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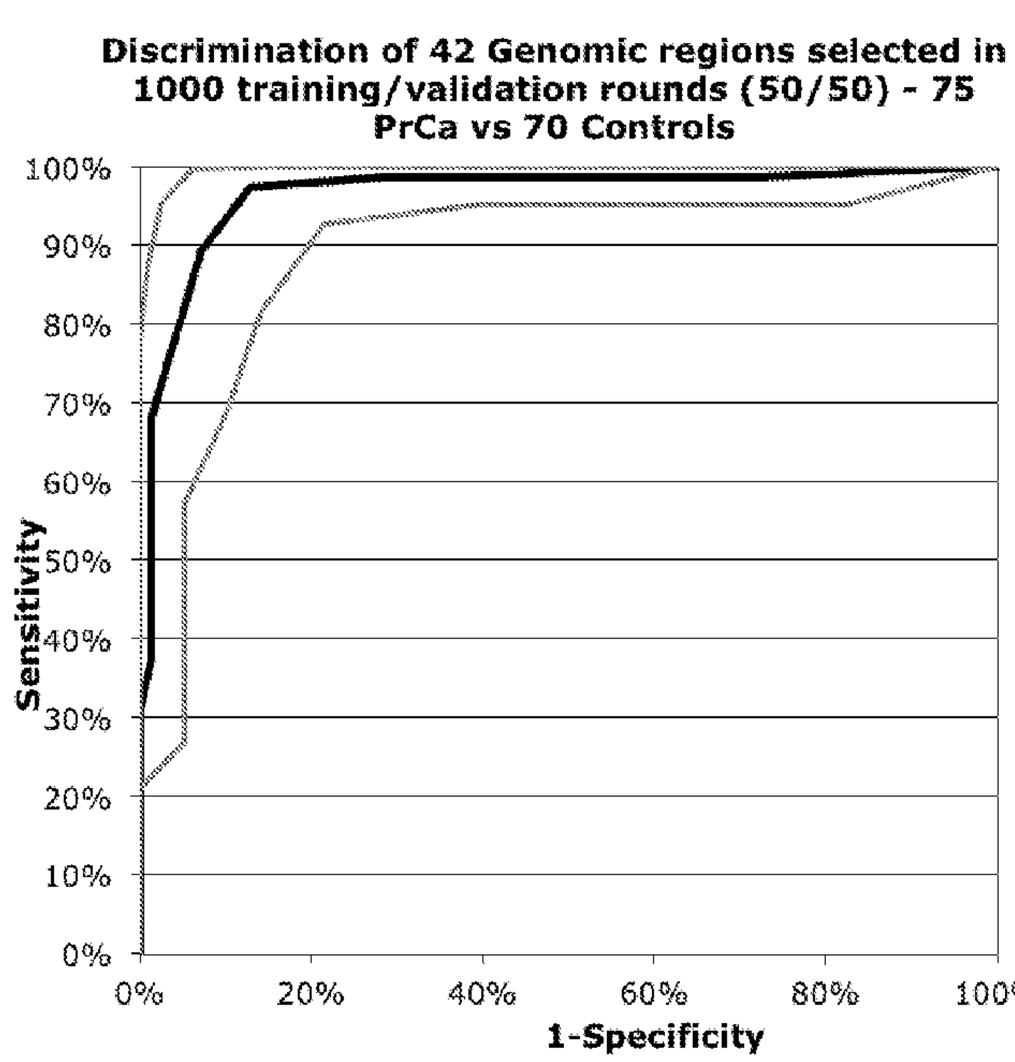
(54) Titre : BIOMARQUEURS D'ACIDES NUCLEIQUES CIRCULANTS ASSOCIES AU CANCER DE LA PROSTATE
(54) Title: PROSTATE CANCER ASSOCIATED CIRCULATING NUCLEIC ACID BIOMARKERS



(57) Abrégé/Abstract:
Methods and reagents for diagnosing prostate cancer are disclosed, wherein said methods comprise detection of circulating nucleic acid biomarkers from a patient to be evaluated.

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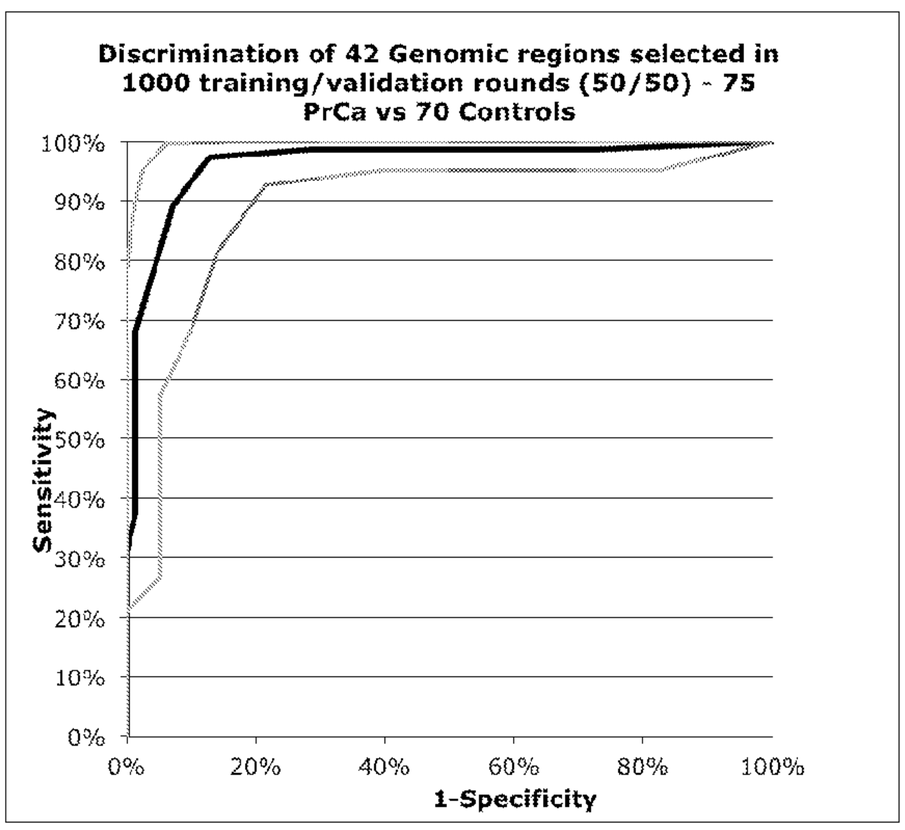
(54) **Title**: PROSTATE CANCER ASSOCIATED CIRCULATING NUCLEIC ACID BIOMARKERS

(57) **Abstract**: Methods and reagents for diagnosing prostate cancer are disclosed, wherein said methods comprise detection of circulating nucleic acid biomarkers from a patient to be evaluated.

Figure 1



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WHAT IS CLAIMED IS:

1. A method of detecting a biomarker that is associated with prostate cancer in a patient, the method comprising:

obtaining the sequence of substantially all circulating cell-free DNA having a length of between 50 and 400 consecutive nucleotides isolated from a sample obtained from blood, serum, or plasma of a patient that has been diagnosed with prostate cancer or is suspected of having prostate cancer;

comparing each sequence, free of repetitive elements, to the sequences set forth in Table B to determine whether a sequence of a circulating cell-free DNA falls within a chromosomal region set forth in Table 3;

wherein detecting a sequence in the circulating nucleic acids that is unambiguously assigned to a chromosomal region set forth in Table 3 is indicative of an increased likelihood of prostate cancer or recurrence of prostate cancer.

2. The method of claim 1, further comprising:

comparing the sequences free of repetitive elements from the circulating nucleic acids to the sequences set forth in Table A, C, or D to determine whether a sequence of a circulating cell-free DNA falls within a chromosomal region set forth in Table 2, 4, or 5; wherein detecting a sequence in the circulating nucleic acids that is unambiguously assigned to a chromosomal region set forth in Table 2 or 4 is indicative of an increased likelihood of prostate cancer or recurrence of prostate cancer; and detecting a sequence in the circulating nucleic acids that is unambiguously assigned to a chromosomal region set forth in Table 5 is indicative of a decreased likelihood of prostate cancer or recurrence of prostate cancer.

3. The method of claim 1, further comprising:

comparing the sequences free of repetitive elements from the circulating nucleic acids to the sequences set forth in Table A, C, and D to determine whether a sequence of a circulating cell-free DNA falls within a chromosomal region set forth in Table 2, 4, and 5; wherein detecting a sequence in the circulating nucleic acids that is unambiguously assigned to a chromosomal region set forth in Table 2 or 4 is indicative of an increased likelihood of prostate

cancer or recurrence of prostate cancer; and detecting a sequence in the circulating nucleic acids that is unambiguously assigned to a chromosomal region set forth in Table 5 is indicative of a decreased likelihood of prostate cancer or recurrence of prostate cancer.

4. A kit comprising a plurality of oligonucleotides, wherein each oligonucleotide has about 18 to 100 nucleotides and has a nucleotide sequence falling within a chromosomal region that is set forth in Table 3; wherein said plurality comprises oligonucleotides corresponding to each and every chromosomal region set forth in Table 3; and wherein said oligonucleotides are free of repetitive element;

optionally wherein said oligonucleotides are attached to a solid substrate.

5. A method of diagnosing or screening for prostate cancer in a patient, comprising:

providing a sample of circulating cell-free DNA isolated from blood, serum or plasma from said patient;

hybridizing the sample to a plurality of probes to determine if one of the circulating cell-free DNA molecules hybridizes to any one of the plurality of probes under stringent conditions, where the plurality of probes comprises a probe set for all of the chromosomal regions set forth in Table 3; and

correlating the presence of a cell free DNA that falls within a chromosomal region of Table 3 with an increased likelihood that said patient has prostate cancer.

6. The method of claim 5, wherein the plurality of probes comprises a probe set for the chromosomal regions set forth in Table 2, 4, or 5.

7. A system for analyzing circulating cell-free DNA, comprising:

a sample analyzer that determines the presence or absence, or the amount of, a circulating cell-free DNA having a nucleotide sequence of at least 25 nucleotides falling within each chromosomal region set forth in Table 3;

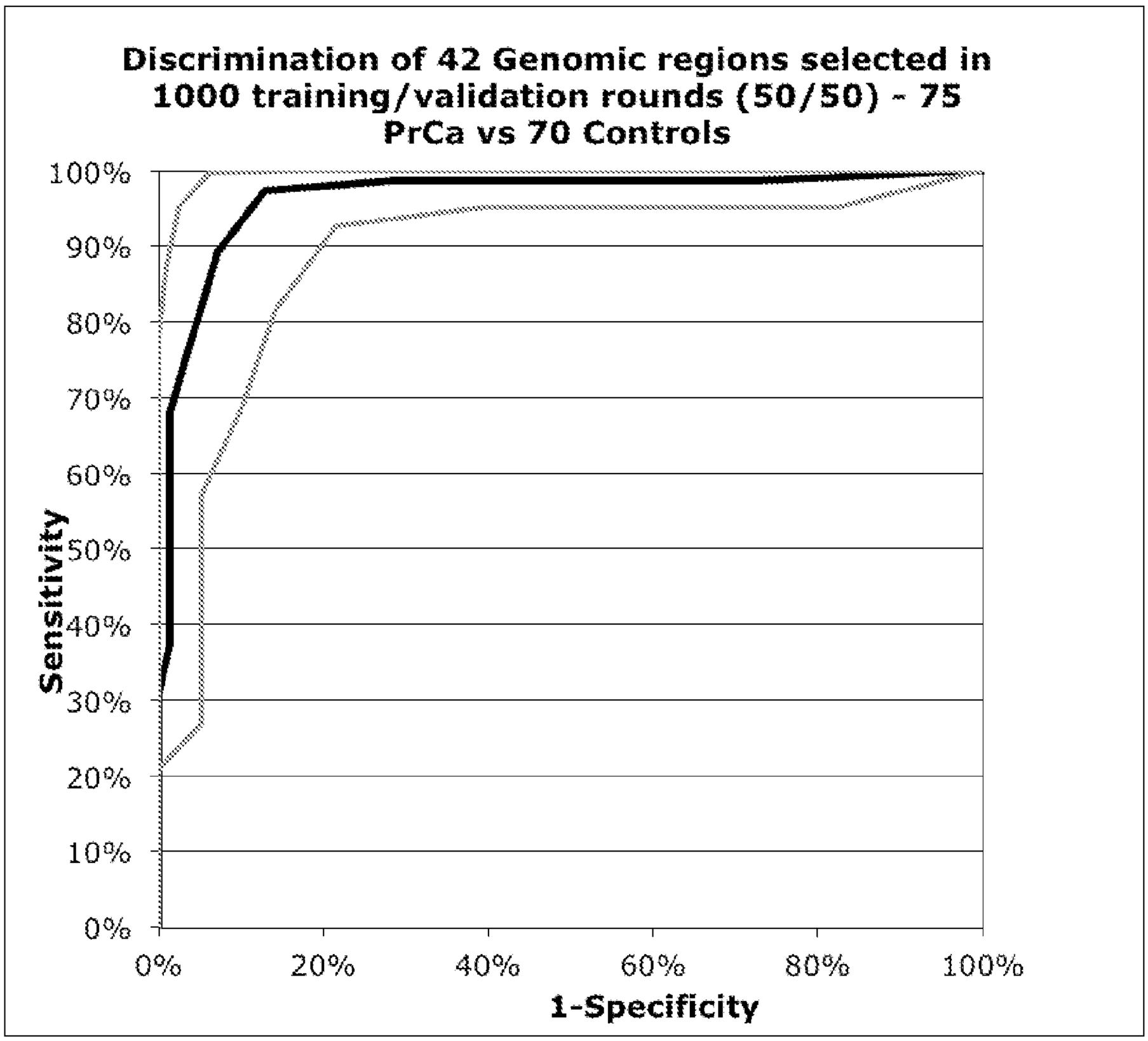
a computer system that automatically receives and analyzes data obtained in step (1), and that correlates the presence of, or an increased amount of, said circulating cell-free DNA with a diagnosis of prostate cancer;

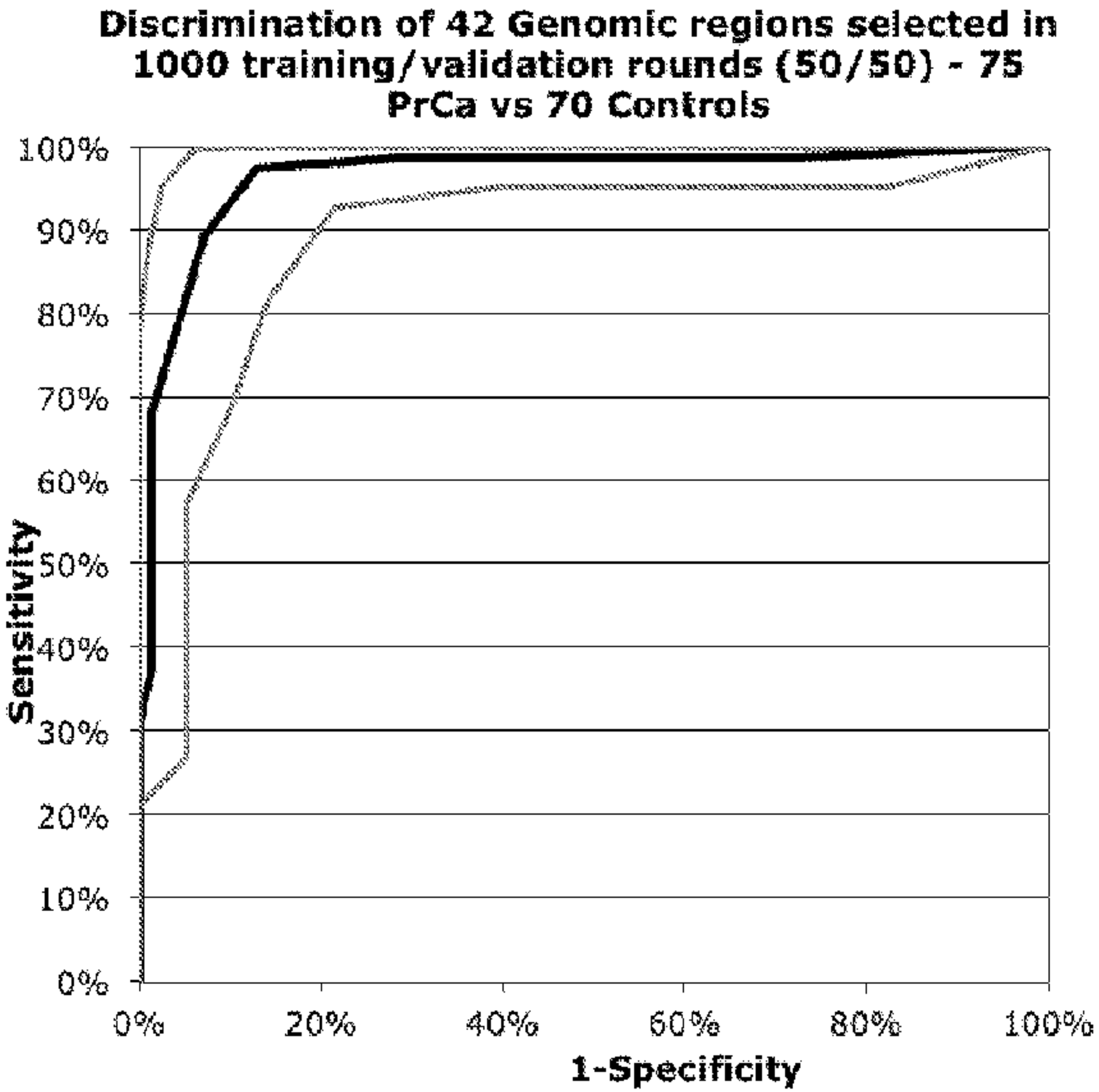
optionally further comprising a display module that displays the result of the correlating step.

8. The system of claim 7, wherein the sample analyzer determines the presence or absence, or the amount of, a circulating cell-free DNA having a nucleotide sequence of at least 25 nucleotides falling within each chromosomal region set forth in Table 2 or Table 4.

9. The system of claim 7, wherein the sample analyzer determines the presence or absence, or the amount of, a circulating cell-free DNA having a nucleotide sequence of at least 25 nucleotides falling within each chromosomal region set forth in Table 2 and Table 4.

Figure 1


Discrimination of 42 Genomic regions selected in 1000 training/validation rounds (50/50) - 75 PrCa vs 70 Controls
Sensitivity
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
0%
20%
40%
60%
80%
100%
1-Specificity


Discrimination of 42 Genomic regions selected in 1000 training/validation rounds (50/50) - 75 PrCa vs 70 Controls
100%
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Sensitivity
0%
20%
40%
60%
80%
100%
1-Specificity