CLAIMS

1. A method of determining a risk of gastrointestinal cancer in a human subject, the method comprising:

determining in a fluid biological sample of the subject, whether mutation is present in one or more focal regions with high mutation rates, wherein the one or more focal regions is selected from the group consisting of:

CTCF-binding sites (CBS) overlapping regions set forth in the table 1 below:

Chromosome	Start site	End site
6	50570094	50570120
8	71000992	71001012
1	209422184	209422222
2	49173770	49173816
4	182064578	182064613
X	104435106	104435140
14	70285576	70285601
6	73122084	73122123
8	70576141	70576184
13	36552821	36552860
3	164903700	164903728

or portions or flanking sequences thereof,

and non-CBS regions set forth in the table 2 below:

Chromosome	Start site	End site
7	68391104	68391132
7	136495924	136495948
2	57627616	57627640
16	8381278	8381302
5	23824204	23824224
7	67614923	67614943

8	65161396	65161420
7	4937707	4937736
12	126996666	126996686
4	5415060	5415082
X	137405623	137405655
3	171164993	171165017
4	144748744	144748764
9	25481736	25481758
2	77150455	77150477
3	104801455	104801477
X	125548690	125548710
14	83046706	83046744

or portions or flanking sequences thereof,

wherein presence of mutation in the one or more focal regions is indicative of a risk of gastrointestinal cancer in the subject,

wherein the fluid biological sample is selected from the group consisting of blood, plasma, serum, and combinations thereof, and wherein the flanking sequence is a continuous sequence of no more than 10 nucleotides immediately contiguous to the 5' end and the 3' end of the CBS and/or non-CBS overlapping region.

2. The method of claim 1, further comprising determining in the subject, whether mutation is present in at least one of the genes selected from the group consisting of: *KRAS*, *TP53, RHOA, ARID1A, PIK3CA, ERBB3 and PTEN*, wherein presence of mutation in the one or more focal regions, and/or at least one of the genes is indicative of a risk of gastrointestinal cancer in the subject.

3. The method of claim 1 or 2, wherein determining whether mutation is present in the one or more focal regions does not comprise determining whether mutation is present in a region spanning more than 50 nucleotides.

4. The method of any of claims 1-3, wherein determining whether mutation is present in the CBS overlapping region(s), or portions or flanking sequences thereof, comprises contacting the biological sample with a primer having at least 85% sequence identity to a sequence selected from the group consisting of: SEQ ID NO. 35, SEQ ID NO. 36, SEQ ID NO. 39, SEQ ID NO. 40, SEQ ID NO. 45, SEQ ID NO. 46, SEQ ID NO. 47, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 50, SEQ ID NO. 51, SEQ ID NO. 52, SEQ ID NO. 57, SEQ ID NO. 58, SEQ ID NO. 59, SEQ ID NO. 60, SEQ ID NO. 65, SEQ ID NO. 66, SEQ ID NO. 77, SEQ ID NO. 78, SEQ ID NO. SEQ ID NO. 83, SEQ ID NO. 84 and combinations thereof and/or wherein determining whether mutation is present in the non-CBS region(s), or portions or flanking sequences thereof, comprises contacting the biological sample with a primer having at least 85% sequence identity to a sequence selected from the group consisting of: SEQ ID NO. 37, SEQ ID NO. 38, SEQ ID NO. 41, SEQ ID NO. 42, SEQ ID NO. 43, SEQ ID NO. 44, SEQ ID NO. 53, SEQ ID NO. 54, SEQ ID NO. 55, SEQ ID NO. 56, SEQ ID NO. 61, SEQ ID NO. 62, SEQ ID NO. 63, SEQ ID NO. 64, SEQ ID NO. 67, SEQ ID NO. 68, SEQ ID NO. 71, SEQ ID NO. 72, SEQ ID NO. 75, SEQ ID NO. 76, SEQ ID NO. 81, SEQ ID NO. 82, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 87, SEQ ID NO. 88, SEQ ID NO. 89, SEQ ID NO. 90, SEQ ID NO. 91, SEQ ID NO. 92, and combinations thereof.

5. The method of any of claims 1-4, wherein the method comprises determining whether mutation is present in at least two of the CBS overlapping regions, or portions or flanking sequences thereof, set forth in the table 1, optionally wherein the method comprises determining whether mutation is present in all of the CBS overlapping regions, or portions or flanking sequences thereof, set forth in the table 1, further optionally wherein the method comprises determining whether mutation is present in all of the CBS overlapping regions, or

portions or flanking sequences thereof, and all of the non-CBS regions, or portions or flanking sequences thereof, set forth in the tables 1 and 2.

6. The method of any of claims 1-5, wherein the method of determining a risk of gastrointestinal cancer has a detection sensitivity of no less than 50%.

7. The method of any of claims 1-6, wherein if the biological sample shows a presence of mutation in the one or more focal regions, and optionally a mutation is present in at least one of the genes selected from the group consisting of: *KRAS*, *TP53*, *RHOA, ARID1A, PIK3CA, ERBB3 and PTEN*, the subject is to be administered a therapeutic agent for treating gastrointestinal cancer.

8. The method of claim 7, wherein the therapeutic agent is selected from the group consisting of chemotherapy, radiation therapy, immunotherapy and combinations thereof.

9. The method of any of claims 1-8, wherein the gastrointestinal cancer is selected from the group consisting of gastric cancer, colorectal cancer, colon cancer, rectal cancer, esophagael cancer, liver cancer, and pancreatic cancer.

10. The method of any one of claims 1 to 9, wherein the method comprises determining whether mutation is present in all of the focal regions set forth in Tables 1 and 2, wherein presence of mutation in one or more of the focal regions is indicative of a risk of gastrointestinal cancer in the subject and wherein the gastrointestinal cancer is selected from the group consisting of gastric cancer, colorectal cancer, colon cancer, rectal cancer, esophageal cancer, liver cancer and pancreatic cancer.

~~11. A kit for detecting gastrointestinal cancer from a fluid biological sample of a human subject, the kit comprising:~~

~~an agent for detecting mutation in one or more focal regions with high mutation rates,~~

~~wherein the one or more focal regions is selected from the group consisting of:~~

~~CBS overlapping regions set forth in the table 1 below:~~

~~Chromosome~~	~~Start site~~	~~End site~~
~~6~~	~~50570094~~	~~50570120~~
~~8~~	~~71000992~~	~~71001012~~
~~1~~	~~209422184~~	~~209422222~~
~~2~~	~~49173770~~	~~49173816~~
~~4~~	~~182064578~~	~~182064613~~
~~X~~	~~104435106~~	~~104435140~~
~~14~~	~~70285576~~	~~70285601~~
~~6~~	~~73122084~~	~~73122123~~
~~8~~	~~70576141~~	~~70576184~~
~~13~~	~~36552821~~	~~36552860~~
~~3~~	~~164903700~~	~~164903728~~

~~or portions or flanking sequences thereof,~~

~~and non-CBS regions set forth in the table 2 below:~~

~~Chromosome~~	~~Start site~~	~~End site~~
~~7~~	~~68391104~~	~~68391132~~
~~7~~	~~136495924~~	~~136495948~~
~~2~~	~~57627616~~	~~57627640~~
~~16~~	~~8381278~~	~~8381302~~
~~5~~	~~23824204~~	~~23824224~~
~~7~~	~~67614923~~	~~67614943~~
~~8~~	~~65161396~~	~~65161420~~
~~7~~	~~4937707~~	~~4937736~~
~~12~~	~~126996666~~	~~126996686~~

~~4~~	~~5415060~~	~~5415082~~
~~X~~	~~137405623~~	~~137405655~~
~~3~~	~~171164993~~	~~171165017~~
~~4~~	~~144748744~~	~~144748764~~
~~9~~	~~25481736~~	~~25481758~~
~~2~~	~~77150455~~	~~77150477~~
~~3~~	~~104801455~~	~~104801477~~
~~X~~	~~125548690~~	~~125548710~~
~~14~~	~~83046706~~	~~83046744~~

~~or portions or flanking sequences thereof,~~

~~wherein the fluid biological sample is selected from the group consisting of blood, plasma, serum and combinations thereof.~~

~~12. The kit of claim 11, further comprising an agent for detecting mutation in at least one of the genes selected from the group consisting of: *KRAS, TP53, RHOA, ARID1A, PIK3CA, ERBB3, PTEN*.~~

~~13. The kit of claim 11 or 12, wherein the agent for detecting mutation in the CBS overlapping region(s), or portions or flanking sequences thereof, comprises a primer having at least 85% sequence identity to a sequence selected from the group consisting of: SEQ ID NO. 35, SEQ ID NO. 36, SEQ ID NO. 39, SEQ ID NO. 40, SEQ ID NO. 45, SEQ ID NO. 46, SEQ ID NO. 47, SEQ ID NO. 48, SEQ ID NO. 49, SEQ ID NO. 50, SEQ ID NO. 51, SEQ ID NO. 52, SEQ ID NO. 57, SEQ ID NO. 58, SEQ ID NO. 59, SEQ ID NO. 60, SEQ ID NO. 65, SEQ ID NO. 66, SEQ ID NO. 77, SEQ ID NO. 78, SEQ ID NO. SEQ ID NO. 83 and SEQ ID NO. 84 and/or wherein the agent for detecting mutation in the non-CBS region(s), or portions or flanking sequences thereof, comprises a primer having at least 85% sequence identity to a sequence selected from the group consisting of: SEQ ID NO. 37, SEQ ID NO. 38, SEQ ID NO. 41, SEQ ID NO. 42, SEQ ID NO. 43, SEQ ID NO. 44, SEQ ID NO. 53, SEQ ID NO. 54, SEQ ID NO. 55, SEQ ID NO. 56, SEQ ID~~

~~NO. 61, SEQ ID NO. 62, SEQ ID NO. 63, SEQ ID NO. 64, SEQ ID NO. 67, SEQ ID NO. 68, SEQ ID NO. 71, SEQ ID NO. 72, SEQ ID NO. 75, SEQ ID NO. 76, SEQ ID NO. 81, SEQ ID NO. 82, SEQ ID NO. 85, SEQ ID NO. 86, SEQ ID NO. 87, SEQ ID NO. 88, SEQ ID NO. 89, SEQ ID NO. 90, SEQ ID NO. 91 and SEQ ID NO. 92.~~

~~14The kit of any of claims 11-13, the kit comprising agents for detecting mutation in at least two of the CBS overlapping regions, or portions or flanking sequences thereof, set forth in the table 1, optionally wherein the kit comprises agents for detecting mutation in all of the CBS overlapping regions, or portions or flanking sequences thereof, set forth in the table 1, further optionally wherein the kit comprises agents for detecting mutation in all of the CBS overlapping regions, or portions or flanking sequences thereof, and all of the non-CBS regions, or portions or flanking sequences thereof, set forth in the tables 1 and 2.~~

~~15. The kit of any one of claims 11 to 14 wherein the kit comprises agents for detecting mutation in all of the focal regions set forth in Tables 1 and 2, and wherein the gastrointestinal cancer is selected from the group consisting of gastric cancer, colorectal cancer, colon cancer, rectal cancer, esophageal cancer, liver cancer and pancreatic cancer.~~

~~16~~11. The method ~~or the kit~~ of any one of claims 1-~~15~~10, wherein the human subject is an Asian subject.

~~17. The method or the kit of any one claims 1 to 16, wherein the flanking sequence is a continuous sequence of no more than 10 nucleotides immediately contiguous to the 5' end and the 3' end of the CBS and/or non-CBS overlapping region.~~