Claims:

Claim 1. A method for detecting and/or identifying a target in a cell sample comprising:

forming a modified moiety by conjugating a nucleic acid sequence to a moiety directed to the target;

forming a nucleic acid nanostructure comprising a polyhedron shape, optionally a tetrahedron, and a segment sequence complementary to a portion of the nucleic acid sequence of the modified moiety;

incubating the cell sample with the modified moiety to form a complex between the modified moiety and the target;

removing modified moieties that do not form a complex with the target;

allowing the complementary segment sequence of the nanostructure to hybridize to the portion of the nucleic acid sequence of the modified moiety to which it is complementary;

forming a nucleic acid barcode comprising the complementary segment sequence of the nanostructure;

detecting the nucleic acid barcode, whereby the detection of the nucleic acid barcode indicates that the target is present in the sample;

forming at least two different location identifiers wherein each location identifier comprises a nucleic acid sequence comprising a segment sequence complementary to a second portion of the nucleic acid sequence of the modified moiety and a unique identifier;

permeabilizing a first cell sample with a first permeabilization buffer to allow a first location identifier to enter a first subcellular location of the cell and permeabilizing a second cell sample with a second permeabilization buffer to allow a second location identifier to enter a second subcellular location of the cell wherein the first and second location identifier are directed to a specific subcellular location by the size of the unique identifier; and

detecting the first, or second location identifier indicates the target was present in the first or second subcellular location.

Claim 2. The method according to claim 1, wherein the nucleic acid sequence of the modified moiety is 50 nucleotides or less.

Claim 3. The method according to claim 1 or 2, wherein a plurality of modified moieties directed to a plurality of targets and a plurality of nucleic acid nanostructures comprising a segment sequence complementary to a portion of each of the plurality of nucleic acid sequences of the modified moieties are formed.

Claim 4. The method according to any one of claims 1 to 3, wherein the at least two different location identifiers comprises at least three different location identifiers, a first location identifier wherein the unique identifier comprises a nucleic acid sequence, a second location identifier wherein the unique identifier comprises a nucleic acid sequence conjugated to a nanoparticle having a diameter between 60nm and 10nm and a third location identifier wherein the unique identifier comprises a nucleic acid sequence conjugated to a nanoparticle having a diameter between 100nm and 300nm wherein detection of the first location identifier indicates the target was present at any location within the cell or cellular environment, detection of the second location identifier indicates the target was present at any location within the cell or cellular environment outside the nucleus or detection of the third location identifier indicates the target was present external cellular environment including on the cell surface.

Claim 5. The method according to any one of claims 1 to 4, further comprising ligating the complementary segment sequence of the nanostructure with the complementary segment sequence of the location identifier; forming a nucleic acid barcode comprising the ligated complementary segment sequence of the nanostructure and the complementary segment sequence of the location identifier.

Claim 6. The method according to any one of claims 1 to 5, further comprising: determining the relative location of at least two reference target proteins, each having a different known cellular distribution, with a set of interacting nucleic acid structures comprising

i) a modified antibody having a nucleic acid sequence conjugated thereto directed to each reference target protein;

ii) a nucleic acid nanostructure comprising a segment sequence complementary to a portion of the nucleic acid sequence conjugated to the modified antibody; and

iii) a unique identifier by detecting at least two reference barcodes formed comprising the complementary segment sequence of the nanostructure, the complementary segment sequence of the second portion of the nucleic acid sequence of the modified antibody and a unique identifier;

determining the relative amount and/or location of at least one target protein with a set of interacting nucleic acid structures comprising

i) a modified moiety having a nucleic acid sequence conjugated thereto directed to each target protein;

ii) a nucleic acid nanostructure comprising a segment sequence complementary to a portion of the nucleic acid sequence conjugated to the modified moiety; and

iii) a unique identifier, by detecting at least one barcode comprising the complementary segment sequence of the nanostructure, the complementary segment sequence of the second portion of the nucleic acid sequence of the modified moiety and the unique identifier;

analyzing the at least two reference barcodes formed when the reference target proteins are present and comparing the relative distribution of the at least two reference barcodes with the at least one barcode formed when the target protein is present and determining the relative cellular location of the target protein.

Claim 7. The method according to claim 4, wherein the nanoparticle comprises mesoporous silica nanoparticle.

Claim 8. The method according to any one of claims 1 to 7, wherein the nucleic acid sequence of nanostructures is further modified chemically at the 5'-end and the nucleic acid segment sequence of the location identifiers complementary to a portion of the nucleic acid sequence of the modified moiety is modified chemically at the 5'-end to facilitate enzymatic or chemical ligation.

Claim 9. The method according to any one of claims 1 to 8, wherein the moiety is an antibody, and/or the antibody is modified with at least two nucleic acid sequence strands and/or the target is a target protein.

Claim 10. A set of interacting nucleic acid structures for use in detecting and/or identifying a target comprising:

a nucleic acid sequence capable of being conjugated to a moiety directed to the target;

a nucleic acid nanostructure comprising a polyhedron shape, optionally a tetrahedron, and a segment sequence complementary to a portion of the nucleic acid sequence capable of being conjugated to a moiety directed to the target; and

at least two different location identifiers wherein each location identifier comprises a nucleic acid sequence comprising a segment sequence complementary to a second portion of the nucleic acid sequence of a modified moiety and a unique identifier, wherein the unique identifier of a first location identifier comprises a nucleic acid sequence and the unique identifier of a second location identifier comprises a nucleic acid sequence conjugated to a nanoparticle, wherein the nanoparticle is selected from a nanoparticle having a diameter of between 60 and 10nm and a nanoparticle having a diameter of between 100 nm and 300 nm.

Claim 11. The set of interacting nucleic acid structures according to claim 10, wherein the nucleic acid sequence of the modified moiety is 50 nucleotides or less.

Claim 12. The set of interacting nucleic acid structures according to claim 10 or 11, wherein the at least two different location identifiers comprises at least three different location identifiers, a first location identifier wherein the unique identifier comprises a nucleic acid sequence a second location identifier wherein the unique identifier comprises a nucleic acid sequence conjugated to a nanoparticle having a diameter between 60nm and 10nm and a third location identifier wherein the unique identifier comprises a nucleic acid sequence conjugated to a nanoparticle having a diameter between 100nm and 300nm.

Claim 13. The set of interacting nucleic acid structures according to any one or claims 10 to 12, further comprising at least two modified antibodies directed to at least two reference target proteins having a known cellular location.

Claim 14. The set of interacting nucleic acid structures according to any one or claims 10 to 13, wherein the nucleic acid sequence capable of being conjugated to a moiety is conjugated to a moiety directed to the target.

Claim 15. The set of interacting nucleic acid structures according to claim 14, wherein the moiety comprises an antibody and the target is a protein target.

Claim 16. A system for detection and/or identification of a target in a sample comprising:

a modified moiety comprising a nucleic acid sequence conjugating to a moiety directed to the target in a mixing chamber for mixing the sample with the modified moiety;

a filter for capturing a complex between the modified moiety and the target;

a nucleic acid nanostructure comprising a polyhedron shape, optionally a tetrahedron, and a segment sequence complementary to a portion of the nucleic acid sequence of the modified moiety and at least two different location identifiers comprising a nucleic acid sequence, a segment sequence complementary to a second portion of the nucleic acid sequence of the modified moiety and a unique identifier, the nucleic acid nanostructure and the at least two different location identifiers in a reservoir for incubating the moiety complex with the nucleic acid nanostructure and the at least two different location identifiers wherein the unique identifier of a first location identifier comprises a nucleic acid sequence and the unique identifier of a second location identifier comprises a nucleic acid sequence conjugated to a nanoparticle, wherein the nanoparticle is selected from a nanoparticle having a diameter of between 60 and 10nm and a nanoparticle having a diameter of between 100 nm and 300 nm; and

a detection chamber for detecting a nucleic acid barcode comprising the nucleic acid segment sequence complementary to the portion of the nucleic acid of the modified moiety, that can be used to determine the cell or subcellular location of the target when the location identifiers bind to the second portion of the nucleic acid sequence of the modified moiety.

Claim 17. The system according to claim 16, wherein the mixing chamber comprises a serpentine channel.

Claim 18. The system according to claim 16 or 17, wherein the filter comprises a porous membrane.

Claim 19. The system according to any one of claims 16 to 18, wherein the detection chamber comprises a plurality of detection chambers for detection of a plurality of barcodes indicative of a plurality of targets.

Claim 20. The system according to any one of claims 16 to 19, further comprising a heating element.

Claim 21. An *in vitro* method comprising:

forming a modified antibody by conjugating a nucleic acid sequence to an antibody directed to a target protein associated with a disease;

forming a nucleic acid nanostructure comprising a polyhedron shape, optionally a tetrahedron, and a segment sequence complementary to a portion of the nucleic acid sequence of the modified antibody;

forming at least two location identifiers wherein each location identifier comprises a nucleic acid sequence comprising a segment sequence complementary to a second portion of the nucleic acid sequence of the modified antibody and a unique identifier;

incubating a sample with the modified antibody to form a complex between the modified antibody and the target protein, and removing modified antibodies that do not form a complex with the target protein;

permeabilizing a first cell sample with a first permeabilization buffer to allow a first location identifier to enter a first subcellular location of the cell and permeabilizing a second cell sample with a second permeabilization buffer to allow a second location identifier to enter a second subcellular location of the cell wherein the first and second location identifier are directed to a specific subcellular location by the size of the unique identifier;

incubating the complex with the nucleic acid nanostructure, the first and the second location identifier to form a super complex between the modified antibody, the target protein and the first or the second location identifier;

ligating the nucleic acid of the super-complex between the segment sequence complementary to the portion of the nucleic acid nanostructure and the complementary segment sequence of the first or the second location identifier;

forming a nucleic acid barcode comprising the ligated sequence complementary to the portion of the nucleic acid sequence of the modified antibody and the sequence complementary to the second portion of the nucleic acid sequence of the modified antibody; and

detecting and analyzing the nucleic acid barcode to determine the amount and/or subcellular distribution of target proteins, whereby the amount and/or subcellular distribution of target protein indicates presence of the disease in the sample.

Claim 22. The method according to claim 21, further comprising: measuring at least two reference target proteins, each having a known cellular location using a modified antibody directed to each reference target protein by determining the relative location of the at least two reference target proteins, each having a different known cellular distribution, with a set of interacting nucleic acid structures comprising a modified antibody having a nucleic acid sequence conjugated thereto directed to each reference target protein; a nucleic acid nanostructure comprising a segment sequence complementary to a portion of the nucleic acid sequence conjugated to the modified antibody by detecting at least two reference barcodes formed comprising the complementary segment sequence of the nanostructure, the complementary segment sequence of the second portion of the nucleic acid sequence of the modified antibody and a unique identifier;

determining the amount of at least two target proteins with a set of interacting nucleic acid structures comprising a modified moiety having a nucleic acid sequence conjugated thereto directed to each target protein; a nucleic acid nanostructure comprising a segment sequence complementary to a portion of the nucleic acid sequence conjugated to the modified moiety by detecting; at least two barcodes comprising the complementary segment sequence of the nanostructure, the complementary segment sequence of the second portion of the nucleic acid sequence of the modified moiety and a unique identifier;

analyzing the at least two reference barcodes formed when the reference target protein is present and comparing the relative distribution of the at least two reference barcodes with the at least two barcodes formed when the target protein is present and determining the relative cellular location of the target protein.

Claim 23. The method according to claim 21 or 22, wherein the disease is a disease subtype selected from a cancer subtype an aggressive cancer subtype, and/or wherein the disease subtype, the cancer subtype or the aggressive cancer subtype is breast cancer.

Claim 24. The method according to claim 23, wherein detection of more of the nucleic acid barcode comprising a unique identifier located in a nucleus compared to the nucleic acid barcode comprising a unique identifier located in other subcellular locations indicates the breast cancer is aggressive wherein the target protein associated with cancer is selected from the group consisting of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and a combination thereof.

Claim 25. The method according to any one of claims 21 to 23, wherein the target protein associated with cancer is selected from the group consisting of estrogen receptor (ER), progesterone receptor (PR), human epidermal growth factor receptor 2 (HER2) and a combination thereof.

Claim 26. The method according to claim 24 or 25, wherein the breast cancer is subtyped into luminal, non-luminal or triple negative based the expression of ER, PR and HER2, wherein detection of the nucleic acid barcode comprising the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to the ER, and/or detection of the nucleic acid barcode comprising the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to the PR, and/or detection of the nucleic acid barcode comprising the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to the HER2 indicates the breast cancer is a luminal subtype; or wherein detection of the nucleic acid barcode comprising the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to HER2 but not the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to ER or PR indicates the breast cancer is a non-luminal subtype; or wherein the absence of the nucleic acid barcode comprising the segment sequence complementary to the portion of the nucleic acid sequence of the modified antibody directed to the ER, PR and HER2 indicates the breast cancer is a triple negative subtype.