claim 1, further comprising measuring the reference level for the first macromolecule.

4. The method of claim 1, further comprising measuring the reference level for the other macromolecule.

5. The method of claim 1, wherein the compound preferentially increases the level of association of the first macromolecule with the one or more target condensates if the compound increases the level of association of the first macromolecule as compared to the reference level for the first macromolecule more than the compound increases the level of association of the other macromolecule as compared to the reference level for the other macromolecule.

6. The method of claim 5, wherein the compound results in the first macromolecule associating with the one or more target condensates.

7. The method of claim 1, wherein the compound preferentially decreases the level of association of the first macromolecule with the one or more target condensates if the compound decreases the level of association of the first macromolecule as compared to the reference level for the first macromolecule more than the compound decreases the level of association of the other macromolecule as compared to the reference level for the other macromolecule.

8. The method of claim 7, wherein the compound results in the first macromolecule not associating with the one or more target condensates.

9. The method of claim 1, wherein the compound alters the level of association of the first macromolecule with the one or more target condensates as compared to the reference level for the first macromolecule at least about 0.25 fold.

10. The method of claim 1, further comprising assessing at least one characteristic of the one or more target condensates.

11. The method of claim 10, wherein the characteristic of the one or more target condensates is selected from the group consisting of: size, number, shape, composition, surface area, location, functional activity, stability, liquidity, and solidification.

12. The method of claim 10, wherein the assessing the at least one characteristic of the one or more target condensates is performed using a microscopy technique.

13. The method of claim 1, further comprising causing the formation of the one or more target condensates.

14. The method of claim 1, wherein the first macromolecule and the other macromolecule are each independently selected from the group consisting of: a polypeptide, a DNA, and an RNA.

15. The method of claim 14, wherein the first macromolecule or the other macromolecule is aberrantly present in a disease state.

16. The method of claim 14, wherein the first macromolecule or the other macromolecule comprises a mutation.

17. The method of claim 1, wherein the first macromolecule comprises a first label.

18. The method of claim 17, wherein the other macromolecule comprises a second label.

19. The method of claim 18, wherein the first label and the second label are distinguishable.

20. The method of claim 19, wherein the first macromolecule and the first label are a fusion protein, and the other macromolecule and the second label are a fusion protein.

21. The method of claim 19, further comprising labeling the first macromolecule and the other macromolecule.

22. The method of claim 21, wherein the labeling comprises contacting the first macromolecule with an antibody or antigen-binding fragment thereof comprising the first label, and contacting the other macromolecule with another antibody or antigen-binding fragment thereof comprising the second label.

23. The method of claim 19, wherein the first label and the second label are each independently selected from the group consisting of: a radioactive label, a colorimetric label, and a fluorescent label.

24. The method of claim 1, wherein measuring the co-localization of the first macromolecule and the other macromolecule comprises use of an imaging technique.

25. The method of claim 1, wherein the cellular composition comprises an animal cell.

26. The method of claim 25, wherein the animal cell has one or more features of a neurodegenerative, proliferative, immunological, cardiac, or metabolic disease.