Claim 4. The method of any of claims 1-3, wherein step (1)(d) comprises,

(i) generating an initial image of at least part of the sample from the detected fluorescent signals; and

(ii) selecting a region of interest from the initial image, and detecting by fluorescence, signals from at least the first binder and the fluorescent marker to generate the first image at a higher resolution than the initial image.

Claim 5. The method of claim 4, wherein the composite image is generated by combining signal information from the higher resolution image and the second image.

Claim 6. The method of any of claims 4-5, comprising registering the location of signals from the fluorescent marker in the higher resolution image with the location of signals from the fluorescent marker in the second image.

~~Claim 7: The method of any of the preceding claims, wherein the detecting step in generating the first image or the detecting step in generating the second image further comprises detecting autofluorescense of the biological sample.~~

~~Claim 8: The method of any of the preceding claims, wherein generation of the composite image comprises registering the location of signals from the fluorescent marker acquired in step 1 with the location of signals from the fluorescent marker acquired in step 2.~~

~~Claim 9: The method of any of the preceding claims, wherein the step of generating the first image further comprises: prior to generating the image of the sample, generating a lower resolution image of the entire solid support and locating the sample on the solid support.~~

Claim 7~~10~~: The method of any of the preceding claims, wherein generating the first image and/or generating the second image comprises generating a brightfield type image that resembles a brightfield stain, wherein said brightfield type images resemble a simulated H&E image or a simulated DAB image.

~~Claim 11: The method of claim 11, wherein the brightfield type images resemble a simulated H&E image.~~

~~Claim 12: The method of claim 11, wherein the brightfield type images resemble a simulated DAB image.~~

Claim 813: The method of ~~any of~~ claims 710-12, wherein the regions of interests are selected at least in part based on morphological information from the brightfield type image of the first image.

~~Claim 14: The method of any of the preceding claims, further comprising an antigen retrieval step prior to the contacting step (1)(a).~~

~~Claim 15: The method of any of the preceding claims, further comprising, in step (1)(a), physically binding the first binder with the target protein.~~

Claim 916: The method of any of the preceding claims, wherein said binder is an antibody specific for the target protein.

Claim 1017: The method of claim 916, wherein said antibody is labeled with a fluorophore.

~~Claim 18: The method of any of the preceding claims, wherein said target protein is selected from the group consisting of cytokeratin, cyclin D1, cyclin B1, Ki67, ER, AR, PI3K, cMET, EGFR, cMyc, PTEN, MAPK, EGFR and HER2.~~

Claim 1119: The method of any of the preceding claims, wherein in step (1)(a), the sample is also contacted with at least one additional binder that provides additional morphological information; and in step (1)(c), signals from the at least one additional binder is also detected by fluorescence.

~~Claim 20: The method of claim 19, wherein said at least one additional binder comprise antibody for keratin 15, 19, E-cadherin, Na+K+ATPase, Claudin 1, Collagen IV, EPCAM, fibronectin, glut-1, SMA, vimentin, smooth muscle actin, CD31 and pan-cytokeratin antibodies.~~

~~Claim 21: The method of claim 19, wherein said additional morphological information comprises tissue origin, cell origin, tumor, normal, and stromal regions, cell types, and subcellular structure such as cell membrane, cytoplasm, nucleus.~~

~~Claim 22: The method of claim 19, wherein said additional morphological information comprises information about cytoplasm location of cells of epithelial origin.~~

~~Claim 23: The method of any of claims 19-22, further comprising, in step (1)(a), physically binding the first binder with the protein, and binding the at least one additional binder with proteins which are located in specific compartments of the sample.~~

~~Claim 24: The method of any of the preceding claims, wherein said fluorescent marker comprises 4',6-diamidino-2-phenylindole (DAPI), Eosin, Hoechst 33258 and Hoechst 33342 (two bisbenzimides), Propidium Iodide, Quinacrine, Fluorescein-phalloidin, Chromomycin A-3, Acriflavine-Feulgen reaction, Auramine O-Feulgen reaction and Ethidium Bromide.~~

~~Claim 25: The method of any of the preceding claims, wherein said fluorescent marker stains the nucleus of a cell.~~

Claim 12~~26~~: The method of any of the preceding claims, further comprising digesting the sample by a proteinase prior to step (2)(a).

Claim 13~~27~~: The method of any of the preceding claims, wherein in step (2)(a), said hybridizing reaction is selected from the group consisting of FISH, IQ-FISH, in-situ PCR, rolling circle amplification and primed in situ labeling.

~~Claim 28: The method of any of the preceding claims, wherein said hybridizing reaction is FISH, and the reaction further comprises probes that identify each of the chromosomes on which the nucleic acid sequences of interest reside.~~

~~Claim 29: The method of any of the preceding claims, wherein said probe comprises a nucleic acid probe, a peptide nucleic acid probe, a locked nucleic acid probe, mRNA probe, miRNA probe or siRNA probe.~~

~~Claim 30: The method of any of the preceding claims, wherein said probe is fluorescently labeled.~~

~~Claim 31: The method of any of the preceding claims, wherein said target nucleic acid comprises nucleic acid sequences for EGFR, TOP2A, cMyc, ALK, FGFR1 and HER2.~~

Claim 14~~32~~: The method of any of the preceding claims, wherein after step (1)(d), fluorescent signal from the first binder is modified.

~~Claim 33: The method of claim 32, wherein the fluorescent signal is modified by a chemical agent.~~

Claim 15~~34~~: The method of claim 14~~32~~, wherein steps (1)(a) through (1)(d) are repeated with another binder for a different protein.

Claim 16~~35~~: The method of any of the preceding claims, wherein after step (2)(d), fluorescent signal from the probes is modified by oxidation, stripping, photobleaching, or a mixture thereof, and steps (2)(a) through (2)(d) are repeated with probes for additional nucleic acid sequences of interest.

Claim 17~~36~~: A method of analyzing a biological sample, comprising providing a composite image of the biological sample according to claim 1, and analyzing the expression of the protein and the nucleic acid sequences of interest from the composite image.

~~Claim 37: The method of claim 36, wherein said sample comprises a cell or a tissue sample.~~

~~Claim 38: The method of any of claims 36-37, wherein said sample comprises a Formalin-Fixed, Paraffin-Embedded (FFPE) tissue sample.~~

Claim 1839: The method of ~~any of~~ claims ~~36-38~~17, wherein in step (1)(a), the sample is also contacted with at least one additional binder that provides additional morphological information; and in step (1)(c), signals from the at least one additional binder is also detected by fluorescence, and the method further comprising creating a color blended composite image for the first image, said composite image includes the image of the target protein, the morphological information represented by the at least one additional binder, and the fluorescent marker.

~~Claim 40: The method of any of claims 36-39, further comprising creating a RGB color blend heatmap image of the target protein expression level by mapping the fluorescent signal from the first binder to a reference color lookup table.~~

~~Claim 41: The method of claim 39, further comprising creating a color blended composite image for the first image, said composite image includes the image of the target protein, the morphological information represented by the at least one additional binder, and the fluorescent marker.~~

~~Claim 42: The method of any of claims 36-41, wherein the sample is an FFPE tissue sample, the first binder is an antibody for HER2, the one or more additional binders is a pan-cytokeratin antibody cocktail, the fluorescent marker is DAPI, and the nucleic acid sequence of interest is HER2.~~

Claim 1943: A kit, comprising components for fluorescent detection of a protein as well as fluorescent detection of a target nucleic acid sequence on the same biological sample.

Claim 2044: A system, comprising means for performing fluorescent detection of a protein as well as a target nucleic acid sequence on the same biological sample.

Claim 2145: A method for generating a first and a second image of a single biological sample, comprising the steps of:

(1) generating the first image of the biological sample, comprising the steps of:

a. contacting the sample on a solid support with a first binder for a target protein;

b. staining the sample with a fluorescent marker that provides morphological information;

c. detecting, by fluorescence, signals from the first binder and the fluorescent marker;

d. generating a first image of at least part of the sample from the detected fluorescent signals; and then

(2) generating the second image of the biological sample, comprising the steps of:

a. contacting the same sample from step (1) with a probe for each of at least one target nucleic acid sequence thus hybridizing the probes with the target nucleic acid sequence;

b. optionally, staining the sample with the fluorescent marker;

c. detecting, by fluorescence, signals from the probes for each of the target nucleic acid sequences and the fluorescent marker; and

d. generating a second image of at least part of the sample from the detected fluorescent signal.

~~Claim 46. The method of claim 45, wherein generating the first image comprises, after detecting, by fluorescence, signals from the first binder and the fluorescent marker,~~

~~(i) generating an initial image of at least part of the sample from the detected fluorescent signals; and~~

~~(ii) selecting a region of interest from the initial image, and detecting by fluorescence, signals from at least the first binder and the fluorescent marker to generate the first image at a higher resolution than the initial image.~~