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(71) Applicant: **FREENOME HOLDINGS, INC.** [US/US];
259 East Grand Avenue, 5th Floor, South San Francisco,
California 94080 (US).

(72) Inventors: **ST. JOHN, John**; 259 East Grand Avenue,
5th Floor, South San Francisco, California 94080 (US).
KOTHEN-HILL, Steven; 259 East Grand Avenue, 5th
Floor, South San Francisco, California 94080 (US). **YANG,
Rui**; 259 East Grand Avenue, 5th Floor, South San Fran-
cisco, California 94080 (US). **DRAKE, Adam**; 259 East
Grand Avenue, 5th Floor, South San Francisco, California
94080 (US).

(74) Agent: **CHOW, Carmen**; Wilson Sonsini Goodrich &
Rosati, 650 Page Mill Road, Palo Alto, California 94304
(US).

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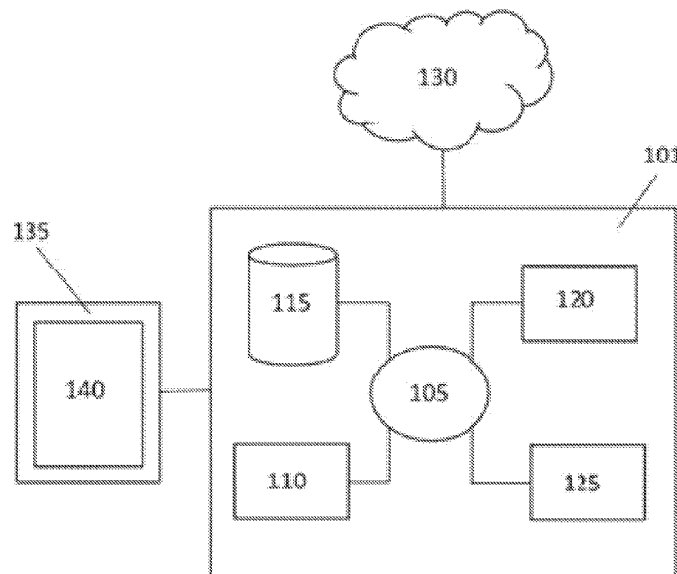


FIG. 1

(57) Abstract: The present disclosure provides methods and systems for screening or detecting a colorectal cancer or following colorectal disease progression that may be applied to cell-free nucleic acids such as cell-free DNA. The method may use detection of methylation signals within a single sequencing read in identified genomic regions as input features to train a machine learning model and generate a classifier useful for stratifying populations of individuals. The method may comprise extracting DNA from a cell-free sample obtained from a subject, converting the DNA for methylation sequencing, generating sequencing reads, and detecting colon proliferative cell disorder-associated signals in the sequencing information and training a machine learning model to provide a discriminator capable of distinguishing groups in a subject population such as healthy, cancer or distinguishing disease subtype or stage. The method may be used for, e.g., predicting, prognosticating, and/or monitoring response to treatment, tumor load, relapse, or colorectal

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