In yet another example, responsive to the determination of the presence of the KIF5B-RET fusion, the method includes administering a kinase inhibitor, *e.g.*, a kinase inhibitor as described herein, to the subject.

In one aspect, the present disclosure refers to a method of determining the presence of a Kinesin Family Member 5B - RET proto-oncogene (KIF5B-RET) fusion, comprising acquiring knowledge by sequencing, e.g., next-generation sequencing (NGS) or sequencing by mass spectrometry, that a nucleic acid molecule encoding the KIF5B-RET fusion or a KIF5B-RET fusion polypeptide is present in a sample from a subject having cancer, wherein the cancer is chosen from a colorectal cancer or a lung cancer, optionally wherein the lung cancer is a NSCLC, a SCLC, a SCC, or a combination thereof, and wherein responsive to the acquisition of knowledge of the presence of the KIF5B-RET fusion:

(i) the subject is classified as a candidate to receive treatment with an anti-cancer agent; and/or

(ii) the subject is identified as likely to respond to a treatment that comprises an anti-cancer agent, wherein the anti-cancer agent is selected from:

(a) a multi-kinase inhibitor that inhibits RET kinase activity or a RET-specific inhibitor; or

(b) a nucleic acid molecule selected from the group consisting of antisense molecules, ribozymes, siRNA, and triple helix molecules, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule encoding the KIF5B-RET fusion, thereby blocking or reducing mRNA expression of the nucleic acid molecule encoding the KIF5B-RET fusion,

said method optionally further comprising providing a report to another party, wherein said report comprises:

information on the role of a KIF5B-RET fusion, or wildtype sequence, in disease;

information on prognosis, resistance, or potential or suggested therapeutic options for the subject;

information on the likely effectiveness of a therapeutic option, the acceptability of a therapeutic option, or the advisability of applying a therapeutic option to the subject; or

information, or a recommendation on, the administration of a drug to the subject.

We Claim:

1. A method of determining the presence of a Kinesin Family Member 5B - RET proto-oncogene (KIF5B-RET) fusion, comprising acquiring knowledge by sequencing, e.g., next-generation sequencing (NGS) or sequencing by mass spectrometry, that a nucleic acid molecule encoding the KIF5B-RET fusion or a KIF5B-RET fusion polypeptide is present in a sample from a subject having cancer, wherein the cancer is chosen from a colorectal cancer or a lung cancer, optionally wherein the lung cancer is a NSCLC, a SCLC, a SCC, or a combination thereof, and wherein responsive to the acquisition of knowledge of the presence of the KIF5B-RET fusion:

(i) the subject is classified as a candidate to receive treatment with an anti-cancer agent; and/or

(ii) the subject is identified as likely to respond to a treatment that comprises an anti-cancer agent, wherein the anti-cancer agent is selected from:

(a) a multi-kinase inhibitor that inhibits RET kinase activity or a RET-specific inhibitor; or

(b) a nucleic acid molecule selected from the group consisting of antisense molecules, ribozymes, siRNA, and triple helix molecules, wherein the nucleic acid molecule hybridizes to a nucleic acid molecule encoding the KIF5B-RET fusion, thereby blocking or reducing mRNA expression of the nucleic acid molecule encoding the KIF5B-RET fusion,

said method optionally further comprising providing a report to another party, wherein said report comprises:

information on the role of a KIF5B-RET fusion, or wildtype sequence, in disease;

information on prognosis, resistance, or potential or suggested therapeutic options for the subject;

information on the likely effectiveness of a therapeutic option, the acceptability of a therapeutic option, or the advisability of applying a therapeutic option to the subject; or

information, or a recommendation on, the administration of a drug to the subject.

2. The method of claim 1, wherein the sample:

(i) comprises fluid, cells, and/or a tissue, e.g., a tumor tissue;

(ii) is a nucleic acid sample or a protein sample;

(iii) is acquired from the subject;

(iv) comprises a tumor biopsy or a circulating tumor cell or nucleic acid; and/or

(v) is chosen from one or more of: tissue, e.g., cancerous tissue such as a tissue biopsy, whole blood, serum, plasma, buccal scrape, sputum, saliva, cerebrospinal fluid, urine, stool, circulating tumor cells, circulating nucleic acids, or bone marrow.

3. The method of claim 1, wherein a nucleic acid molecule encoding the KIF5B-RET fusion is determined to be present in a sample from the subject having cancer, and wherein the method further comprises a method chosen from one or more of: a nucleic acid hybridization assay, an amplification-based assay, a PCR-RFLP assay, real-time PCR, a screening analysis, FISH, spectral karyotyping or MFISH, comparative genomic hybridization, *in situ* hybridization, SSP, HPLC or mass-spectrometric genotyping.

4. The method of claim 1, wherein the method further comprises: contacting the sample with a reagent which specifically binds to a KIF5B-RET fusion polypeptide, wherein the sample is a protein sample; and detecting the formation of a complex of the KIF5B-RET fusion polypeptide and the reagent, optionally wherein: the reagent is labeled with a detectable group to facilitate detection of the bound and unbound reagent; and/or the reagent is an antibody molecule.

5. The method of claim 1, wherein:

(i) the level or activity of the KIF5B-RET fusion is evaluated;

(ii) the KIF5B-RET fusion is detected prior to initiating a treatment with the anti-cancer agent in the subject;

(iii) the KIF5B-RET fusion is detected at the time of diagnosis of the subject with a cancer; and/or

(iv) the KIF5B-RET fusion is detected at a pre-determined interval, e.g., a first point in time and at least at a subsequent point in time.

6. The method of claim 1, further comprising, responsive to a determination of the presence of the KIF5B-RET fusion, one or more of:

(i) stratifying a patient population;

(ii) identifying or selecting the subject as likely or unlikely to respond to a treatment;

(iii) selecting a treatment option for the subject, optionally wherein the treatment option comprises administering an anti-cancer agent chosen from lenvatinib, sorafenib, sunitinib, vandetanib, NVP-AST487, regorafenib, motesanib, cabozantinib, apatinib, or DCC-2157; or

(iv) prognosticating the time course of the cancer in the subject.

7. The method of claim 1, further comprising:

identifying, selecting, or obtaining information or knowledge that the subject has participated in a clinical trial or has been treated for cancer,

wherein the presence of the KIF5B-RET fusion identifies the subject as having an increased risk for, or having, a cancer associated with the KIF5B-RET fusion.

8. The method of any one of claims 1-7, wherein the anti-cancer agent is a multi-kinase inhibitor that inhibits RET kinase activity.

9. The method of claim 8, wherein the multi-kinase inhibitor is lenvatinib, sunitinib, vandetanib, or cabozantinib.

10. The method of any one of claims 1-7, wherein the anti-cancer agent is a RET-specific inhibitor.

11. The method of any one of claims 1-10, wherein the cancer is a colorectal cancer.

12. The method of any one of claims 1-10, wherein the cancer is a lung cancer.

13. The method of clam 12, wherein the lung cancer is a NSCLC, a SCLC, a SCC, or a combination thereof.