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Titolo

NUOVI MARCATORI DI METILAZIONE DEL DNA UTILI PER LA DIAGNOSI DI MALATTIE
NEOPLASTICHE

DESCRIZIONE dell'invenzione industriale dal titolo:

"Nuovi marcatori di metilazione del DNA utili per la diagnosi di malattie neoplastiche"

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DESCRIZIONE

La presente invenzione riguarda un procedimento in vitro per la rivelazione di neoplasie dell'uomo tramite analisi dello stato di metilazione del DNA di specifiche regioni del DNA tumorale, nonché acidi nucleici e oligonucleotidi utili in tale procedimento e kit comprendenti tali oligonucleotidi.

La metilazione del DNA, ossia il legame di gruppi metilici ($-CH_3$) a citosine presenti nel DNA nel contesto del dinucleotide CpG (C = citosina; G = guanina; p = monofosfato) è la più comune e nota modificazione epigenetica a cui il DNA può andare incontro nelle cellule di mammifero. Di norma, una volta stabilito lo schema di metilazione del DNA, la cellula madre lo trasmette fedelmente a tutte le cellule figlie.

Nel genoma umano, sono presenti numerose migliaia di regioni particolarmente ricche di CpG - le cosiddette isole CpG (CpG islands). Queste regioni, spesso localizzate nei promotori genici, sono generalmente prive di metilazione.

E' noto dalla letteratura scientifica che svariate isole CpG presentano metilazione aberrante nei tumori umani. Ciò spesso si associa con l'inibizione della trascrizione dei geni ad esse collegate, suggerendo che l'alterato stato di metilazione del DNA riscontrato nei tumori umani possa avere un ruolo nel processo tumorigenico. In ogni caso, la presenza di alterata metilazione si presenta come un utile marcatore di diagnosi di malattie neoplastiche nell'uomo. Inoltre, poichè alterazioni nello stato di metilazione si riscontrano già nelle fasi iniziali del processo neoplastico, questi marcatori sono utili anche per una diagnosi precoce.

La letteratura scientifica e brevettuale riporta infatti numerosi studi sullo stato di metilazione di geni implicati nello sviluppo di tumori umani e sui metodi utili per la loro rivelazione.

Vi è peraltro la continua necessità di individuare nuovi marcatori di malattie neoplastiche che da un lato consentano di ampliare le conoscenze attualmente disponibili sui meccanismi molecolari alla base della canceroge-

nesi, e dall'altro contribuiscano a fornire nuovi strumenti per la diagnosi precoce di tumori umani.

La presente invenzione si basa su studi effettuati dai presenti inventori, con i quali è stato identificato un gruppo di isole CpG associate a geni umani (elencati in tabella 1) che si sono rivelati utili come marcatori di metilazione del DNA. Specificamente, tutte le isole CpG elencate in tabella 1 sono state inizialmente identificate attraverso un unico esperimento di analisi del profilo trascrizionale nella linea cellulare umana RKO trattata con farmaco demetilante.

Più specificamente, gli inventori hanno trovato che lo stato di metilazione delle isole CpG elencate in tabella 1 è alterato in tumori umani e che l'analisi dello stato di metilazione delle isole CpG di tali geni costituisce un marcatore utile per la diagnosi di diversi tipi di neoplasie umane, comprendenti sia tumori solidi sia neoplasie ematologiche.

Più specificamente, gli inventori hanno trovato che le isole CpG riportate in tabella 1 presentano, in cellule derivate da neoplasie umane, una frequenza di metilazione superiore a quella osservata nei controlli normali, che risultano non metilati o metilati con bassa frequenza.

Lo stato di metilazione di tali isole CpG, la cui localizzazione genomica ed estensione è specificata in ta-

bella 1, costituiscono quindi un utile marcatore di tumori solidi e neoplasie ematologiche nell'uomo.

Le isole CpG si trovano tutte all'estremità 5' di geni umani elencati in tabella 1 e coprono regioni variabili da circa 1,3 kb a circa 7,5 kb.

Un oggetto della presente invenzione è quindi un procedimento per la diagnosi di tumori solidi e neoplasie ematologiche, caratterizzato dal fatto di comprendere, in un campione di DNA genomico, la fase di analizzare lo stato di metilazione dell'isola CpG di un gene scelto dal gruppo che consiste dei geni umani elencati in tabella 1, la localizzazione genomica dell'isola CpG di ciascuno di detti geni umani essendo come indicata in tabella 1, la metilazione di detta isola CpG essendo indicativa di malattia neoplastica.

In una forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene ARGAP20 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 42.661 e 45.840 della sequenza Genbank AP003460, versione 3 (SEQ ID NO: 1), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene CDH11

compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 52.081e 55.500 della sequenza Genbank AC137643, versione 3 (SEQ ID NO: 2), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene FLI1 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 40.001 e 47.460 della sequenza Genbank AP001122, versione 5 (SEQ ID NO: 3), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene FOSL2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 52.801 e 57.000 della sequenza Genbank AC104695, versione 2 (SEQ ID NO: 4), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene HES2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 31.741 e 34.020 della sequenza Genbank AL031848, versione 11 (SEQ ID NO: 5), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene HTR6 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 92.521 e 95.340 della sequenza Genbank AL031727, versione 43 (SEQ ID NO: 6), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene LHX3 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 111.001 e 116.040 della sequenza Genbank AL138781, versione 13 (SEQ ID NO: 7), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene LOC51149 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 117.001 e 119.700 della sequenza Genbank AC008393, versione 7 (SEQ ID NO: 8), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene MAP1B

compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 39.361 e 41.460 della sequenza Genbank AC093218, versione 2 (SEQ ID NO: 9), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene MDM2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 140.401 e 141.660 della sequenza Genbank AC025423, versione 32 (SEQ ID NO: 10), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene NID1 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 36.661 e 38.520 della sequenza Genbank AL122018, versione 37 (SEQ ID NO: 11), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene NID2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 75.001 e 77.340 della sequenza Genbank AL008557, versione 5 (SEQ ID NO: 12), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene PNU TL2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 108.541 e 111.200 della sequenza Genbank AC005666, versione 1 (SEQ ID NO: 13), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene PRPH compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 149.821 e 152.460 della sequenza Genbank AC125611, versione 4 (SEQ ID NO: 14), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene PTGER3 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 123.001 e 124.560 della sequenza Genbank AL031429, versione 11 (SEQ ID NO: 15), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

In un'altra forma di attuazione, il procedimento dell'invenzione comprende la fase di analizzare lo stato di metilazione della sequenza nucleotidica del gene PTPRM compresa tra le posizioni nucleotidiche corrispondenti ai

nucleotidi 64.321 e 66.660 della sequenza Genbank AP001091, versione 5 (SEQ ID NO: 16), la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

La tabella 1 riassume la corrispondenza delle isole CpG di ciascuno dei geni sopra menzionati con le coordinate nucleotidiche delle rispettive sequenze Genbank.

Tabella 1. Nuovi marcatori genici di metilazione aberrante in tumori umani e localizzazione loro

isole CpG

Gene symbol	Isola CpG						SEQ ID NO:			
	Genbank n.	Genbank version	da nt	a nt	Dimensione	seq WT	Seq meti- lata top	Seq meti- lata bot- tom	Seq non metilata top	Seq non metilata bottom
ARHGAP20	AP003460	AP003460.3	45.840	42.661	3.180	1	17	18	19	20
CDH11	AC137643	AC137643.3	52.081	55.500	3.420	2	21	22	23	24
FLI1	AP001122	AP001122.5	40.001	47.460	7.460	3	25	26	27	28
FOSL2	AC104695	AC104695.2	52.801	57.000	4.200	4	29	30	31	32
HES2	AL031848	AL031848.11	31.741	34.020	2.280	5	33	34	35	36
HTR6	AL031727	AL031727.43	92.521	95.340	2.820	6	37	38	39	40
LHX3	AL138781	AL138781.13	116.040	111.001	5.040	7	41	42	43	44
LOC51149	AC008393	AC008393.7	119.700	117.001	2.700	8	45	46	47	48

MAP1B	AC093218	AC093218.2	39.361	..	41.460	2.100	9	49	50	51	52
MDM2	AC025423	AC025423.32	141.660	..	140.401	1.260	10	53	54	55	56
NID1	AL122018	AL122018.37	38.520	..	36.661	1.860	11	57	58	59	60
NID2	AL118557	AL118557.5	77.340		75.001	2.340	12	61	62	63	64
PNUTL2	AC005666	AC005666.1	111.200	..	108.541	2.660	13	65	66	67	68
PRPH	AC125611	AC125611.4	152.460	..	149.821	2.640	14	69	70	71	72
PTGER3	AL031429	AL031429.11	124.560	..	123.001	1.560	15	73	74	75	76
PTPRM	AP001091	AP001091.5	64.321	..	66.660	2.340	16	77	78	79	80

Lo stato di metilazione dell'isola CpG viene analizzato utilizzando tecniche che includono il trattamento chimico del DNA con un reagente capace di trasformare le differenze di metilazione in differenze di sequenza. Preferibilmente, a tale scopo viene utilizzato un reagente chimico capace di trasformare le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina.

Un reagente preferito per questo scopo è il bisolfito, preferibilmente sodio bisolfito, in combinazione con idrochinone. In questa reazione chimica, le citosine non metilate presenti nel DNA vengono infatti deaminate ad uracile che, in termini di appaiamento delle basi, corrisponde alla timidina. Le citosine metilate sono invece resistenti al trattamento chimico e pertanto non subiscono alcuna modificazione. Conseguentemente, le metilcitosine presenti nel DNA originario, che inizialmente non potevano essere distinte dalle citosine poiché presentavano le stesse proprietà di appaiamento, rimangono le uniche citosine presenti nel DNA trattato chimicamente e possono quindi essere identificate utilizzando tecniche standard di biologia molecolare.

La sequenza di basi del DNA trattato chimicamente può ad esempio essere analizzata mediante sequenziamento diretto. In alternativa possono essere utilizzate tecniche,

quale ad esempio la Methylation Specific PCR (MSP), basate sull'amplificazione metilazione-specifica di segmenti dell'isola CpG del DNA campione trattato chimicamente. Tali tecniche utilizzano oligonucleotidi capaci di ibridarsi selettivamente alle sequenze modificate dell'isola CpG metilata o non metilata ottenute mediante il trattamento chimico sopra descritto.

Trattando chimicamente come descritto sopra un campione di DNA genomico includente l'isola CpG di uno dei geni descritti in tabella 1, si ottengono per ciascun gene due filamenti modificati, ciascuno dei quali è derivato da uno dei due filamenti del DNA genomico trattato, i quali tuttavia non sono più tra loro complementari.

Le sequenze denominate SEQ ID NO: 17 e SEQ ID NO: 18 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene ARHGAP20 sono metilati.

Le sequenze denominate SEQ ID NO: 19 e SEQ ID NO: 20 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene ARHGAP20 è metilato.

Le sequenze denominate SEQ ID NO: 21 e SEQ ID NO: 22 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene CDH11 sono metilati.

Le sequenze denominate SEQ ID NO: 23 e SEQ ID NO: 24 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene CDH11 è metilato.

Le sequenze denominate SEQ ID NO: 25 e SEQ ID NO: 26 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene FLI1 sono metilati.

Le sequenze denominate SEQ ID NO: 27 e SEQ ID NO: 28 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene FLI1 è metilato.

Le sequenze denominate SEQ ID NO: 29 e SEQ ID NO: 30 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene FOSL2 sono metilati.

Le sequenze denominate SEQ ID NO: 31 e SEQ ID NO: 32 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene FOSL2 è metilato.

Le sequenze denominate SEQ ID NO: 33 e SEQ ID NO: 34 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene HES2 sono metilati.

Le sequenze denominate SEQ ID NO: 35 e SEQ ID NO: 36

sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene HES2 è metilato.

Le sequenze denominate SEQ ID NO: 37 e SEQ ID NO: 38 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene HTR6 sono metilati.

Le sequenze denominate SEQ ID NO: 39 e SEQ ID NO: 40 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene HTR6 è metilato.

Le sequenze denominate SEQ ID NO: 41 e SEQ ID NO: 42 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene LHX3 sono metilati.

Le sequenze denominate SEQ ID NO: 43 e SEQ ID NO: 44 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene LHX3 è metilato.

Le sequenze denominate SEQ ID NO: 45 e SEQ ID NO: 46 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene LOC51149 sono metilati.

Le sequenze denominate SEQ ID NO: 47 e SEQ ID NO: 48 sono le sequenze nucleotidiche dei due filamenti modifica-

ti che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene LOC51149 è metilato.

Le sequenze denominate SEQ ID NO: 49 e SEQ ID NO: 50 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene MAP1B sono metilati.

Le sequenze denominate SEQ ID NO: 51 e SEQ ID NO: 52 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene MAP1B è metilato.

Le sequenze denominate SEQ ID NO: 53 e SEQ ID NO: 54 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene MDM2 sono metilati.

Le sequenze denominate SEQ ID NO: 55 e SEQ ID NO: 56 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene MDM2 è metilato.

Le sequenze denominate SEQ ID NO: 57 e SEQ ID NO: 58 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene NID1 sono metilati.

Le sequenze denominate SEQ ID NO: 59 e SEQ ID NO: 60 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi

dell'isola CpG originaria del gene NID1 è metilato.

Le sequenze denominate SEQ ID NO: 61 e SEQ ID NO: 62 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene NID2 sono metilati.

Le sequenze denominate SEQ ID NO: 63 e SEQ ID NO: 64 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene NID2 è metilato.

Le sequenze denominate SEQ ID NO: 65 e SEQ ID NO: 66 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene PNUTL2 sono metilati.

Le sequenze denominate SEQ ID NO: 67 e SEQ ID NO: 68 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene PNUTL2 è metilato.

Le sequenze denominate SEQ ID NO: 69 e SEQ ID NO: 70 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene PRPH sono metilati.

Le sequenze denominate SEQ ID NO: 71 e SEQ ID NO: 72 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene PRPH è metilato.

Le sequenze denominate SEQ ID NO: 73 e SEQ ID NO: 74 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene PTGER3 sono metilati.

Le sequenze denominate SEQ ID NO: 75 e SEQ ID NO: 56 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene PTGER3 è metilato.

Le sequenze denominate SEQ ID NO: 77 e SEQ ID NO: 78 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando tutti i dinucleotidi dell'isola CpG originaria del gene PTPRM sono metilati.

Le sequenze denominate SEQ ID NO: 79 e SEQ ID NO: 80 sono le sequenze nucleotidiche dei due filamenti modificati che si ottengono quando nessuno dei dinucleotidi dell'isola CpG originaria del gene PTPRM è metilato.

Le sequenze SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19 e SEQ ID NO: 20 sono state determinate sulla base della sequenza Genbank AP003460, versione 3 (nucleotidi 42661-45840) del gene ARHGAP20.

Le sequenze SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23 e SEQ ID NO: 24 sono state determinate sulla base della sequenza Genbank AC137643, versione 3 (nucleotidi 52081-55500) del gene CDH11.

Le sequenze SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27

e SEQ ID NO: 28 sono state determinate sulla base della sequenza Genbank AP001122, versione 5 (nucleotidi 40001-47460) del gene FLI1.

Le sequenze SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31 e SEQ ID NO: 32 sono state determinate sulla base della sequenza Genbank AC104695, versione 2 (nucleotidi 52801-57000) del gene FOSL2.

Le sequenze SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35 e SEQ ID NO: 36 sono state determinate sulla base della sequenza Genbank AL031848, versione 11 (nucleotidi 31741-34020) del gene HES2.

Le sequenze SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39 e SEQ ID NO: 40 sono state determinate sulla base della sequenza Genbank AL031727, versione 43 (nucleotidi 92521-95340) del gene HTR6.

Le sequenze SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43 e SEQ ID NO: 44 sono state determinate sulla base della sequenza Genbank AL138781, versione 13 (nucleotidi 111001-116040) del gene LHX3.

Le sequenze SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 47 e SEQ ID NO: 48 sono state determinate sulla base della sequenza Genbank AC008393, versione 7 (nucleotidi 117001-119700) del gene LOC51149.

Le sequenze SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 51 e SEQ ID NO: 52 sono state determinate sulla base della

sequenza Genbank AC093218, versione 2 (nucleotidi 39361-41460) del gene MAP1B.

Le sequenze SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55 e SEQ ID NO: 56 sono state determinate sulla base della sequenza Genbank AC025423 versione 32 (nucleotidi 140401-141660) del gene MDM2.

Le sequenze SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59 e SEQ ID NO: 60 sono state determinate sulla base della sequenza Genbank AL122018, versione 37 (nucleotidi 36661-38520) del gene NID1.

Le sequenze SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63 e SEQ ID NO: 64 sono state determinate sulla base della sequenza Genbank AL118557, versione 5 (nucleotidi 75001-77340) del gene NID2.

Le sequenze SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67 e SEQ ID NO: 68 sono state determinate sulla base della sequenza Genbank AC005666, versione 1 (nucleotidi 108541-111200) del gene PNUF2.

Le sequenze SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71 e SEQ ID NO: 72 sono state determinate sulla base della sequenza Genbank AC125611, versione 4 (nucleotidi 149821-152460) del gene PRPH.

Le sequenze SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75 e SEQ ID NO: 76 sono state determinate sulla base della sequenza Genbank AL031429, versione 11 (nucleotidi 123001-

124560) del gene PTGER3.

Le sequenze SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79 e SEQ ID NO: 80 sono state determinate sulla base della sequenza Genbank AP001091, versione 5 (nucleotidi 64321-66660) del gene PTPRM.

La tabella 1 riassume la corrispondenza tra i diversi geni e le SEQ ID.

Oligonucleotidi di almeno 10 nucleotidi di lunghezza complementari o identici ad un segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, 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: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59 e SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ

ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79 e SEQ ID NO: 80 costituiscono un utile strumento per l'analisi dello stato di metilazione delle isole CpG dei geni elencati in tabella 1 in un campione di DNA genomico, poiché la loro ibridazione dipende dallo stato di metilazione dell'isola CpG originaria del campione. Tali oligonucleotidi rientrano nell'ambito della presente invenzione. Preferibilmente, gli oligonucleotidi dell'invenzione sono complementari o identici a un segmento di una sequenza bersaglio come definita sopra comprendente almeno un dinucleotide CpG.

Nel procedimento diagnostico dell'invenzione, gli oligonucleotidi sopra definiti possono essere utilizzati come primers di amplificazione o come sonde di ibridazione. Nel secondo caso, essi hanno preferibilmente una lunghezza di almeno 18 nucleotidi.

A titolo di esempio, la tabella 2a riporta primers oligonucleotidici specifici basati su alcune delle sequenze bersaglio sopra elencate, utili nel procedimento diagnostico dell'invenzione.

Le caratteristiche del prodotto amplificato con i primers della tabella 2a sono riportate in tabella 2b.

Tabella 2a. Primers oligonucleotidici specifici per isole CpG elencate in Tabella 1

Gene	Primer 1	Sequenza Oligonucleotidica	Seq ID NO.	Primer 2	Sequenza Oligonucleotidica	Seq ID NO.
ARHGAP20	ARHGAP20_MF	AGTTTTTATTGTCGGCGCGC	81	ARHGAP20_MR	ACGAAAAACGACGACGCTACC	82
CDH11	CDH11_MF	CGCGGACGGGGTCGGTTTTC	83	CDH11_MR	TACTCTCGACCCGCGAC	84
FLI1	FLI1_MF	TAAGCGCGGGGTACCGAC	85	FLI1_MR	CGCCTAACCGACTAACCGC	86
FOSL2	FOSL2_MF	TCGTTGAGTTTCGGTTGCGGC	87	FOSL2_MR	TACGGCGCTCGTTCTCGCGC	88
HES2	HES2_MF	TTGGGGGTCGTTATTTCG	89	HES2_MR	CAAACGAATACGGCCCC	90
HTR6	HTR6_MF	GCGTACGTTTCGGCGGC	91	HTR6_MR	AAAAACGACCGCGAACCGAAC	92
LHX3	LHX3_MF	CGGTGTTTCGTTTTCGGGTC	93	LHX3_MR	CTAACCGAACGAAAAACGAAAC	94
LOC51149	LOC51149_MF	CGGTTTTCGTTAGACGACGAGTC	95	LOC51149_MR	CCTACGGCGTCTCGCATAC	96
MAP1B	MAP1B_MF	ATAAAGCGCGGTCGTTTTC	97	MAP1B_MR	CTATACCTCGACGAAATATCTC	98

MDM2	MDM2_MF	TTAGGGCGTCTGTGTTTTCGGCG	99	MDM2_MR	ACCGCCGCGAATAACCGTCC	100
NID1	NID1_MF	GAGGGTTTCGTTTCGTTTAGC	101	NID1_MR	AACGCCGTTTCGCTAAAAATCG	102
NID2	NID2_MF	TAGTATTGGTAACGACGATAGTATC	103	NID2_MR	AAATTCGAAACTAACGCGACACG	104
PNUTL2	PNUTL2_MF	TTTCGCTATTTCGGGGTTCGC	105	PNUTL2_MR	GACCCGCGACGAAACTACGC	106
PRPH	PRPH_MF	TTCTCGGGGTTTTTCGGGTC	107	PRPH_MR	AAAACGCCCGCTCCCGCTC	108
PTGER3	PTGER3_MF	GGATTCGGTATTTTCGGCGC	109	PTGER3_MR	GAACGACGACGAAAAATCGAC	110
PTPRM	PTPRM_MF	TACGTTTTTTTAGCGGGTCCG	111	PTPRM_MR	CGAAACCCCGAACTACCGACC	112

Tabella 2b. Caratteristiche dei prodotti amplificati con i primers descritti in tabella 2a

Gene	Primer 1	Primer 2	T (°C) annealing	Prodotto amplificato			
				Dimensione (nt)	da nt	a nt	da SEQ ID NO.
ARHGAP20	ARHGAP20_MF	ARHGAP20_MR	56°C	153	1777	1930	18
CDH11	CDH11_MF	CDH11_MR	59°C	246	2098	2343	21
FLI1	FLI1_MF	FLI1_MR	60°C	199	5744	5909	25
FOSL2	FOSL2_MF	FOSL2_MR	60°C	264	2496	2760	29
HES2	HES2_MF	HES2_MR	57°C	205	972	1177	33
HTR6	HTR6_MF	HTR6_MR	66°C	134	719	853	37
LHX3	LHX3_MF	LHX3_MR	57°C	164	2814	2978	42

LOC511149	LOC511149_MF	LOC511149_MR	58°C	176	1284	1460	46
MAP1B	MAP1B_MF	MAP1B_MR	53°C	216	315	531	49
MDM2	MDM2_MF	MDM2_MR	62°C	328	578	906	54
NID1	NID1_MF	NID1_MR	58°C	144	1228	1371	57
NID2	NID2_MF	NID2_MR	58°C	140	1237	1377	61
PNUTL2	PNUTL2_MF	PNUTL2_MR	60°C	216	826	1042	66
PRPH	PRPH_MF	PRPH_MR	61°C	198	100	297	70
PTGER3	PTGER3_MF	PTGER3_MR	57°C	191	388	579	74
PTPRM	PTPRM_MF	PTPRM_MR	57°C	245	741	986	77

Il procedimento diagnostico dell'invenzione può ad esempio essere un procedimento di rivelazione basato sull'amplificazione del DNA, eventualmente seguito da rivelazione dei frammenti di DNA amplificati tramite una sonda di ibridazione. In tale procedimento un campione di DNA genomico da esaminare viene pre-trattato chimicamente con un reagente atto a convertire le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina. Il campione di DNA genomico da analizzare è preferibilmente ottenuto da una fonte quale sangue, siero, plasma, lavaggio bronchiale, espettorato, saliva, lavaggio intestinale, urina, feci, eiaculato, tamponi di varia origine, ago aspirati, biopsie linfonodali, o loro combinazioni. Il suddetto pretrattamento chimico del DNA genomico viene effettuato preferibilmente con sodio bisolfito e idrochinone. A seguito del pretrattamento chimico, dal DNA genomico originario a doppio filamento si ottengono due filamenti modificati che tuttavia non sono più tra loro complementari.

Dopo la fase di pretrattamento chimico, uno qualsiasi dei filamenti modificati ottenuti dal pretrattamento del DNA genomico può essere sottoposto a una reazione di amplificazione degli acidi nucleici, utilizzando come primers di amplificazione una coppia di oligonucleotidi di almeno 10 nucleotidi di lunghezza, in cui uno di detti o-

lignonucleotidi è complementare a un primo segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO:17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77 e SEQ ID NO: 78 e l'altro di detti oligonucleotidi è identico a un secondo segmento di detta sequenza bersaglio, il secondo segmento essendo localizzato a valle del primo segmento.

Secondo una forma di attuazione, almeno uno di detti primo e secondo segmento della sequenza bersaglio comprende almeno un dinucleotide CpG. In tal caso, la reazione di amplificazione è metilazione-specifica, nel senso che la coppia di primers oligonucleotidici utilizzata è disegnata per amplificare specificamente un filamento modificato derivante dalla sequenza dell'isola CpG originaria metilata. In questa forma di attuazione, la rivelazione dei frammenti di DNA amplificati, se presenti, può essere effettuata con qualsiasi procedimento di per sé noto, ad esempio mediante elettroforesi su gel di agarosio e colorazione con

un agente intercalante del DNA, quale ad esempio bromuro di etidio.

Secondo un'altra forma di attuazione, né il primo né il secondo segmento della sequenza bersaglio comprende un dinucleotide CpG. In tal caso la reazione di amplificazione non è metilazione-specifica. Conseguentemente, la rivelazione dei frammenti amplificati, se presenti, verrà effettuata mediante ibridazione con una sonda oligonucleotidica di almeno 18 nucleotidi di lunghezza complementare a un terzo segmento della sequenza bersaglio, detto terzo segmento essendo situato tra i suddetti primo e secondo segmento e comprendendo almeno un dinucleotide CpG. Il terzo segmento della sequenza bersaglio può eventualmente essere parzialmente sovrapposto al primo o al secondo segmento.

In entrambe le forme di attuazione sopra descritte, la reazione di amplificazione è preferibilmente una reazione a catena della polimerasi (PCR). Ancora più preferibilmente, è una reazione di amplificazione in due fasi che comprende una PCR primaria seguita da una PCR secondaria semi nested o nested.

Poiché il DNA modificato che costituisce il bersaglio della reazione di amplificazione è inizialmente a singolo filamento, nel primo ciclo di PCR al filamento bersaglio si ibriderà inizialmente uno solo dei due primers. Il pri-

mo primer ibridato verrà esteso da una polimerasi utilizzando come stampo il filamento bersaglio. Successivamente, il secondo primer si ibriderà alla catena neosintetizzata e verrà esteso dalla polimerasi utilizzando come stampo la catena neosintetizzata. In tal modo, il DNA bersaglio iniziale a singolo filamento verrà trasformato in DNA a doppio filamento. Invece, nei successivi cicli della reazione PCR i due primers di amplificazione si ibrideranno simultaneamente ciascuno ad un filamento del DNA bersaglio a doppio filamento.

In tabella 2a sono riportati alcuni esempi specifici di oligonucleotidi adatti come primers o sonde nel procedimento diagnostico dell'invenzione.

Gli oligonucleotidi ARHGAP20_MF (SEQ ID NO: 81) e ARHGAP20_MR (SEQ ID NO: 82) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 18. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi ARHGAP20_MF e ARHGAP20_MR amplifica una sequenza di 153 bp compresa tra il nucleotide 1777 ed il nucleotide 1930 di SEQ ID NO: 18.

Gli oligonucleotidi CDH11_MF (SEQ ID NO: 83) e CDH11_MR (SEQ ID NO: 84) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 21. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi CDH11_MF e CDH11_MR amplifica una sequenza di 246

bp compresa tra il nucleotide 2098 e il nucleotide 2343 di SEQ ID NO: 21.

Gli oligonucleotidi FLI1_MF (SEQ ID NO: 85) e FLI1_MR (SEQ ID NO: 86) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 25. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi FLI1_MF e FLI1_MR amplifica una sequenza di 199 bp compresa tra il nucleotide 5744 ed il nucleotide 5909 di SEQ ID NO: 25.

Gli oligonucleotidi FOSL2_MF (SEQ ID NO: 87) e FOSL2_MR (SEQ ID NO: 88) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 29. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi FOSL2_MF e FOSL2_MR amplifica una sequenza di 264 bp compresa tra il nucleotide 2496 e il nucleotide 2760 di SEQ ID NO: 29.

Gli oligonucleotidi HES2_MF (SEQ ID NO: 89) e HES2_MR (SEQ ID NO: 90) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 33. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi HES2_MF e HES2_MR amplifica una sequenza di 205 bp compresa tra il nucleotide 972 e il nucleotide 1177 di SEQ ID NO: 33.

Gli oligonucleotidi HTR6_MF (SEQ ID NO: 91) e HTR6_MR (SEQ ID NO: 92) sono stati disegnati per ibridarsi speci-

ficamente in SEQ ID NO: 37. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi HTR6_MF e HTR6_MR amplifica una sequenza di 134 bp compresa tra il nucleotide 719 e il nucleotide 853 di SEQ ID NO: 37.

Gli oligonucleotidi LHX3_MF (SEQ ID NO: 93) e LHX3_MR (SEQ ID NO: 94) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 42. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi LHX3_MF e LHX3_MR amplifica una sequenza di 164 bp compresa tra il nucleotide 2814 e il nucleotide 2978 di SEQ ID NO: 42.

Gli oligonucleotidi LOC51149_MF (SEQ ID NO: 95) e LOC51149_MR (SEQ ID NO: 96) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 46. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi LOC51149_MF e LOC51149_MR amplifica una sequenza di 176 bp compresa tra il nucleotide 1284 e il nucleotide 1460 di SEQ ID NO: 46.

Gli oligonucleotidi MAP1B_MF (SEQ ID NO: 97) e MAP1B_MR (SEQ ID NO: 98) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 49. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi MAP1B_MF e MAP1B_MR amplifica una sequenza di 216 bp compresa tra il nucleotide 315 e il nucleotide 531 di

SEQ ID NO: 49.

Gli oligonucleotidi MDM2_MF (SEQ ID NO: 99) e MDM2_MR (SEQ ID NO: 100) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 54. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi MDM2_MF e MDM2_MR amplifica una sequenza di 328 bp compresa tra il nucleotide 578 e il nucleotide 906 di SEQ ID NO: 54.

Gli oligonucleotidi NID1_MF (SEQ ID NO: 101) e NID1_MR (SEQ ID NO: 102) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 57. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi NID1_MF e NID1_MR amplifica una sequenza di 144 bp compresa tra il nucleotide 1228 e il nucleotide 1371 di SEQ ID NO: 57.

Gli oligonucleotidi NID2_MF (SEQ ID NO: 103) e NID2_MR (SEQ ID NO: 104) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 61. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi NID2_MF e NID2_MR amplifica una sequenza di 140 bp compresa tra il nucleotide 1237 e il nucleotide 1377 di SEQ ID NO: 61.

Gli oligonucleotidi PNU TL2_MF (SEQ ID NO: 105) e PNU TL2_MR (SEQ ID NO: 106) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 66. Quando utilizzati

come primers in una amplificazione PCR, la coppia di oligonucleotidi PNUTL2_MF e PNUTL2_MR amplifica una sequenza di 216 bp compresa tra il nucleotide 826 e il nucleotide 1042 di SEQ ID NO: 66.

Gli oligonucleotidi PRPH_MF (SEQ ID NO: 107) e PRPH_MR (SEQ ID NO: 108) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 70. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi PRPH_MF e PRPH_MR amplifica una sequenza di 198 bp compresa tra il nucleotide 100 e il nucleotide 297 di SEQ ID NO: 70.

Gli oligonucleotidi PTGER3_MF (SEQ ID NO: 109) e PTGER3_MR (SEQ ID NO: 110) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 74. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi PTGER3_MF e PTGER3_MR amplifica una sequenza di 191 bp compresa tra il nucleotide 388 e il nucleotide 579 di SEQ ID NO: 74.

Gli oligonucleotidi PTPRM_MF (SEQ ID NO: 111) e PTPRM_MR (SEQ ID NO: 112) sono stati disegnati per ibridarsi specificamente in SEQ ID NO: 77. Quando utilizzati come primers in una amplificazione PCR, la coppia di oligonucleotidi PTPRM_MF e PTPRM_MR amplifica una sequenza di 245 bp compresa tra il nucleotide 741 e il nucleotide 986 di SEQ ID NO: 77.

Nell'ambito della presente invenzione rientra inoltre un kit per l'esecuzione del procedimento diagnostico dell'invenzione, che può essere composto, ad esempio, da una coppia di primers di amplificazione come definiti in precedenza eventualmente in combinazione con un reagente atto a convertire le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina, ad esempio sodio bisolfito in combinazione con idrochinone. Il kit può inoltre comprendere mezzi di rivelazione del DNA, come ad esempio una sonda di ibridazione metilazione-specifica come definita in precedenza, e/o mezzi di amplificazione del DNA, ad esempio un enzima polimerasi. In alternativa alla sonda di ibridazione, il kit può comprendere un reagente di rivelazione del DNA quale un agente intercalante del DNA, per esempio bromuro di etidio.

Il kit dell'invenzione può anche comprendere una seconda coppia di primers di amplificazione di almeno 10 nucleotidi di lunghezza, uno di detti oligonucleotidi essendo complementare a un primo segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 48,

SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60 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: 79 e SEQ ID NO: 80 e l'altro oligonucleotide essendo identico a un secondo segmento di detta sequenza bersaglio, il secondo segmento essendo localizzato a valle del primo segmento. Preferibilmente, almeno uno di tali primo e secondo segmento della sequenza bersaglio comprende almeno un dinucleotide TpG. La seconda coppia di primers è utilizzata come controllo dell'avvenuta modifica del DNA a seguito del trattamento con bisolfito, permettendo la convalida di un risultato negativo dell'amplificazione con primers disegnati sulla base delle sequenze nucleotidiche modificate derivate dall'isola CpG metilata.

Sezione sperimentale (esempi)

E' stato analizzato lo stato di metilazione delle isole CpG dei geni indicati in tabella 1 in campioni tumorali e normali umani, utilizzando i primers e le condizioni di reazione indicate in tabella 2. I risultati ottenuti sono riassunti sotto in tabella 3.

Tabella 3

	Tessuto	ARRGAP20	CDH11	FLI1	POSL2	HES2	MYR6	LEK3	LOC51149
Colon	Carcinoma	61% (17/28)	47% (9/19)	82% (45/50)	nd	0% (0/28)	11% (2/19)	32% (6/19)	nd
	Mucosa normale	0% (0/10)	0% (0/10)	21% (5/24)	70% (7/10)	0% (0/10)	0% (0/10)	0% (0/10)	60% (6/10)
Stomaco	Carcinoma	58% (11/19)	84% (16/19)	86% (13/16)	nd	21% (3/19)	32% (6/19)	37% (7/19)	nd
	Mucosa normale	0% (0/10)	8% (1/13)	31% (4/13)	40% (4/10)	0% (0/10)	8% (1/13)	0% (0/13)	82% (9/11)
Fegato	Carcinoma	14% (4/28)	10% (2/20)	25% (6/24)	69% (18/26)	14% (4/28)	14% (3/21)	0% (0/21)	81% (17/21)
	Epatociti	0% (0/9)	0% (0/9)	22% (2/9)	22% (2/9)	0% (0/9)	44% (0/9)	0% (0/9)	0% (0/9)
Mammella	Carcinoma	25% (7/28)	0% (6/19)	69% (35/51)	68% (19/28)	4% (1/28)	nd	0% (0/19)	nd
	Tessuto normale	nd	nd	0% (0/9)	0% (0/9)	nd	nd	nd	nd

continuazione Tabella 3

Tessuto	MAP1B	MDM2	NID1	NID2	PNUTL2	PRPH	PTGER3	PTPRN	
Colon	Carcinoma	43% (12/28)	nd	69% (33/48)	29% (14/48)	0% (0/28)	79% (15/19)	61% (17/28)	75% (21/28)
	Mucosa normale	0% (0/10)	40% (4/10)	33% (8/24)	0% (0/24)	0% (0/10)	0% (0/10)	0% (0/10)	0% (0/10)
	Carcinoma	26% (5/19)	nd	90% (18/20)	95% (19/20)	26% (5/19)	nd	68% (13/19)	74% (14/19)
Stomaco	Mucosa normale	0% (0/10)	30% (3/10)	38% (5/13)	0% (0/13)	0% (0/10)	77% (10/13)	0% (0/10)	0% (0/10)
	Carcinoma	29% (7/23)	50% (13/26)	29% (8/28)	25% (7/28)	0% (0/24)	nd	36% (10/28)	17% (4/23)
Fegato	Epatociti	0% (0/9)	0% (0/9)	0% (0/9)	0% (0/9)	0% (0/9)	78% (0/9)	11% (1/9)	0% (0/9)
Mammella	Carcinoma	4% (1/28)	nd	62% (30/48)	40% (19/47)	7% (2/28)	90% (18/20)	11% (3/28)	50% (14/28)
	Tessuto normale	nd	nd	nd	nd	nd	33% (1/3)	nd	0% (0/9)

Dall'analisi effettuata su campioni tumorali e normali si evincono le percentuali di metilazione per ciascun gene nei diversi tessuti analizzati. I tessuti analizzati derivano da colon, stomaco, fegato e mammella. Questo risultato indica che le isole CpG elencate in tabella 1 sono frequentemente metilate in almeno uno dei tessuti tumorali analizzati. Questi tumori sono da considerarsi un esempio indicativo della alta frequenza con cui questi geni sono metilati in malattie neoplastiche non limitatamente agli esempi descritti in tabella 3.

Le sequenze nucleotidiche a cui si fa riferimento nella presente descrizione sono illustrate nell'annessa lista delle sequenze, in cui:

SEQ ID NO. 1 è la CpG island di ARHGAP20, corrispondente al segmento di 3.180 nt compreso tra i nt 45840-42661 della versione 3 della sequenza Genbank AP003460; SEQ ID NO. 2 è la CpG Island del gene CDH11, corrispondente al segmento di 3.420 nt compreso tra i nt 52021-55500 della versione 3 della sequenza Genbank AC137643; SEQ ID NO: 3 è la CpG Island di FLI1 corrispondente al segmento di 7.460 nt compreso tra i nt 40001-47460 della versione 5 della sequenza Genbank AP001122; SEQ ID NO: 4 è la CpG Island di FOSL2 corrispondente al segmento di 4.200 nt compreso tra i nt 52801-57000 della versione 2 della sequenza Genbank AC104695; SEQ ID NO: 5 è la CpG Island di

HES2 corrispondente al segmento di 2.280 nt compreso tra i nt 31741-34020 della versione 11 della sequenza Genbank AL031848; SEQ ID NO: 6 è la CpG Island di HTR6 corrispondente al segmento di 2.820 nt compreso tra i nt 92521-95340 della versione 43 della sequenza Genbank AL031727; SEQ ID NO: 7 è la CpG Island di LHX3 corrispondente al segmento di 5.040 nt compreso tra i nt 111001-116040 della versione 13 della sequenza Genbank AL138781; SEQ ID NO: 8 è la CpG Island di LOC51149 corrispondente al segmento di 2.700 nt compreso tra i nt 117001-119700 della versione 7 della sequenza Genbank AC008393; SEQ ID NO: 9 è la CpG Island di MAP1B corrispondente al segmento di 2.100 nt compreso tra i nt 39361-41460 della versione 2 della sequenza Genbank AC093218; SEQ ID NO: 10 è la CpG Island di MDM2 corrispondente al segmento di 1.260 nt compreso tra i nt 140401-141660 della versione 32 della sequenza Genbank AC025423; SEQ ID NO. 11 è la CpG island del gene NID1, corrispondente al segmento di 1.860 nt compreso tra i nt 36661-38520 della sequenza Genbank AL122018, versione 37; SEQ ID NO. 12 è la CpG island del gene NID2, corrispondente al segmento di 2.340 nt compreso tra i nt 75001-77340 di Genbank AL118557, versione 5; SEQ ID NO. 13 è la CpG island del gene PNUTL2, corrispondente al segmento di 2.660 nt compreso tra i nt 108541-111200 di Genbank AC005666, versione 1; SEQ ID NO. 14 è la CpG island del

gene PRPH, corrispondente al segmento di 2.640 nt compreso tra i nt 149821-152460 di Genbank AC125611, versione 4; SEQ ID NO. 15 è la CpG island del gene PTGER3, corrispondente al segmento di 1.560 nt compreso tra i nt 123001-124560 di Genbank AL031429, versione 11; SEQ ID NO. 16 è la CpG island del gene PTPRM, corrispondente al segmento di 2.340 nt compreso tra i nt 64321-66660 di Genbank AP001091, versione 5; SEQ ID NO. 17 è la sequenza derivata dalla sequenza metilata del gene ARHGAP20 (top strand), derivata da SEQ ID NO. 1; SEQ ID NO. 18 è la sequenza derivata dalla sequenza metilata del gene ARHGAP20 (bottom strand), derivata da SEQ ID NO. 1; SEQ ID NO. 19 è la sequenza derivata dalla sequenza non metilata del gene ARHGAP20 (top strand), derivata da SEQ ID NO. 1; SEQ ID NO. 20 è la sequenza derivata dalla sequenza non metilata del gene ARHGAP20 (bottom strand), derivata da SEQ ID NO. 1; SEQ ID NO. 21 è la sequenza derivata dalla sequenza metilata del gene CDH11 (top strand), derivata da SEQ ID NO. 2; SEQ ID NO. 22 è la sequenza derivata dalla sequenza metilata del gene CDH11 (bottom strand), derivata da SEQ ID NO. 2; SEQ ID NO. 23 è la sequenza derivata dalla sequenza non metilata del gene CDH11 (top strand), derivata da SEQ ID NO. 2; SEQ ID NO. 24 è la sequenza derivata dalla sequenza non metilata del gene CDH11 (bottom strand), derivata da SEQ ID NO. 2; SEQ ID NO. 25 è la sequenza derivata

dalla sequenza metilata del gene FLI1 (top strand), derivata da SEQ ID NO. 3; SEQ ID NO. 26 è la sequenza derivata dalla sequenza metilata del gene FLI1 (bottom strand), derivata da SEQ ID NO. 3; SEQ ID NO. 27 è la sequenza derivata dalla sequenza non metilata del gene FLI1 (top strand), derivata da SEQ ID NO. 3; SEQ ID NO. 28 è la sequenza derivata dalla sequenza non metilata del gene FLI1 (bottom strand), derivata da SEQ ID NO. 3; SEQ ID NO: 29 è la sequenza derivata dalla sequenza metilata del gene FOSL2 (top strand), derivata da SEQ ID NO. 4; SEQ ID NO: 30 è la sequenza derivata dalla sequenza metilata del gene FOSL2 (bottom strand), derivata da SEQ ID NO. 4; SEQ ID NO: 31 è la sequenza derivata dalla sequenza non metilata del gene FOSL2 (top strand), derivata da SEQ ID NO. 4; SEQ ID NO: 32 è la sequenza derivata dalla sequenza non metilata del gene FOSL2 (bottom strand), derivata da SEQ ID NO. 4; SEQ ID NO: 33 è la sequenza derivata dalla sequenza metilata del gene HES2 (top strand), derivata da SEQ ID NO.5; SEQ ID NO: 34 è la sequenza derivata dalla sequenza metilata del gene HES2 (bottom strand), derivata da SEQ ID NO.5; SEQ ID NO: 35 è la sequenza derivata dalla sequenza non metilata del gene HES2 (top strand), derivata da SEQ ID NO.5; SEQ ID NO: 36 è la sequenza derivata dalla sequenza non metilata del gene HES2 (bottom strand), derivata da SEQ ID NO.5; SEQ ID NO: 37 è la sequenza derivata

dalla sequenza metilata del gene HTR6 (top strand), derivata da SEQ ID NO.6; SEQ ID NO: 38 è la sequenza derivata dalla sequenza metilata del gene HTR6 (bottom strand), derivata da SEQ ID NO.6; SEQ ID NO: 39 è la sequenza derivata dalla sequenza non metilata del gene HTR6 (top strand), derivata da SEQ ID NO.6; SEQ ID NO: 40 è la sequenza derivata dalla sequenza non metilata del gene HTR6 (bottom strand), SEQ ID NO: 41 è la sequenza derivata dalla sequenza metilata del gene LHX3 (top strand), derivata da SEQ ID NO.7; SEQ ID NO: 42 è la sequenza derivata dalla sequenza metilata del gene LHX3 (bottom strand), derivata da SEQ ID NO.7; SEQ ID NO: 43 è la sequenza derivata dalla sequenza non metilata del gene LHX3 (top strand), derivata da SEQ ID NO.7; SEQ ID NO: 44 è la sequenza derivata dalla sequenza non metilata del gene LHX3 (bottom strand), SEQ ID NO: 45 è la sequenza derivata dalla sequenza metilata del gene LOC51149 (top strand), derivata da SEQ ID NO.8; SEQ ID NO: 46 è la sequenza derivata dalla sequenza metilata del gene LOC51149 (bottom strand), derivata da SEQ ID NO.8; SEQ ID NO: 47 è la sequenza derivata dalla sequenza non metilata del gene LOC51149 (top strand), derivata da SEQ ID NO.8; SEQ ID NO: 48 è la sequenza derivata dalla sequenza non metilata del gene LOC51149 (bottom strand), SEQ ID NO: 49 è la sequenza derivata dalla sequenza metilata del gene MAP1B (top strand), derivata da SEQ ID NO.9;

SEQ ID NO: 50 è la sequenza derivata dalla sequenza metilata del gene MAP1B (bottom strand), derivata da SEQ ID NO.9; SEQ ID NO: 51 è la sequenza derivata dalla sequenza non metilata del gene MAP1B (top strand), derivata da SEQ ID NO.8; SEQ ID NO: 52 è la sequenza derivata dalla sequenza non metilata del gene MAP1B (bottom strand), derivata da SEQ ID NO.8; SEQ ID NO: 53 è la sequenza derivata dalla sequenza metilata del gene MDM2 (top strand), derivata da SEQ ID NO.10; SEQ ID NO: 54 è la sequenza derivata dalla sequenza metilata del gene MDM2 (bottom strand), derivata da SEQ ID NO.10; SEQ ID NO: 55 è la sequenza derivata dalla sequenza non metilata del gene MDM2 (top strand), derivata da SEQ ID NO.10; SEQ ID NO: 56 è la sequenza derivata dalla sequenza non metilata del gene MDM2 (bottom strand), derivata da SEQ ID NO.10; SEQ ID NO: 57 è la sequenza derivata dalla sequenza metilata del gene NID1 (top strand), derivata da SEQ ID NO.11; SEQ ID NO: 58 è la sequenza derivata dalla sequenza metilata del gene NID1 (bottom strand), derivata da SEQ ID NO.11; SEQ ID NO: 59 è la sequenza derivata dalla sequenza non metilata del gene NID1 (top strand), derivata da SEQ ID NO.11; SEQ ID NO: 60 è la sequenza derivata dalla sequenza non metilata del gene NID1 (bottom strand), derivata da SEQ ID NO.11; SEQ ID NO: 61 è la sequenza derivata dalla sequenza metilata del gene NID2 (top strand), derivata da SEQ ID NO.12; SEQ ID

NO: 62 è la sequenza derivata dalla sequenza metilata del gene NID2 (bottom strand), derivata da SEQ ID NO.12; SEQ ID NO: 63 è la sequenza derivata dalla sequenza non metilata del gene NID2 (top strand), derivata da SEQ ID NO.12; SEQ ID NO: 64 è la sequenza derivata dalla sequenza non metilata del gene NID2 (bottom strand), derivata da SEQ ID NO.12; SEQ ID NO: 65 è la sequenza derivata dalla sequenza metilata del gene PNUTL2 (top strand), derivata da SEQ ID NO.13; SEQ ID NO: 66 è la sequenza derivata dalla sequenza metilata del gene PNUTL2 (bottom strand), derivata da SEQ ID NO.13; SEQ ID NO: 67 è la sequenza derivata dalla sequenza non metilata del gene PNUTL2 (top strand), derivata da SEQ ID NO.13; SEQ ID NO: 68 è la sequenza derivata dalla sequenza non metilata del gene PNUTL2 (bottom strand), derivata da SEQ ID NO.13; SEQ ID NO: 69 è la sequenza derivata dalla sequenza metilata del gene PRPH (top strand), derivata da SEQ ID NO.14; SEQ ID NO: 70 è la sequenza derivata dalla sequenza metilata del gene PRPH (bottom strand), derivata da SEQ ID NO.14; SEQ ID NO: 71 è la sequenza derivata dalla sequenza non metilata del gene PRPH (top strand), derivata da SEQ ID NO.14; SEQ ID NO: 72 è la sequenza derivata dalla sequenza non metilata del gene PRPH (bottom strand), derivata da SEQ ID NO.14; SEQ ID NO: 73 è la sequenza derivata dalla sequenza metilata del gene PTGER3 (top strand), derivata da SEQ ID NO.15; SEQ ID NO:

74 è la sequenza derivata dalla sequenza metilata del gene PTGER3 (bottom strand), derivata da SEQ ID NO.15; SEQ ID NO: 75 è la sequenza derivata dalla sequenza non metilata del gene PTGER3 (top strand), derivata da SEQ ID NO.15; SEQ ID NO: 76 è la sequenza derivata dalla sequenza non metilata del gene PTGER3 (bottom strand), derivata da SEQ ID NO.15; SEQ ID NO: 77 è la sequenza derivata dalla sequenza metilata del gene PTPRM (top strand), derivata da SEQ ID NO.16; SEQ ID NO: 78 è la sequenza derivata dalla sequenza metilata del gene PTPRM (bottom strand), derivata da SEQ ID NO.16; SEQ ID NO: 79 è la sequenza derivata dalla sequenza non metilata del gene PTPRM (top strand), derivata da SEQ ID NO.16; SEQ ID NO: 80 è la sequenza derivata dalla sequenza non metilata del gene PTPRM (bottom strand), derivata da SEQ ID NO.16; SEQ ID NO: 81 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO: 18; SEQ ID NO: 82 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:18; SEQ ID NO: 83 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO: 21; SEQ ID NO: 84 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:21; SEQ ID NO: 85 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su

SEQ ID NO:25; SEQ ID NO: 86 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:25; SEQ ID NO: 87 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:29; SEQ ID NO: 88 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:29; SEQ ID NO: 89 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:33; SEQ ID NO: 90 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:33; SEQ ID NO: 91 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:37; SEQ ID NO: 92 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:37; SEQ ID NO: 93 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:42; SEQ ID NO: 94 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:42; SEQ ID NO: 95 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:46; SEQ ID NO: 96 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:46; SEQ ID NO: 97 è la sequenza oligonu-

cleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:49; SEQ ID NO: 98 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:49; SEQ ID NO: 99 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:54; SEQ ID NO: 100 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:54; SEQ ID NO: 101 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:57; SEQ ID NO: 102 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:57; SEQ ID NO: 103 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:61; SEQ ID NO: 104 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:61; SEQ ID NO: 105 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:66; SEQ ID NO: 106 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:66; SEQ ID NO: 107 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:70; SEQ ID NO: 108 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare

invertita di SEQ ID NO:70; SEQ ID NO: 109 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:74; SEQ ID NO: 110 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:74; SEQ ID NO: 111 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:77; SEQ ID NO: 112 è la sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:77.

Lista delle sequenze nucleotidiche

SEQ ID NO. 1

CpG island di ARHGAP20, corrispondente al segmento di 3.180 nt compreso tra i nt
42661-45840 della versione 3 della sequenza Genbank AP003460

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1 cactacagcc catacatcat caagttcacg gacacccta gatggctccg tgacacggtc
61 aaggtccttg ggaactccca cacatttcta tactcggcac accgatcacc tctcttcaac
121 tgacctctag ccaacctaa atcctggtgg gaagatttat gaaaggcagt aaaatcaaga
181 caagcagggg acctgcgtaa cccctttaag tctctaata aacaaatgca atcccttaag
241 atatttctta aggaaaagct agaagatgcc tctaatacga acttggttcc agaaaagctg
301 gaagggcacc actaagacaa ggcaaaaaa aaaaaaagg caaatatcg gaaagtctta
361 tgctggaagc gggggtgggg aggcggggga caggcagaca gggctagaaa caccctaatc
421 aattctctag ggagcgaaac ggcagaggcc ggcagccgc ggcacagtg cacttgctca
481 gggaaccgtt ccagcgaaac ctgaccgga tcggaatcct cccgcagcac agcggccgtg
541 tttatcgga tggaacgcta caagttgtca cctgcaccc tctccagct ttgacagggg
601 aacgcgctg ccccaagcc cacaccgaca cccgatccc tatccagccc ggccagagtc
661 ccaggggcca gggaccagtg cagggagaag gtccccacc tcagccctca ggaccccaa
721 ccacagccca ccgcgccca cctgctcgg ttctaggccc agccgaacct acatgtcccc
781 gtagtgtcga gcgttatcat ccacagtcgc cctcaaact gtgacccca cctgggagac
841 ccggaatcat ccaggaccct ggtgtgggg gcagtactcc ccatatctgc cccccaaaa
901 ctgctatgga gcagcgcgc ctgcggggc aggtgagggg gccgagccca ccagcgcgc
961 agccccgtg cctaccttct tcagcgcgg ctgcgcctc cgggcagaca tcgcggccc
1021 tgactttggg gctgacacg ccaaaggga gtcagtgtc gccagggcca cttcgggagg
1081 ccaggggga cggcgaggg tcggggaag gcgatcgcc actacagccc gcgcgcctag
1141 actgaggag gagccggct gcagaaccg cggcgatgg agacgggag gaggtgcga
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1201 ggtcgctcga ggagagacta aggtctctaga aacggagaag cgggcgctct ggggagggcg
 1261 gcggcgctgc cgctggcgt caagggcggg aagtgttctg ggactctcat taggggccgc
 1321 gagcctcgag ogtaaaattc ccgcggcgtc cgcttagcgc gctgctgtgg cgggcgcgga
 1381 gggcgcgcg cggcagtggt ggctgcggcg gcggagggca cgggcccccg ctcagcgtec
 1441 tcaccttctt ggtgcagctg cctcccgga gccgagacac tcctgtcagg gaagaggagc
 1501 gccccggctg tccccctaga gtctctgct ggggggacat cgcttccatg aagaaaatct
 1561 tcaaacaat cccagcccag gaggaggcta caogatcatg tccggggct gccggccgga
 1621 ggggcgagga cgcgcggcg gaggcgcggc tgcgtgtc aggcaggag cagagctccg
 1681 ggtgctcgcc gcgcgctcc ogtcggggcc atgtacctcc gcctgcgtc gacacggcg
 1741 gctggaggcg agtgcagcg cgacagcccg tcagcgccgc ggcccgccc gcctcgggc
 1801 cgcacctcc gctccggcg cctgcgcgg gggcccgccc ccgcagcct cctcagcct
 1861 cctccagctt gggccctct agcctcgtec cagcctgcgg cgcgcctggc gggcgtctct
 1921 ctatatatgt tagcacacc gccacggct gacctttcg gtctgtgact cgcgtgggt
 1981 gcagcccgca ggagctcat gcctgtgtc acgcaaggcg gcctctagt caggacacg
 2041 cgcctctcc gccacctgc cactcccacc agaccccat cctcccgcg cgtgcccgc
 2101 ggcggaaggc gccctgcag cgcgtgcac cgcggagcgg tggcgacct agcctgagca
 2161 gaggagtgc agtgattcct gcctcgctt cagcggactg cggagggaat ccccccccc
 2221 accccactgg ggatagggtg gcacgtcgca gagtgtcgca gctgtacaaa ttggaagcc
 2281 cacagcatcg cctgacctct tgtgcaatc cgaacgctag cctgttcggg taacctgag
 2341 tgggcttctg cagccgtca tgcagcggc ccctgcacat ttgcaccgc ggtttcgct
 2401 gtctgcaggc tgcagagac ggggcattcc aaacgtgaaa gagcaatgaa ggaaatgca
 2461 gacagagcga ggacgcgaa atttgctaa gctattgaga aggtacaat atgtggaagt
 2521 gtttatcaga tatctgcgc gagagcataa ctctctgtca gcccaaatag aggcacaaat
 2581 attttaagg ccaaagaata atcagaggga gaggatttg agctgaccgc cgttgagctg
 2641 agtgttgctg cactttgcgg ggctggtga ctggtacgga tgattcgga gatggcattc

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2701 ttcccttgga gtcaggacta gagaagcagt ggcggattag tgaggaagga caccacgcta
2761 tgatattagg ttgtggaagg ggtttggttt gcttttgtgg taagaagaaa aaaatcgagg
2821 ttctgccag gttaggctgt tattaggaca ggtttagaa gaatagggct ctggccggct
2881 ctgtccaag gaagggatgc tgtccaacac aactcgcgc gcgcacacat caccaccatg
2941 ccaggaatg gtttattgtg gaaataatag ggggaaaatg ttccagcccg ttttaagcct
3001 tgtccacctc aactgttta aagtaggctt acataggctt tataaatcac acacacgtat
3061 aatcacaca caagtataaa tcacatgtat gatttgtaaa tcactatta ttgtgtttat
3121 gtatgtgtgc atatacacac acagtttttc atggctactc tctttttgca gctgagacct

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SEQ ID NO: 2

CpG Island del gene CDH11 corrisponde al segmento di 3.420 nt compreso tra i nt 52801-55500 di Genbank AC137643, versione 3

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1 acttcacact cctctagga ccacgtggaa gggttgagaa aatccaggca atagtttgta
61 gccaaacaag agcaaaactc gactacctct gagggaaagc cggacccctt gtccatcctc
121 tctgtgtaa gtaacttcat ttataagctg aatgacgcc accagatcat cctattacca
181 tcacatgcc tcattagagt ggggactttc ggoggtggct tgggaagtac ccaaagtttt
241 aggggttaca gcagaggcca aaaaggcaga cagaggaagc agggtagagc tctgaaaagg
301 ttcagggccca gggaccaca gggggaggca ggagtggcag gcaccaogat ctgctctctg
361 gcgctctaca ggaaagcacc gggagtcaat gtctcgcgc gtccttgcg cagagtgtgg
421 tgcagaggtg gggggttact ggagaccag ggggctatca ccttgacac ctatggtggg
481 gggagggctg aggagtaaga taacgggca gctggaaact tacagctctt ccccgagcgt
541 ggaggaatga ggagtcaaaa ggccacgtcc acacagaggg tgacagaggc atcctctccg
601 cgcaggacgc ggactggggg caggcacgca gcgccaccg gatcctggag tcgtcaagaa
661 aaacgcgggc gcgcaggccg aagagggtag gtcgggggc agcctcgccg gcaccggccc

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721 ccgcgggcgt ctccccaagc cgtgtggaaa cccgggcggc tgcgggcgt cgggaccgc
781 gggctggga ccaggagctg gagggcaggg ctggccgt ctgacctag cccgcactg
841 gggttccttc cccatgcgt caggatcca agctttctct tccgttttcg gcctctttt
901 ccgttaactc ctgggccgt ctctccctc ctagccctt caaactgctt ggctgtggc
961 cccagcttcc cctccgcgc ctcttccc gtcttttcg cgggtccatc tcttctctt
1021 tcccagctc atcccgtcc cctaggcgg tctctttta gccttcccc actggcgtct
1081 ccaccttctc cgcctctc tcttgctcc acctcccacc ctgcaaactt gttcaagcca
1141 ggggtcccca cacaggcatg gttgttccct gctgggtgtg cggatcccca cgcgttccc
1201 ggtaccgcga gcgccccgc cagtcttgg cgtgattct aagccccgc cctgccagcc
1261 ctttctcccg gcgactcggg gagggagggc aggaagcagg cccggggaac cctcacgga
1321 gcgagtcgtc agtgaggga acagcggagg aaggagctag gactccggcg ctgcgcccc
1381 ttaggcctt tctccgtag aaacgcacac tccaccggc cctggcgggt ctgtagcgag
1441 ggagtggcaa caagtacac tacggcggg ggccactgat acctggctgg ggtaggggcc
1501 aaggcaccct cccaaaagct ggagcgaggc cgacccccgc gaagcgtcc cgcgcaccc
1561 ctctccgagg cgttgcgtg ggggcactag acgagaggag agctgagaga gaacggagac
1621 tgggtctctc ccaagtcta agtctctc cccgccgac ttcaccacca gagccaccag
1681 aagagtttgc aagggatgg agattgagag ggggtggggc tgggcaggag ccgccaacgt
1741 tgagggattt ttggaagggt ggggtgtgga gtgagaaaga atagaacgcg ctcccgaaat
1801 cccaattgct tccctcactt ggacgatacc tcccccaac caccatcccg gcccgccagg
1861 cgagagccca gcctggccag ctggagcga tttgggggaa ggaggaaaat gggggctccc
1921 aaccctctc cagcttccct cgcgcgcct cctgattgg ctgtgcgtcc ctggagccca
1981 acttcagtgc ctccagactc catctgagcc ctgaggaggt cggagcgcg cgcacgggg
2041 cgggaggggc ggccacgaat ccaggggtta gcatctctg gccctgggg ggaggggcg
2101 ggaagggtc ggcgccgca gcctctgca ggcacatct gctgcctct gcagcctcg
2161 cttctctcag ccccgccct tcttccct cacagcgca gcctccctc tccgcccc

2221 cccgccccgc acccgctgc ccgcccgcga cctcccccg gtttctcatt cctgccacta
 2281 gcgcgctcgg cggctcattc cgcggccgcc gccagctgag gggagcgtcg cgggccgagg
 2341 agcagatgcc gcgggggccc ctgcagcccg ccgctgactt gtgaatggga cggggactgg
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 2461 tccacctca agggcccag gtgaggtgcg ccgccagtcc ctctctctcg cctggttggg
 2521 gcttcttggg atggggggca ggattttctc aggaagagaa tgtcttggcg gggcggggtg
 2581 gtgaggggga cggtggtatc tgagtcgaga aggcttact aacgcaaagc aaaagggagg
 2641 gagagatttg tttaaaaatc agaaaggag aaggagcca gctgtggcg cgggcaaagc
 2701 aggggacgga ggcttcagat gtgcgtcca cgaactctcc tggctccgc ctctgtggg
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 3361 ctgccccgga acgcgagcgg ggaggtggga agcactgaga agctggccag atggggagga

SEQ ID NO: 3

CpG Island di FLI1 corrispondente al segmento di 7.460 nt compreso tra i nt

40001-47460 della versione 5 della sequenza Genbank AP001122

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1 ggctcaggag ttgttgacaa acaccgcagg cccaggcgcc caggcccat gagggaggag
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121 ggtctgggct ctgaggggtc ccacagagag gtaaaggagg taattgccca cataagagcg
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301 tcagatctta ccttcgccag ccgctgctct aagcgttggt tctgtattag ctcatttaat
361 attaacaaca atcttaggag gtagtcatt ctgcaggcga gaaactgagg cattgtgagg
421 ttaatgtgat gtgaggggca gagccaagat acatagagta atgacaaagt tgtgctggct
481 gccaggcaag ttctaaaggc ttatttcgtc ttacaacag cccttgaga taagtcctat
541 tataaccca ttgtacagat gaggacagtg aggcacaggg aggttaagta acttggtcaa
601 gccctcagag ctagtaagtg tagagctaga attcaaacct aggtgcgcta gtctcaaac
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721 agtggagtaa cctgacccg cacctgcaog atgcccgcg agtgcaaagc actttctct
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1381 ctaaggcaag aaccagcgtg gggagcggc caggcgaca gaggctctaa atcttcttc
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1441 actctgtgag tagatgaagt ctgagaaaca aattcaaagc aggcgcgcct gcagagcctt
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2461 cccaagctg ggcccagaga ctaaggaaag aggaaggaga gaagagagga gggagaggag
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2641 aaaacaatgt gagctgccag gatcaaacca tcttccaga tgtctggtg taaccacatt
2701 aaacagggtg gacttgttta ctattgtgct tggtagggc gcttcccca tccctttca
2761 ggatttaaaa aagcagcagt agcagtgag ttgaccatca aacctgagt tacataaaa
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2941 ggagcttctc ccagggggct gaaaatcgcc aacaacagtg gcaccagtgc cagtctgtga
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 6061 gagtcaaggc cgagagacct cgggggtccac cactcccacc gacacccggg gctcccggtg
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 7381 tgaaggctc tctgatcca gaagggtggg aagatggcct cagggtcttg atgtggacac

7441 cctaaggaaa agtgaagaaa

SEQ ID NO: 4

CpG Island di FOSL2 corrispondente al segmento di 4.200 nt compreso tra i nt 52801-57000 della versione 2 della sequenza Genbank AC104695

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1 ggactgattc gttttgcgtc aaaggactgc atttactcag tcttgcctggg agaggcgcgt
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301 tgaccccgag tattgttttg gattaccgta tcttggggcc cttggggcgg ccagatgccg
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661 ccattcacac acaccatcat ctacagcgaa ggattggagc tccagagcag agaaggccct
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1081 ccggaatgtc ttgactggtt aatttcattc tcaaggctac tctaacgaa ttaactgtag
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4141 ctatacctgg tgagtcccca aaatggcttt tctgtcttcc ctctgectcc catggtgctc

SEQ ID NO: 5

CpG Island di HES2 corrispondente al segmento di 2.280 nt compreso tra i nt
31741-34020 della versione 11 della sequenza Genbank AL031848

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1021 atccccggg gcgtcgoggt ctcctctccc ggtccccc tgccaggaa caaaggcagg
1081 aggtgggacc agcgggcggc cggactccgc ggggcggggc ggggcgggcg agccgctccc

1141 ttaaagctcg gccgcgggcg gggcgcgcac tcgtctggca ccagcccggg ccgcgcccgg
 1201 gacctcattt cggacctcgg tttccctttg cgtggggctc gcagctgcca ccgttcccc
 1261 gcggagcatg gggctgcctc gccgggcagg ggacgcggcg gagctgcgca aggtgggtac
 1321 cggggactgg gggcggggct ggggactcgg gggaccgctc taaccaccgc gccgcccgtc
 1381 cgcagagcct gaagccgctg ctggagaagc gccggcgcg cgcctcaac cagagcctga
 1441 gccagcttaa ggggtcctc ctgcccgtgc tgggccggga ggtgagcgcg cccgggcgga
 1501 gggcagaggg tcttggggcg cggagcgggg gcagggggac ggggtgctcc tgcgggagga
 1561 acccaccagg gggttccgcg cggcgccoga ggcggagcct ggggtgggtg ggcgcgtcgg
 1621 agcggacccc cagcaggcca cggcgcgccc cacaccagc tcccactag agcgagggtg
 1681 cgcacggtag ccggccaaag ttctgtcttg gtggttctct gtgcctcttc ctgtggcg
 1741 ggcgcagaac tccaactgct cgaagctaga gaaggcagac gtcttgaaa tgaccgtgcg
 1801 cttcctgcag gagctgcctg cgtcctcatg gccacggca gcgcccgtg agtgagcct
 1861 cctgcctcg ccgcgcgctc tgcacccgc acccggcacc ctaccccgcg cctcagcgg
 1921 ctctccgccc gcagtgcctt gcgacagcta ccgcgagggc tacagcgct gtgtggcg
 1981 cctggcccgc gtgctgccc cctgcctgt cctggagccc gccgtgagcg cgcgctgct
 2041 ggagcacctg tggcgagag cggccagcgc caccctggac ggcgggcgcg ctggggattc
 2101 cagtggcccg tctgccccg cccagcgcc cgcgtctgcc ccagagccc catccgctcc
 2161 ggtgcctcg ccgcctcgc ctccctcgg ccctggcctc tggcgccgt ggtagccct
 2221 cggccgatcc acagaccctg ccgactgctt gggacottgg ggcactggac aggttgaagc

SEQ ID NO: 6

CpG Island di HTR6 corrispondente al segmento di 2.820 nt compreso tra i nt
 92521-95340 della sequenza Genbank AL031727, versione 43

1 catctagtgg atgcgcctta aaagatgcat tgaagtatct gttcaatgaa tgaatgaata

61 acagtattaa cctgcacagc agtgtaggc agagactctt ctcagccaga ggggagacgt
 121 acagaggag gtcacacca ggggaaacca caccacacgc ctctgcctgc agcagactctt
 181 aacacacctg gcctggggat tctcaaatct gttaacgctc tgtagacta ggagcgccaa
 241 cagctcaggg acttcatcct tagtacctgg cccctttggg gatcgggatg gtttctgcgg
 301 gaaaggccct ggggaagggt agcttcttgc tcaactaac ggtgaagaat gccagaatt
 361 actaaccat ttacagata tggcaactga ggccagagg ggtgtcaggc gatttgtcca
 421 atatttcca actcctggct cccctgaaag cccggtgacc cgttgtgag tggcaggca
 481 ccattagag agcagccct ggataagggc aggtcacagc cccctgctcc cagttcggc
 541 tgcccgccg ccacgtgtgg gttgggagg gcacttgagg gtgtggggc tgccacagcc
 601 cgggaggtga cccctgcag ctggggcgct ctgatcttcg gccacaggc cgggggtgc
 661 gggacccgc cctcctgcag ggccagggt cggctctccc cggccaccg gaggcgggc
 721 gcacgtccg cggcgggg accgcgcct ccaggtgca cccggcctct cctccgcg
 781 tgccggccc tcggcgccc tccgggctc gggagaccg gtcccgccg cggccggc
 841 cggcgccgc tcttctctc gcagccccc ggcccttgc gcagtcgag gggcgaggc
 901 agccagagc cccaggtac cagtgcggc gggagacga ggcgacctg ctgcgggtg
 961 gggaggggc gcgcgcggc cgtgcctc ctcttcccg ggggctggc gggccggc
 1021 aaccccgcg ccgcacaggc cgtgtgccc ggatccggg gctccgcg cagctgagc
 1081 ctgccttcc cagggcggc ttgtctcgg cccctaggc cccgcctg taccacac
 1141 gccacccgc cgggggagc ctgctccgc ccgagagc ccattaccc cctcacca
 1201 cctcccgcg tcccacttc ccgcactct gaccggccg gacgcccct cctatctg
 1261 cggccgccc cctcagggg gctctgctc caccacagg agccatccg acctctgtt
 1321 gacttcccg cgttctctc aggggctcg gctcatcgg tgccctccc caaacttca
 1381 accggttgc tccaggagt cctgcccac cccgagggc gccaaatag ccacactgt
 1441 tctcctgta gtcgtgccc cctgacctg cggagaccg cggcccgcc catgtcccc
 1501 cactcacct cccgggggg cgtggtgagt cgggtctgt tctacggac ggtcccgct

1561 cagcctgcgc ttgcggggg cctcatctg ctttccgcc accctatcac tccttgccg
 1621 tccacctcg gtctcatgg tccagagcc gggcccaacc gccaatagca cccggcctg
 1681 gggggcagg cogccgtcg cccgggggg cagcggttg gtggcgccg cgtgtgct
 1741 ggtcatcgcg ctgacggcg oggccaactc gctgctgac ggcctcatct gcaactagcc
 1801 cgcgtgcgc aacacgtcca acttcttct ggtgtcgctc ttcacgtctg acctgatggt
 1861 ggggctggtg gtgatgcgc cggccatgct gaacgcgtg tacgggcgct ggggtgctggc
 1921 ggcgggcctc tgctgtctct ggacgcctt cgacgtgatg tgctgcagcg cctccatcct
 1981 caacctctgc ctcatcagcc tggaccgcta cctgtctatc ctctgcgcgc tgcgtacaa
 2041 gctgcgcctg acgccctgc gtgcctggc cctagtctg ggcgcctgga gcctgcgcg
 2101 tctgcctcc ttctgcccc tgctgtggg ctggcacgag ctgggccacg cagggccacc
 2161 cgtccctggc cagtgcgcc tgctggccag cctgcctttt gtcttctgg cgtcgggcct
 2221 cactttcttc ctgcctcgg gtgccatag cttaacctac tgcaggatcc tgctagctgc
 2281 cgcgaagcag gcgtgcagg tggcctccct caccacggc atggccagtc aggcctcgga
 2341 gacgtgcag gtacctggg tgccagggg gaccgggct gtgggataga gaggaatgag
 2401 cagcccttg ggacccctg ggcacccca cttagcacac atttgcctat ggcctgcgt
 2461 ggctgttg agcgccacc tttcttctga actccagagc caatgcctga cccaccacc
 2521 acaggatagc tcgtcagga tttgggggca ggcttctccc aggtaccatg tacaacaggg
 2581 aatttatggt ggcccaactc tcccattct tgcctccctg gtcttcccca tcatggcaaa
 2641 tggcaccatt gcggcatcac atgccaggaa cttaggaata cttttctccc tcacctcat
 2701 gccattcatt agcgagacct gttggcgctg ctctaaacag gtgccatctc cctgcact
 2761 tctaccggg gaggtgtgt agacttctcc tggctccct gcttctgccg cagaccagc

SEQ ID NO: 7

CpG Island di LHX3 corrispondente al segmento di 5.040 nt compreso tra i nt

111001-116040 della sequenza Genbank AL138781, versione 13

```
1 ccggcagga aacatagga aacgggtctt caccatcacc tggagctggg gcaccccatc
61 gggctctctt catgttaagc gtcattggcca ctctttctag ggactcctcg caaatgtggc
121 tgccttgctt ggtggcctg tctgcaggcc tccggggtaa atatcaatgc cttcccatc
181 attgggcagc cgcaaaatta cttatgagtg gactggacaa gccgatccac tgcctttgtg
241 tcaggcgtgg gtgcccccaa caccgtcaga gttactcaaa cgtctggett cccgctgett
301 ctgcccccca caccacactt oggtactgca ggccccctgg aggaaccaca ctggggaggt
361 ccaagggtgc cctgtgggag cctogagtct gtgagcgggt ttccaggtg tcaagggtg
421 aggactcctt cttcacttag aaaaagtctc tgggaagagag gagtgcctcg tgaagggacc
481 gggatttact gacatattgc accgcctcc ctggctgtgg accccgcggg ctccagccca
541 tctccagtg ggtgagagac accaggaagg ggctccctcg acctcggcg gaaaaaactg
601 ggctgcgctt cccacgcag tggcgggaaa cggcgatga atgcgcccc catccggcaa
661 aacgcagct cgggtgcgg agcgtcagg acccgtgcg cggcgggggt ccccatcgtg
721 ggcagcagtc gcaggcgagg acccggctcg gagcggggcg gcccgacagg cgcacacagc
781 gcggattcag caccgcggac cggacagcgc ctccgcgcga gctcgcgcg ggcgccgcg
841 tcgggcaaaa gccgccccag cccacccgc gccgcgccg cgaacccagc cttacgtgc
901 atggcgactc cagccctggc gggggtctct gtgtcaggga tggcggggtc ggcggagcct
961 ggaagccagc cggccgcgc cggccagctc tcccagcgc ggcgcgcag tctctcttc
1021 tccctccctc tctccgccc ccagccccg cggccaacc ctcccaggaa cgtcgaaaa
1081 ataaataaat aagtagggaa ccgcagccc ccacagcctg gatgtaacc cttcccgcc
1141 ggcgggtccc tctactccc cactggctcc ggggctctct tcccatcct goggtccag
1201 ctggccggg agtcaggag aactgccag gttccctaag aaccaaagt ctgggagcta
1261 gagtgggtcc accaggaagc tggggggcct ggagaagaga ggctttttcc tacagacggg
1321 cctgagcgg ggataaacg agcgggtgct tgtgggcga gacgtgaaa cctgacttcg
1381 gggagaccga cgtcggagt tcagctcgac cttggccct gcactgact ctgttcgct
```

1441 ggaacgtgga aagagtccgg ctggggcggc cttcttgggg accctcctgt cccgtgggtca
1501 ctgccccgcc actgctccct gcgcctcttc cagcccaggg agctggctcc gggctgcaga
1561 ggtctcctaa gccacacctg gaccccgag agctccctgg ccggagcagc gcagtgccac
1621 aacctcactc actccctgac aaccaggcc aggggcccctg caacaaatac aggctgaggc
1681 gccaggcgc ggacgttcg gggctctcgc gccactccc gccagatcc tctagctcct
1741 gccagcctcc ggggccaggc ccggaaaggc ctgaggatct cctggtctcc ccggtgcagc
1801 cactcggccc gggcacccac ctgggcgag gtccgccctc cgcgccagca gtgctagcag
1861 caggtcgctt ccgcgcgact ccggggcgg gccagctcc ccgcgcgct ccatgggtcc
1921 cgcgcgcggc cgtcgccact ctccagtcgc gaactttccc gggcccagcg accccacccc
1981 gcaatagccc cgaaccggcg tccaagcgac tccgggtgct gctgggcgct gcgcccgcgg
2041 gccgccctgg gggccggagc ctctggccga gcggaggcgc gagcgcccg ggggcggggc
2101 cgcggggcgg ggcggggcgg ggggtcgcgg agaccagccc gggccactgc ggactctgag
2161 cgcttttgcg ccgggaacctg cggtgcccag aggcgcgcc cgtgcccgg ccgaggggcg
2221 ggcaccggta agggaggggc caggtcaggg cttcccgcca gcgttcgtcc cggccccgca
2281 gcttctctcg ccggagcggc ccagaggcag aggcctgagc tggagcacac gccaggaggg
2341 ctaaggttcc cgggagaggg gtcgagaagg cagcagggtc ctcccgcgc tgaggtttgg
2401 cctcgggagc agcagatggt cggcgggagc tcaaccgaa accgagaagg ggtgagtgtg
2461 gcgcggaggg ctgcgtaccg gaaccgcaag gtgccggacc gatcccagat gctaacaggc
2521 ttctgggctc cacccttga actgcggccc cggacggctc agggaggaag ggcaatcctt
2581 gagagagaac aggtctctgt tcttgacac gcagccaaga cctcgggtcg tgaggggcgg
2641 agctggggaa gcccagggc acacctcca ttccagccc ccagcactcc ggtccattg
2701 gaacacggtc cttacctga tatttcagcc tcttgccca gtccacacag gtgagctctc
2761 cagaaccac ctgtccttgc aggcagaggc acgcaccac ccctgccag agggccctgg
2821 gccagcacca gcctgggca gccaccggg gaagaacaca gcagtgggtg gcctcggca
2881 gcacaggact tgcaaaagg aggggtgccc tggcagtgcg cagaaacaca caggaagggt

2941 tgggggacca ggggctgatg ccctcctgca ggtccctctc cctgtgggtc tcacagcaat
 3001 actctgtcca ctctgcctat ggcttctgga ctgtgagctt taagggccca ggcccagaag
 3061 gatgggcaca agaaaccaca gtccctccct cctagctccc agcaggtccg atgtgtccgt
 3121 tttgagcagt ggcccatgca gccagctttc tgcccttca ctttgacag cacttgttac
 3181 ccaagaaggg ccagggaag gacacgggg tgcaaagccg agtgtgtgag ggtgtgtctg
 3241 ggtgcagggt gctgagtgtc agctgtgcc gaagcgatca ggggtcgtgt gtggcaggac
 3301 tggggaaggg gcggcgag gttaaggagg cggcccacc tgctggcatc tggccagccc
 3361 tccaacaatg cctccattat tcccagcgt cgtggtgat ggaatggccc ttggggaggg
 3421 tgggtcaggc gggagacaca ggcttgggtc ccctgctgtg gggccagag acctgggccg
 3481 ggctgtgtgc aagagctgac gggcactggt caccggggga acctagcacc ccttggtcgg
 3541 ccccatcgcc cccagctgt gctgcgatg ccccttttt ttctaggggc ctccactcca
 3601 accgctgtcc cgcactcttg caggccagcg tcaggccctc cccgccacc tgggatctgg
 3661 aaactcactc tctgcagttt ccctctctgt gtcccgctg cagagcggcg ggactttctt
 3721 tgctggccg ctggccctgc acgcacccc ttctcggc ctctgcgc cttgcgttt
 3781 ctgtcctcag tgctctgtg gggcttacc cagtcctgc ccaaggtgca gacggcgcg
 3841 gcccggggcc tgcctgggtc gcgtcgagc cccgtttcca gcagcatgc ggccaccagg
 3901 ccagtggtg cgagacgcgc tcctcctagg tcagcgtccc ctggagggtt cggggctccc
 3961 aagtcctgcc gcgtcgtgc gggcaggag cccgggagcc actgggctg gcgtgtccg
 4021 cggctgtgaa ggaggcgccc gctgcccgcc cgcgcgcgc gcccgccac ctcccgggc
 4081 cctctctgtc gcccggtcc caccctcgc ctctgcccg tgcgggggc gctccctcc
 4141 ctggctgggt tgggcgcac tcaaggcagc cccgcctc accctctga gaccagggt
 4201 ggccgtgcc gctcctccct aagctccagg cctgctgag gcgtgggat tgcgcagtt
 4261 tcgcagcaag cgggtgtcc agccgcagg caggaggaca ctgacctac cttctggcg
 4321 tgcagcctct ggaaggcagt gccaggccg tgccccggg cagcccatg cgtgatcaac
 4381 tccagcccag ggctcactgg ggcactctc tgcagggtt ttgctggtca gggaaacttc

4441 cactcttaac ctcttgaac tcaaccccca acttctggga ggagctcagc ccgcaccct
 4501 ccgggctgcc aggaggagag gcacctgcag tccctgtaa caaaagcact gctgaggact
 4561 caagaccttg ggcataggca gggcctgaag gaatcgcca gtacacacc aggctgggt
 4621 ctgctcgtg cctgacgagt gactgagtia ctgccagcct ctgcacagcc tggccagga
 4681 ggtgccaacc ggcttctcc acagccacag gcaagactgt tgaccactgc cctgccccca
 4741 ctggcacagc aaaagtaggg gaggggcaga agacaacag ggtcaaggg cccccacag
 4801 aacaccacaa acagccttag caggacactc acaccagga agcagagga tggccactca
 4861 agcaagctgg ggttctctg aggtgccctc aggtgggct gccgcgctg ctctttgaag
 4921 tgtgtagctg acatgcatct cagctgcct ttaacctgt taaaatcaag ggtctgtcc
 4981 tgtgagtctc gtccagatca gctccagga gatgatctat cactgcttc catcttctac

SEQ ID NO: 8

CpG Island di LOC51149 corrispondente al segmento di 2.700 nt compreso tra i nt
 117001-119700 della sequenza Genbank AC008393, versione 7

1 gcattaaatg caagcttaca gacacatact cagcatcttg ctgacttttt aacatacctc
 61 ttaaacaagt ctgatccag ccgggcacaa tggctctcgc ctgtaatccc agcactttgg
 121 gagggcagg caggcgggtc acctgaggtc aggagttcga gaccggcctg accaactgg
 181 agaaaccctg tctctattaa aaacacaaaa ttagctgggc atggtgggc atgctgtaa
 241 tccagctact cgggaggctg aggcaggaga attgcttgaa cctgggaggc ggaggttgog
 301 gtgagccgag atcgcccat tgcactccag cctgggcaac aagagcgaaa ctccgtctca
 361 aaaaaaaaaa aaaaagaaga agaagtctga tgctattctt tctcagggca tagcagatta
 421 ccaataatta ggaggagggt actatcagaa gcagatacgg tgactgcagt gttaagtgat
 481 atcaagcagg gagacagggt cgatccggaa aaggttaagt ggcattctct atctggcaog
 541 ctgaaagtta gggaggcaaa tatgtcctag aaacacagat tatctgtctt taagactccg

601 gggcccggtgg tttatgcgtc ggcgaacagc catatcaagt ccctggcccc gcggaacgg
 661 acggcggcag aggcgcgggg cgacggagag ggcgccagg tgtggagcag ggacgcggcc
 721 ggcgcgcgtt cggctctctaa gaacgctcct cccctctca ctgaaactgc gacagcgcta
 781 ctctgtgggg taggctctgc gtaaaggatg ctatactcaa ccgattctc cactacctg
 841 ctacaattca caagaggcca cctccgcaga accattacct ctggtttgta caagaaccaa
 901 acaaaaagct cagaacgtta tgcggggggc accccaatga gaccgcctt cagcggctcc
 961 tgcactcctt cgggcccggg gcatcccgga gccattcgag acaacacca cagccccgc
 1021 actccccgtc cgctgtcccc gcgcggagg aggaggagg ggctggcacc cgcagacct
 1081 ggtgcgcctg gaagaggcgg cagctgcagc agcgtagcac ccgagaacgc tgaagcgacg
 1141 ccatccctgc ttgtgcagtc gccaggcagc caagcgcgtg cgctctgcat ttgtccgc
 1201 gcggccccgc ccacgcacg cgctccgaac cctctagtcc cctacgcgt ctgcgatgc
 1261 cttatactct tcgtccggc cgccggggc cgcctctgc gactgggat cctctagcc
 1321 tgccgcgcct ctgcgtggtc atctgcgcc ctccgacct ggaaagagtc ctgggtcgg
 1381 gattcctggt agccgactcg tcgtctgacc agggccgtgc ccgcatctc ctaaggcact
 1441 ggttcggcc ctggggagac tggaattgag acgacagggc ctccgctgac cagtccctgg
 1501 acacaacgcg gagcggggct gaggggcgc cctgccaggc ctgcgctgc gtgcttttag
 1561 gtagcagcga acagttagcc ttgaaacgg agccgggggt ggaatacggg gagacggagg
 1621 ggctcaccac acccagctt ccggagagg gcggcgagg cgcgggccg ccgagcgga
 1681 agccggtccc cctgcagccc cgggagcgtc ccaggccac cctacggagg gtggaggcgc
 1741 cccgcagcc cgacgctcac gcgcgaacc tgtgtggctt agggttgtaa cctcgttga
 1801 aaataaaata caaaaaatat taaaattacc tcccacgta caaccctcg tctctagggt
 1861 tgtaatttta atttttttt caacttttac acagtgacta tcacaaaaa agcgaggtgt
 1921 ttttttttg tttttgtt ttggagacag tctcgctcag tcgcccaggc tggagtgcg
 1981 tggcgtgatt ctctgcctc agcctctcca gtagctgga ttaaggatgc ccgccaccac
 2041 gccagctaa tttttgtatt ttagtagag acggtgttc tccatgttg ccaggctggt

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2101 ctggaactcc tgacctcagg tgatccaccc gectcggtctt cccaaagtac tgggattaca
2161 gacgtgagcc actgcacccg gcgacactc gcttttaaca gcagaaacca tcccgttgaa
2221 gaaaacaccc aatcctgaca aggggtgcagg gagggctacc cctctgacag ggtgctggga
2281 gaacggtcaa gtgcaaaacc gtggaaagca acctggcaat actgctaccc caagaaagga
2341 atcccttcac ctaggtgatt tattattcat tcctagtgt tcctgaaga atactaggaa
2401 gaaatggaaa tcagtgttct gaagaacggc acggactctt aggcagtcc atcagcaaga
2461 acctgagttt gaagtacaa cgtgctgtgg agaggcaagg ttacagaatt acagtacac
2521 gtttgacttc tgtgacaccg gcattatctt ctggcgtgtg tgtgtgtgtg tgtggctaag
2581 gtctaggtta atgctaattt ttaaattttt ccaacttttg tacagtaagt agttagaaaa
2641 aaaaattgag agacaatatg ccaatagaca atggtcagat aacgaatgac aataaactga

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SEQ ID NO: 9

CpG Island di MAP1B corrispondente al segmento di 2.100 nt compreso tra i nt 39361-41460 della versione 2 della sequenza Genbank AC093218

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1 acaggtgag ggtgaggagt gggcagtggg tgtgtacgtg gtgggtggtg taggttgaga
61 gogtcttccc ccttcacggc tgcagcagga gtcagcggg cyccccagcc ccttggtctg
121 cggccctgcc cggaccattg tccgcacacc tcgtccctcc agcttcggg cggcgggoga
181 gatgatttgc tgcagatgac atcagccccg ggccaaacggc tggaagagcg gaggcagcca
241 cgcgtgagg atgtgcggg tggctcttct ctcctctctc tectctctct cccggtctcc
301 tgctagtct ccatataaaa ggggcgcgc ctcctcgccc tctctcactc cccgtctctc
361 tccgcgcgc actctcgcg gcgtgggag agggcggagg gggaggcggc gcgcggcgcc
421 agaggagggg ggacgcaggg ggcgagcgg agacagtacc ttcggagata atcctttctc
481 ctgcgcaggt ggagaggagc ggccggagcg agacacttgc cggaggcaca gcagccggca
541 ggatggcgac cgtggtggtg gaagccacgc agccggagcc gtcgggcagc atcgccaacc

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601 cggcggcgtc caccctcgct agcctgtcgc accgcttctt tgacagcaag ttctacttgc
 661 tgggtggtcgt cggcgagatc gtgaccgagg agcacctgcg gogtgccatc ggcaacatcg
 721 agctcggtaa gtggcccgcc gccccagag acgcgcgctg ggagacgcgc aaacacgacc
 781 ccaccaggg cgcgacggtc actgcgtcc tcccgcgcgc ccgcaccca tgctctctct
 841 cgtcacctct cataacttgg ccagaccctt tctgggctaa ttaagaataa tccgaattat
 901 tagatatgag acccagaggg agagtctcca ataaccttga gggatctgtc accacgctga
 961 gtcgcagcc tgtgtgagt tggccacgc ctctccgct aagtgaatg caggtgtcag
 1021 gggagcagag gccacaataa agccgcaacc gcaggaggca gaagggtggg ggagacctga
 1081 tgcaaccact cctttcagtc ctctctctgc ctccagaaaa ggctgggacc cccaccacgc
 1141 cagacctggg gccgaagccc atgtgccagg gccgcgctg gattcatctt caccacggt
 1201 acctcagccc ctgagaaacg ccttttctga tttcaaacct ccgatcctt tctttctca
 1261 gaatgactag gctagtctta gggccacgcc cgtcccccc gcccccctt ccccggggag
 1321 atgctgggat gcagaaccgc ctgcgcttcg ccaccagaca gagcccgctt cgtaccgcc
 1381 cttggggcct tggctgcagc tctcagaaag gacaatggga cccaagtgt cggggtgggg
 1441 ctgctgcttt tagaagtcct agcctcggga gtggtagctt gaagggggtc ggtgagggag
 1501 acgtcagcgc gtagggctcag ctctcgcgcc ggtgctcgca ccagtgggc gctctcgga
 1561 ggcgaatag cggtaacgcg gggaccctgg gcggggccgt gagggtcgg cgggcacagc
 1621 ctggggcgca cagagagacc gccccagcc ccaccgagc tgccgcagtg cctcgggacc
 1681 gcccgccaca cctgcccccc cactctcgg cgcctccgc gggcacggtt ggctgggctt
 1741 gcgctcggcc cgggectcgg gctggcggg gcgcgcgcgc ccacacctc agtttgctg
 1801 gctttgttgc cctgggagtc cctgggtggg cagctctggt ctctgccttt cctttatcc
 1861 ctgggtccc ggcctcccc tgcctctga cagaggtgc cgggtccctc cgcagcccca
 1921 gccgcgcgc tattctctg ggggtgtgct gaagcgttc tccgggagac accggttgg
 1981 gggcgtggg cagtcgcac tgcggtctct acggcagccc gaggcggaca aaggcgctt
 2041 acgcagcctt cgttccccac tccccctccc caataaaaga cgaaagaaaa accttgtttt

SEQ ID NO: 10

CpG Island di MDM2 corrispondente al segmento di 1.260 nt compreso tra i nt
140401-141660 della versione 32 della sequenza Genbank AC025423

```
1  cagagaaaaa gtggcgtgcg tccgtgccca caggtctacc ctccaatcgc cactgaacac
61  agctgggaaa atgcatggtt taaatagccc cagctggaga caagtcagga cttaactcct
121 tttactgcag ttctggaacg tgtctgaact tgaccagctc aagaggaaaa gctgagtcaa
181 cctgccact gaaccggccc aatccgccc agactacgcg cagcgttcac actagtgacc
241 cgacaggcac ctgcgatcat ccggacctcc cgcgcgaag cgccccgca gccccggcc
301 cccgtgacct ttacctgaa ctcccgga gacctcgaa ccacccac cccacggcc
361 gcgagagccg tccgaaatcc cgcctctc cctggcggcg actgcctagc ccagttcaa
421 caaacctcc gcaaagccac gtgcccctg ccccgcgccc cgcgcgcga gccccagcc
481 acgaaccgca caaaggctgc gaacggcgag aggtctggaa ccagcgatag aggggacacc
541 gtcagagccc agacccaaaa gtgacgctc gctgcgggc cagtacctgc tctcaccat
601 cgggggtttt cgcgttga gtgggggtc cctcaagact cccagtttc cttacgggg
661 cgcgcgaag cagcagccc tgggctcgg ggatcattcc actctcggg ccagggcact
721 gggcgctcgt acgcactaat ccggggaggg acggtgctcc tggctgcga agcagcagga
781 tctcggtcag aggggtcgg gcgcgcctc gggctcggct tcttgctcca tcttccgac
841 acacagggcc acacagggcc cagaagcagc caagctcgcc gcggtgcctc ggtgcgcgc
901 ccctaccgcc cgaggggagc gcggggtcg tcgcgcgca tccgggcatt tgtgcgcgc
961 cacacaaccg gccccgttc cgccaattg gtccggggt cggcgcacc acctccggg
1021 tgatggagtg ggggtgtcg ccccggggc gcggcggtc gtgaggggg gtgggggtg
1081 tggcogag ctgagaggt ggggtcggc ctggcgga gccagcaagg tttggcgtg
1141 tgacactcct ttagcggtg cgctatgtt gtatttctg tgtttacact tcccgccgc
1201 ggtgaaaact gcgacaaatg cggatctcg tgctcgtgtt accaaaaa aacaaaaat
```

SEQ ID NO. 11

CpG island del gene NID1, corrispondente al segmento di 1.860 nt compreso tra i
nt 36661-38520 della sequenza Genbank AL122018, versione 37

```
1 gcaggacagg ctgcagccgc tgcgtttgca gttccaaccc ccttcccccg gccaaacccc
61 cacacttctg gaatgcacac aagccttata tgaaatccac atggtgggag gccgaggaag
121 gcagcggcac gaaaggactt caacaagttg acagcgaccc caggccccgc cagtcaaggg
181 gaggatccag ggagctgtag gtcactctgt cccgctcttc gtttggggcc tccgtggtga
241 caatgcctgg ccacaggaaa tgggatcact gggagccctg tgtttcccg cctggactct
301 ggactctgaa acgagcccaa ctggaaagca gcatcactgc caagacacat ccggagtcca
361 cacacaaata caggaggctg ccggcgaaac tctcccgag ccacaagagt cccggggccc
421 gcgcgcagac tgcgatccag ctccggctct tgccctgcgg aggcctccgg cgagaacctg
481 gctccaccgg ggaccggcca ggtcctagcc ccgaagggac tggacagccg agggacggcg
541 actgacctcc ctgcggcgat gcagcccaca gccgcggggg aggaagctcc gcgggggtcca
601 tgggtgcggg ggtcacggcc cggggcgccg ggagccaccc agaccocgg acccgctctt
661 cggatagcag ggaccgggtc gggaaagact tcgcggaccc tgcagaggcg ggagacctg
721 cgcctgccc ggtgccccgg cggccagcgg gtcgggttcc ccgctgcta cggccaagtc
781 cgtccggctc cagggcgcc cccggcccg cgcgccctgc agccctcgc ccgccctccc
841 ggggctcact cagtagact gcytcgatgt cggatctgtc gtagaagcgg agcgccccc
901 tcagctccag ggcaggagag acgaagtcac cccgctctc cagctccagg tccccctgtc
961 cggggccgaa gggaaagagc tcttggcgcc tcaggcagcc cacaggcccc gccagcagca
1021 gcggcagcag cagcgcccg gtcacgcag ccgggatccg gctgctcgag gccaacatgt
1081 tcccgaactg cggcccgca aaccgggtcc cggggccagg acagaggaag gcggggatgt
1141 aaccggacgc cctggcagc cccctctct cccgctccc ggcgttccc cccgggaaa
1201 taggggaggg gagcgagggg gagagcggag ggccccccc cgtccagcgg gcgcgcggc
1261 gggcagccca atggccgca gggggagggc gagggcgaa gccgaacctc ccgcttggg
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1321 cgccggtgcc tgcgattctc gaaaccagcc cgactcccag cgaacggcgc ctccgggagg
1381 gggagcagag cgcgggaccc gcaccgtggt cctctgatta ggggtgggtc gtggagagcc
1441 ggcgacgtgg aaacgctccg gattcaggaa cggcgccac cccattgccg ctcgcccgcg
1501 tccggggtcc aattogettg accctggtag gaagacgggg tgggagctgg gaatcagcca
1561 agggacagag ccaccaaacac gttcatgggc tcaccaccc attcattgcg cgttttttga
1621 gtgcctgac ctgtgctccc tattgtggag gttcgccagg aaacggggtc tcaccctccg
1681 aggcaaagtc accagtgtac aacacaagcc agtgtcagat gggggcccca agtcatcaaa
1741 gacattaggg ctggaaaaac tggcggggaa agctgcaggt gggacggcgg gaatcaaccc
1801 ggggtgctctg gaaggaaatgg gatgtcatca ggcggcagag aaggagggtg gaggaccgag

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SEQ ID NO. 12

CpG island del gene NID2, corrispondente al segmento di 2.340 nt compreso tra i
nt 75001-77340 di Genbank AL118557, versione 5

```

1 actccaagc cactccagcc ctgtgcctc caaggtcagg ttcagcgcaa gagtaggctc
61 agaaacaact ccgagccagt ccctgggtcg ctgcccaga atttaagccc atccttcaat
121 ttctcagca gtcaaatatc cctggtcact tacctctccc gagggcagcg ccccgogctt
181 gacctctcg taagcgcta cctgtccca ggtggccagg aaggcgtggg tgggggtaaa
241 gcgcgcagag cgcgggaagc cagcgcgcac atagcggcgg gccaggccca gcactgcggg
301 ggaggtgtcc tctcggtaca ggaactcgcc tctgcctgg ctggtgtoga tgtccgccag
361 aaaagggcgg atggccggga agtcgggtgg gaaatcatag tccacatact gcgtttccct
421 ggggaagtcc tgagtggaga tgatgcggtt ggtgccacc tgggagagga gagggacaaa
481 aaggtgacag tcgctcaagc ccaaggacgc taccctttcg cgcagggagg gaagggaact
541 gacttaggca aaaagcctct ctctccttc cactggcca gggagtctgg attcagggaa
601 acaagcgcaa cttttgcgac tgtcccagct ccgcgtgca gtaggtccag gggccctaaa
661 actggttcac ctatcttctc actccctca caacccgga gcccctgtc ctggagagg

```

721 aagcctccag gtctgaagag ggaacacccc agctccgcag acgggcacag ccttctcgcg
 781 gtcctaactg caaagcccg cggccgcctt agcaacgcca ccttttctgc ctgggaacgg
 841 taactggctg cgaacaattc ttgtctctcc ctccaggtca ttcttgctcc cctacagcag
 901 cggggcaggc agcggcatcg ctctctggcc ggggtaccacc gcaaggggac tggggggctc
 961 caggagtggg gtctgtttcc tccccctgg aggcagggtt tccgtgagac cgaacccagg
 1021 gaagaagctg cgggaaaagt gccaggaggg ggctgaactt acgtagaggt tgctgaatcg
 1081 ggcttcgtag aagtgcaggg gattogccag cttcaccacg gctgagcttt cgtcgtcgcc
 1141 ttcctgcagg agctggctcc cccacgactc cccgtgtggg aagagctcgt ctgggtgcag
 1201 cgccgcggcc cgcaacatta gcaacggcag cagcagtagc actggtaacg acgacagcac
 1261 cggccgcccg gccaccgggt cccccctcat gctcgtctgg cgtgctgctt acccgtgca
 1321 caacgcgtcc cggccggcc tccagccac tctcggcgcc ggcgcagcct cgaacctgga
 1381 tctcggcggg cgctggggg gggcgggact ccaggccac ccagcaagct aattggctga
 1441 ggccctcgcc tggggaccaa tcaccggctc tgagaaagt cggcagtgcc caccacatct
 1501 ggttctcgtt aacttttcta aggcagcgcc cgtcggagca gggggctgg cggggtaaaa
 1561 gctcctggcc agggctgctt ggagctgcc cttccactcc gccccaggg agtccccggg
 1621 tcatcctctc atccgggctg ccccgcgcc cccaaggagc cccaccccg ggaccaaatg
 1681 gcccgcaagg tttggggcag cggcgttgca ggagatgagc tcagcgcaaa gggaaacccg
 1741 cagcggcgag tgcggtgctt ggctgcgcg ctgtggcccc aacaggctgg cagggcgcg
 1801 ggggtggcg ggggtgoggt atgagcttg ctcctgccc tgggtcccg ggcgtcctg
 1861 gctctggagg cctggccatc ggtccgaaaa gcaaaggagc attgtcgtg tccccctggc
 1921 cgcttcgctc caccagaga cgccctgagg agaagcgagc ctttgtaoga aggcagaggg
 1981 ctgactcta agttctgtcc ccctccgaa ggcggcgcc tagggaagac ttggccaccc
 2041 tctggaagta ccttcccccg ggaacacgc agcaggaaa accatgaaat actactgtg
 2101 gtgatccgct cgtttgggg agtaggatga ggcacccgc ttggttacca ggcagaaagg
 2161 ggcgagtcg ggggatggga agaccctgat ctcttggcca ttgtgcggc cgtcggagat

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2221 gccctccccc gcgccacgg aggcggaac ctgagctgct cgcaggact ggaaacgca
2281 caacctcgaa accagctgcg caggagaagg ggaaccccat ccaccataaa catccctct

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SEQ ID NO. 13

CpG island del gene PNUYL2, corrispondente al segmento di 2.660 nt compreso tra i nt 108541-111200 di Genbank AC005666, versione 1

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1 tgggggggtc tccccactg attcccaaag cagctaggac actgacctcc ttgacaaag
61 agacctcat agaggagtct gatctgaacc agtcagccta agaacttggc tggcttgagg
121 gcaggggcct gaggatgggg actttggtga tgggtggttg ggtggagggg ggtgtgtctt
181 taattagaga agaacagtgt ggctctggac aagccgaaag caccaagacc tcagctgaac
241 tgaagttagt gtgtggcaga aaaagccct ctagccctg ctgggcttg cactggggac
301 aatcagtgtc tccttaggtc tccatcccta gaacaatcag tccatccatc caccatgtgg
361 ggagaagtgg gggaaaggaa taaggacagg cctctctcag gaacccctgt tgggggaagg
421 tcacagggtc accaagactt cctggccaag gcttgggcct ctgctggac acagcttgag
481 agacaagagc caaaagggtt ggccctacca aacctgaaag cttctgatcc cagggggccc
541 agggagctcc cttctggagg ctgccacag ccaacatccc gcccacagg ctggtcagtg
601 atccccccct gctgtaaaca gtttgtgtcc ccaatgcag agggcaaagg ctgtggggct
661 tccagactga gaggagagga cgtgtgttg cctagaggtc ctgacacct tacgttattt
721 gtggcaggct ctggcaacaa tgtcaggaga agagattaca tcttcagagc caagcatcaa
781 aaacttcta cctgggcacc tccaggagg ctggtgggg ttactgttc tctccact
841 acaggcaggt ggcagggatg ggtgccccca ccccccacac ctgcagaggg acctggctgg
901 tggggaggga gcgggtagat gcagcaggag gaagctttcc catggttctt gtcccagggg
961 cagaagata tagctaattc caccgggcag gatggtgggc tgggcctccc cctctctggg
1021 gtcccttttg gaaaggcca gggactgcc cttgtcaggc tgagggaagg aggggccaag

```

1081 ogtcttacca tccctcctgg tgaggcaggc agtgtttggt ggcctcctct gcgttttcca
 1141 aatgaagttg gtactggccc ctgtgccag ggtagggtgg tgaggagggg ttactcaggt
 1201 aaaagctgac ccaggcgagg atggggaccc tcacctcgc ttattactga tgcgccttc
 1261 ccagcccaac aagcgctct ccaccagcg gcacctcct cagcacggac ccacccttc
 1321 gtcttagagc gcaggcatca ccagggggtt ggogccact ccgtggctgc tcagaggaa
 1381 aaacttggga gcagcgagc accgcgccc ggcagcagtg ccagcctgtg ccggggcgg
 1441 gcgacggcg ctcaccact gcacagcgc ggtgcggtg ccgggggtcc cctgcagcc
 1501 gccggggagc gaccggcct gcgcaccca gccctgccc gcgcgcgcc gccctgctgc
 1561 ctgccttacc atggctgcag ccggggcgg gccggctcc cctggacag gcccgagga
 1621 ccgcggcgg agctgcgcgc cgacctcga gcaccgcgt caccctccc cctcccag
 1681 tgcggacgc tcggggagg gcccgcggc gggggcgag cagtcggcc ccggggcgg
 1741 gccgtacct cagctgctag cggtgccgc gcgaagtgg tcggggtgcc cagctgggg
 1801 ccggcctgc agccgcgac ccccgatgc gcagagtat cagagtcacc caggacagag
 1861 cggggagcct cagctcctc tccccggc gactggaca cctggtctt tttactcag
 1921 ctccagaagc accgcgggg cttgagccag tcccaaaga aaaaggaac gccacctga
 1981 catccccaga aggagagcc ttggaagg agggggagt gctgcatgag ttggagaga
 2041 accattagt accgcagga ttcaacaagg tttcacaaa gtgaatcgg ctgatgcca
 2101 agttactgat cactacact cctaaaggg aatgtcagat attctccac tccaccgag
 2161 ctgtgaagg gcaggttaga gcagggttc ctcatgcag taccacagat tacagattaa
 2221 agaggatttg ctgcacaaat tatccaggga tcctctgctg gaaggataga agggagaggc
 2281 tgagtggctt taacaggcg gtgtagcct gccctggct gaggacagt gggaggcct
 2341 caggagaggc caaccaggc gtgaccagg ccagctggg ccactcttc tctgacaagc
 2401 aggtgagat ccgaggggac agatgcccc gaagcttag aggcattaga ggctcagaa
 2461 ggtcagagca gcagctagg gaaggcagat gcttgggtg tgggtgttg gtgaggatt
 2521 ccctgagcta agtaggtct gagctgtca ggctcctgt gaagttcca gaagcatgc

2581 ccttcctgac ccgcaagacc cctctctcaa tggcaggctg actggcttct gctgaatac
2641 actctggaca aaactgagac

SEQ ID NO. 14

CpG Island del gene PRPH, corrispondente al segmento di 2.640nt compreso tra i nt
149821-152460 di Genbank AC125611, versione 4

1 aggtacaggc tgtaagccag actcaccagt cgtctttata tttaaggagg caaaagaatg
61 gacgggcacy gagatcctag aggcgaagca agttgtcagc gccctgccc agggcccgcc
121 ctgccggcc cagtccgac ccgccttcg cccgcccag cagctccacc ctcccggt
181 ctctcgccc tccagcagct tgggttaggt ggcgatctcg atgtccagg ccactctgac
241 gttgaggagc tcttggtact cctcaggtg ccgcgccatc tcctcttta gctgtcgag
301 ctctctctcg agccggcag cgcgcctcg gtagccccc gctccaggg cgaactgctc
361 ctccagctct ctcaactgcc tgagcagcg ctcgttctgg ggtaggagag tggaaggggc
421 cagttgcaga acatttcac gtccgctccc cgggcccag cgcgcagctt cgtactcacc
481 gtgcgcgca gcccgccac ctgcacgtt agactctgga tctggcgctg ggactcgttc
541 atctctgct tggcctggcg cagggcctcg tggttccggt tggcagcgc ggacaggtcc
601 gcgtactgag aagtgggggt aaccaggtt ttagtcggct gggacgcgc acaccaccc
661 agcgtccgc ctgcaggcc ctccggctc ttgcacctg gacttgtaac actctcgc
721 ctctgcagg ttcttcggc cgtgctctc gtactgcgc cggatgtccc tcagcgctgc
781 cgtcagctcg ggcttcacg tggcttcac ctccacctgc tgcacctgt ggtctccac
841 actcaactgc aggtctcgca gctcctacg cgggagcag gcagaggatg gacagcgcg
901 caaattccac gcgggccag cagttcgtgc acagaaaaga gaagaaacg ttgaacgaac
961 agaagtggc gccaggagg gcaggcgta cagcctcg ccccgcggg cgcgagacca
1021 gaggccaggt ttggaggta cagccccgt gcccgccc aggtggcgca aggtgggag

1081 tctaaccacc ttagactag ggtggagggg ctggtctac ccagcatcgt cctgatcccc
 1141 agggcgatgc ctccgtcca ccgcccagct ccagcgagac caccacaaa cctcagaaac
 1201 cgcacctgat accgggcca cttacctct cgtgcagctt cttgaggaac tcaatctcat
 1261 ccacagaga ctcaatcttg cgtcttagtt ccaggogga cagagtggca tegtccacgt
 1321 ccttcgaggg gtggcagtg aggttcaaga taagttaggg gctgcgcaga ccaaggaagg
 1381 accaggcctt cctgtctgc ctccaggagc atctgggtta ccccttctc ccgcgcccc
 1441 ccgatgccac ctctggatac tgagatcggg ggtagcgtg gggaggtga actcggagag
 1501 gggctcggac tcaccttgcg gaagagcacg aggttgtgct ccggtctct ccgttgcgc
 1561 gtctctctt ccaacctgac ggaagagcg tgcagaggt gaactgcggg gtgcgcgcc
 1621 agctcgacc ccagacgca cgcacctcag gatccggtta gaggctgtt tgctgccag
 1681 gactctaat ggagggtga ggtgtctaa tggattgcc ccgattgtc tctaaccgac
 1741 tgggagctga aaagggggtt tctcattac tcaggggagg cacagatacc cacttctccc
 1801 acctcccaa aactcagag caaaggggta gggggggca cttggagccc gtgggcaggg
 1861 atgtgcccc cacacacctg ggttggtta gggagccaca ccttgggtt gctgatggag
 1921 aggggaagcg aggggagga agagcagcg cctcgacggc cgttcgacc tgcctcgac
 1981 ggcagcggc cagccctgcc cctgacctc tgcttgagcg ccgcaggtc ctcccgacc
 2041 ccgtcgctt ccacctgac ccgttcacg tcgcggcca acagctccag ctctcgccg
 2101 agctcgcca gctcctgctg gcacagctg tggcgcgcg ccggtctctg gcccgggct
 2161 tggctcagct ccccgcgag ggcgcgtt tgctgctca gaaagctac cttctcgatg
 2221 aagttggcga agcgttgtt gactcctgc agctcctgt tctcgttct gcgcgtggc
 2281 aggaactct ggttgaggg ctccgcatg gagaagtga ggcgtccga ggcagggc
 2341 aggagggcg ccgtccgc tcgggggcta cgaagctgc ccaggcgac caggagctc
 2401 ggggacgcg agccagcag gcgctgctg gagaagogg agctggcga gtaggagaag
 2461 gccccgggg atagtgggg cgttgaccg aaggtacgg ggtatgaggt ggagctgaag
 2521 ccggcccgga ggcgcaggg gtgtggctc attgcggca aggatggga gtcaccttc

2581 gcagagctag gccgggggct gggaaggagc cgcagaccgc tgcgaggcgg ctttatagcc

SEQ ID NO. 15

CpG island del gene PTGER3, corrispondente al segmento di 1.560 nt compreso tra i nt 123001-124560 di Genbank AL031429, versione 11

1 aaccctggaa ctacctacca ggagcggaga ccagcagacc gacagcacgc acatgatccc
61 cataagctga atggcgtct cggctgtgat gggcccccac tgggcactgg actgagatgc
121 cgtggccttg gcccggcagc gggacaccag ggccttaatg gtggccaggt tgcaggaaaa
181 ggtgactgtc agcgccaaga gcccaggaa ggcaaaggca gaggcgaaga aaaggttgcc
241 ccagttatgc gaagagctag tcccgttgcc cctcgcgcg gtgctgatga agcaccacgt
301 cccgggccac tggacggtgt actggccac gccagcacc ggcagcagg cgaaggcgag
361 cacggccagc cacaagcoga gcagcacagc ggggtggca cgcgtcttca tgtggctcgc
421 ataccagtgc ggcgcctga tggccagcgc cgcctcagc gccatggcgc tggcgatgaa
481 caacgaggag agcccgaata cagtcagtgt cagcccgaaa aaggtgcaga gcgcgccga
541 cgggtcgatg tgcctccaac gctgcttga caggtacag acgatgacga cgggggtggt
601 gagaagctgc ccgaccaggt cggtgagcgc cagccagcgc atgcacagca ggaaggactt
661 cttgcgcttg ctctcccgcc gccggtagct gcgcgacagc agcagcatgg ccagtgcgtt
721 gccacgaaa ccagtgagca gcatggtgat cgggaaggcc acggacaccg atccgcaatc
781 ctgcgcagac cctggagggc gcgtgaggtt gcccgcgcgc tcggcggaac gctcgggcgc
841 ccacatgctt gtgtaggagt ggttgaggcg ggtgcagaag ggggcacccc ctccgtagcc
901 cgggtctctc ttcattgttg ctccgaggtg aggggggat ggcgtccaga gagccgcagc
961 gggagggggc agacgcggcg cgggcggcgg cggaggtcgg cgtttaccgc ggctggggct
1021 gggctgcccc ccatggtgcg gggcgcagcc gccgcctac tcgctgctg ggaccgcgcg
1081 cgcggcggcg ccagggtca ctggcccggg agggagccac gccttcctct ctgggaaacc

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1141 tctggtggcg aggcgcgcgg aggtgcgcag tcccctttat aaggccgagg gggcggggcg
1201 cccgtgggtg tggacagaac cgaggtggga ggaggggtgca aagcaactga ggcctctct
1261 tggctgttgc ctatctgat cgcttgggtt gggaagcccc agacggtctc ctctgaaacg
1321 ccttctctct ggcgcgcgcg ggagccact ggggtctctt ccagttctcc gctaaagtgt
1381 cgggtgacgg caagcagcta ataagtagca ctggacttgc ggaccccagg caaactgccg
1441 aggcgcacct gacgctcgt cctctgctt cttcaaccac aaacgctcct acagggacgg
1501 gatccttctc ctgaagtctt ttagtaactc tggtaaagtg aaaatcgctt gtccttaagc

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SEQ ID NO. 16

CpG island del gene PTPRM, corrispondente al segmento di 2.340 nt compreso tra i
nt 64321-66660 di Genbank AP001091, versione 5

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1 agcactttgc accagataca gaaaccacgg gttatgtcca aacctggtt ttggtgtgac
61 caccgccttc cgtgtactgc ctgcggctcg cttcggggcc acacgggaca ccgaggcatg
121 atgaggacgc agaacagcag aagcgcgcgc tgcttcccg ggcagtgctc tggggccag
181 cggcgtgtac ccggcgggcc cggcgcggag cgggctggcg atcgcggggc tggcgcctcc
241 cggctccgc gccatctccc ggcccccgc aacttcgctc cgcgcgggc gtagagaagc
301 tcgcagccct ccggagctc agcagctctc tggctcgctt ttccgcagc cgcgagcag
361 cgcagggccg gcgactcgg gtgcagctgg cctgtgcgg tgacatgcc gtccggcgc
421 aggtcgaag ccgcctggcc gcgcgcgg ggctgcagg cgtggtccc gcccgccgc
481 gtcacaaac tactcgggc togtgaccg ggacaaactt ctggcggcg cgcagctct
541 tccacagtca cctccccag agccagctac caaaatagaa gacgcggccg gggcgaggag
601 gtggcgggg ggagccggg gccgcctct cccgcgcgg ctgacgccg cttcggcgc
661 ggtagtggct gtggcgcgg gccgcgcgc agccagctc ccggaggcg tgggcgcg
721 gccggcggg cagggcgct cagccctct agcgggcgc ggcggcgcg gccggcggtg

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781 acgtgagcgc tcccttcagc cggcctgcgg ggcacogcca gtcagtoggg gagcaagagc
 841 cccgcgcgca gccggcgcgg gctcggteat cggcgcgcg ccgcccgggg ctgggcttgg
 901 ggctgcctgt ggagaggcgg cgggcggaac gcgcgcggcc acggccacgg ccaccgccac
 961 ggccacggcc ggcagctcgg gtcccgggtc ccgggcaggg gaaggggaga ggcggcgagc
 1021 tcagcaaccg gaaccgaggg aagattttgg ctccgcgggc tcgccctccg ctccctctgc
 1081 cagcggcgcc agacgcggag tggggccagg gacaggggag gaggaccag gacctgtgc
 1141 ccgcgccct ggagccgtg gagtccggac ttctgcaact gttggcactt tgggggcttg
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 1441 cgggacgcc gggacgcga cagctccctg gtggtagagc cctaaggctg gcgtcggggc
 1501 cgggcggggg gcgcggcggg ccggacaccg cttctgcctg tgagccgggc gctgggcgag
 1561 gggccgtggg gctggcaggc acccagtcct cgggcgggcg gagcggacgg accccgaggg
 1621 cgagctccc agccgggact gccagctcgg ccgcgcctc tcgcggcct gggctagtgc
 1681 tcaaggttgg gcggcttgca ctcttgagtc cctggccggc tgcaaaagga acagcagaaa
 1741 actttgcttg aagtccag ttgcagcgc cgggcgcct ggctaggcg ctgcgcggtc
 1801 ccgcgcgacc ccgagcagcg gccgggccc ggcgcctggt gttcggtgc gccgcagcg
 1861 atcgcggga actggcgcc gctccggcgg cggcgatctc cgggtgccct gccctccctg
 1921 tcgccccctg ccgcgcgcg ctggcgacc cgggaggtcc ccgcggtcgt gcagcgtctg
 1981 cggagaggct ggggggagtt cctgcgcgt cccagcggta gggcttggcg gccgcggagg
 2041 gaagcgggca ggtcccagg cctggccac ggcctgcgc ccgcctgggc tccccctccc
 2101 caccctcgtc ccctagcgg agcgcgcgg ccagctgcaa ctgttctc cagcccggt
 2161 gcccggggg gccaggtggg aaggagaggc actggcggtg tgcgagcaag cgtgtgagtg
 2221 tgtgcgcgtg tgtgcctgca cgcgcgcgc gggcggttct aagcccagag gaacccctca

2281 cggagaggat ctgtggatcg gagtcggggg tccggcgtgg gggcgaaccc ggcacgctgt

SEQ ID NO. 17

Sequenza metilata del gene ARHGAP20 (top strand), derivata da SEQ ID NO. 1

1 tattatagtt tatatattat taagtttacg gatattttta gatggtttcg tgatacggtt
61 aaggtttttg ggaattttta tatattttta tattcggat atcagattatt ttttttaaat
121 tgatttttag ttaatttaag attttggtgg gaagatttat gaaaggtagt aaaattaaga
181 taagtaggga atttcgtaa tttttttaag tttttaatga aataaatgta attttttaag
241 atatttttta aggaaaagtt agaagatggt ttaaatcgta atttgttttt agaaaagttg
301 gaagggtatt attaagataa ggtaaaaaaa aaaaaaagg taaaatatcg gaaagtttta
361 tgttggaagc gggggtgggg aggcggggga taggtagata gggtagaaa tatttaaatt
421 aatttttttag ggagcgaaac ggtagaggtc ggtagttcgc ggtttacgtg tatttgttta
481 gggaatcgtt ttagcgaaat ttgattcga toggaatttt ttcgtagtat agcggtcgtg
541 tttatcggaa tggaaagtta taagtgtta tttgtatttt ttttttagtt ttgataggga
601 atacgcgttg tttttacgtt tatatcgata ttcggatttt tatttagttc ggtagagtt
661 ttaggggtta gggattagtg tagggagaag gttttttatt ttagttttta ggatttttaa
721 ttatagtta ttcgttttta tttgttcgg ttttaggttt agtcgaattt atatgttttc
781 gtagtgtcga gcgttattat ttatagtcgt tttttaaatt gtgattttta ttggggagat
841 tcggaattat ttaggatttt ggtgtgggg gtagtatttt ttatatttgt tttcgaaaa
901 ttgttatgga gtagtcgcgt ttcggcgggt aggtgagggg gtcaggttta ttagcgtcgt
961 agtttcgttg tttatttttt ttagcgtcgg ttgtcgtttt cgggtagata tcgtcggttt
1021 tgattttggg gttgatatcg ttaaagggtta gttagtgttc gtttaggtta tttcgggagg
1081 tttaggggta cggcgagggg tcggggaaag gcgacgtttt attatagttc gcgcgtttag
1141 attgagggag gagtcgggtt gtagaatcgg cggcggatgg agacgggagg gaggttcga

1201 ggtcgttcga ggagagatta aggttttaga aacggagaag cgggcgtttt gcgggaggcg
 1261 gcggcggtgt cgttggtcgt taagggcggg aagtgttttg ggatttttat taggggtcgc
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 1621 ggggcgagga cgcgcgggcg gaggcgcggt tgcgtgttt aggtaggag tcgagtttcg
 1681 ggtgttcgtc gcgcgttttt cgtcggggtt atgtattttc gtttcggtc gatatcgcg
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 1801 cgtttttttc gtttcgggcg ttttcgcgtc ggggtcgttt tcgtagtttt ttttagtttt
 1861 ttttagtttt ggggtttttt agtttcgttt tagtttcggt cgcgtttggc gggcggtttt
 1921 ttatatatgt tagtatatcg gttatcgggt gatttttttcg gtttggtatt tcgcgtgggt
 1981 gtagttcgta ggagtttacc ggtttgtgtt acgtacgggg gtttttagtg tacggatacg
 2041 cgtttttttc gttatttggt tatttttatt agattttatt ttttttcgcg tcgtgttcgc
 2101 ggcggaaggc gttttttagt cgcgtgtatt cgcggagcgg tggcgatttt agtttgagta
 2161 gaggagtgtg agtgattttt gtttcgtttt tagcggattg cggagggaat tttttatttt
 2221 attttattgg ggataggggt gtacgtcgta gagtgtcgta gttgtataaa tttggaagtt
 2281 tatagtatcg tttgattttt tgtgtaattt cgaacgttag tttgttcggg taattttgag
 2341 tgggtttttg tagtcgggtt tgttagcggg ttttgatat tttgatttcg ggttttcgtt
 2401 gtttgtaggt tgtagagacg ggggtatttt aaacgtgaaa gagtaatgaa ggaaaatgta
 2461 gatagagcga ggacgtcgaa atttggttaa gttattgaga aggttataat atgtggaagt
 2521 gtttattaga tatttcggtc gagagtataa ttttttgta gtttaaatag aggtaaaaat
 2581 attttaaagg ttaaagaata attagaggga gaggatttgg agttgattcg cgttgagttg
 2641 agtgttggtg tattttcggg ggttggttga ttggtacgga tgattcggta gatggatttt

2701 tttttttgga gttaggatta gagaagtagt ggcggattag tgaggaagga tattacgtta
 2761 tgatattagg ttgtggaagg ggtttggttt gttttgtgg taagaagaaa aaaatcgagg
 2821 tttttgttag gttaggttgt tattaggata ggttgtagaa gaatagggtt ttggtcggtt
 2881 ttgttttaag gaagggatgt tgtttaatat atattcgcg gcgtatatat tattattatg
 2941 tttaggaatg gtttattgtg gaaataatag ggggaaaatg ttttagttcg ttttaagttt
 3001 tgtttatttt atattgttta aagtaggttt atataggttt tataaattat atatacgtat
 3061 aaattatata tacgtataaa ttatatgtat gatttgtaaa ttatttatta ttgtgtttat
 3121 gtatgtgtgt atatatatat atagtttttt atggttattt ttttttcta gttgagattt

SEQ ID NO. 18

Sequenza metilata del gene ARHGAP20(bottom strand), derivata da SEQ ID NO. 1

1 gggtttttagt tgtaaaaaga gagtagttat gaaaaattgt gtgtgtatat gtatatatat
 61 ataaatataa taatagatga tttataaatt atatatgtga tttatacgtg tgtgtgattt
 121 atacgtgtgt gtgatttata aagtttatgt aagtttattt taaatagtgt gaggtggata
 181 aggtttaaaa cgggttgga tttttttttt ttattatttt tataataaat ttttttggg
 241 tatggtggtg atgtgtgctg gcgcgagtgt gtgttgata gtattttttt ttggaatag
 301 agtcggtttag agttttattt tttataaatt tgttttaata atagttaat ttggtaggaa
 361 ttctgatttt ttttttttta ttataaaagt aaattaaatt ttttttataa tttaatatta
 421 tagcgtggtg ttttttttta ttaattcgtt attgtttttt tagttttgat ttttaaggaa
 481 gaatgttatt tatogaatta ttcgtattag ttaattagtt tcgtaaagt tagtaatat
 541 tagtttaacg cgggttagtt ttaaattttt ttttttgat tttttttgg tttttaaatt
 601 atttttgttt ttatttgggt tgataggaag ttatgttttc ggcgtagata ttgataaatt
 661 atttttatat attgtagttt ttttaatagt ttagttaaatt ttcggcgttt tcgttttggt
 721 tgtatttttt ttattgttt tttacgttt ggaatgtttt cgtttttgta gttttagat

781 agcggaaatc gcgggtgtaa atgtgtaggg gtcgttgata tgatcggttg tagaagtta
 841 tttagggtta ttcgaatagg ttagcgttcg ggattgtata agaggtagg cgatgttg
 901 ggtttttaaa tttgtatagt tgcgatattt tgcgacgtgt tattttattt ttagtggggt
 961 ggggtggggg atttttttcg tagttcgttg aaagcaggt aggaattatt gtaattttt
 1021 tgtttaggtt gaggtcgta tcgtttcgcg gatgtacgcg ttgtaggggc gtttttcgc
 1081 gcgggtacgc cgcgggaagg gatggggtt ggtgggagtg ggtaggtggc gggagaggcg
 1141 cgtgttcgtg tattagaggt ttcgtgcgt gatataggc gatgagttt tgcgggtgt
 1201 atttacgcg agttatagat cgaagaggt agtcgggtgt cgggtgtta atatatag
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 1681 gtttttttt tttgatagga gtgtttcgt tcgcgggagg tagttgtatt aagaaggtga
 1741 ggacgttgag cgggggttcg tgttttcgt cgtcgtagtt tttattgcg gcgcgcgtt
 1801 ttcgcgttcg ttatagtagc gcgttaggc gacgtcgcg gaatttgacg ttcgaggtc
 1861 gcggttttta atgagagtt tagaatatt ttcgttttg acggttagc gtagcgtcgt
 1921 cgttttcgt agagcgttcg tttttcgtt tttagagtt tagtttttt tcgagcgatt
 1981 tcgtagttt ttttcgtt ttattcgtc tcggtttgt agtcggtt ttttttagt
 2041 ttaggcgcg gggttgtagt ggcgacgt ttttttcga ttttcgtc tgttttggg
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 2161 ggcgcgcga tgtttgttc ggagcgttag tcgcggtga agaaggtagg tagcggggt
 2221 gcggcgttg tgggttcgt tttttattt gttcgtcag gcgcggtgt tttatagtag

2281 ttttcggggg gtagatatgg ggagtattgt tttttatatt agggtttttg atgatttcgg
 2341 gtttttttagg tgggggttat agtttgaggg gcgattgtgg atgataacgt tcgatattac
 2401 ggggatatgt aggttcgggtt gggtttagaa tcgagtaggg tgggggcggg tgggttggtg
 2461 ttgggggttt tgagggttga ggtgggggat ttttttttg tattggtttt tggtttttg
 2521 gattttggtc gggttggata gggattcggg tgcggtgtg ggcgtggggg tagcgcgtgt
 2581 tttttgttaa agttgggaga gggatgtagg tgataatttg tagcgtttta tttcgataaa
 2641 tacggtcgtt gtgttcggg aggatttcga ttccgggttag gtttcgttg aacggttttt
 2701 tgagtaagtg tacgtgggtc gcgggttggt ggtttttgtc gtttcgtttt ttgaggaatt
 2761 gatttgggtg tttttagttt tgtttgttg ttttcgttt tttattttt gtttttagta
 2821 taagattttt cgatattttg ttttttttt tttttttgtt ttgttttagt ggtgtttttt
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 3001 ttttgatttt attgtttttt ataaatttt ttattaggat tttaggttg ttagaggtta
 3061 gttgaagaga ggtgatcgg gtgtcgagta tagaaatgt tgggagtttt taaggatttt
 3121 gatcgtgta cggagttatt taggggtgtt cgtgaatttg atgatgtatg ggttgtagt

SEQ ID NO. 19

Sequenza non metilata del gene ARHGAP20 (top strand), derivata da SEQ ID NO. 1

1 tattatagtt tatatattat taagtttatg gatattttta gatggttttg tgatatggtt
 61 aaggtttttg ggaattttta tatattttta tatttggtat attgattatt tttttttaat
 121 tgatttttag ttaatttaag attttggtg gaagatttat gaaaggtagt aaaattaaga
 181 taagtaggga atttgtgtaa tttttttaag ttttaatga aataaatgta attttttaag
 241 atatttttta aggaaaagt agaagatgtt ttttaattgta atttgttttt agaaaagttg
 301 gaaggggtatt attaagataa ggtaaaaaaa aaaaaaagg taaaatattg gaaagtttta

361 tgttgggaagt gggggtgggg aggtggggga taggtagata gggtagaaa tatttaaatt
 421 aatttttttag ggagtgaat ggtagaggtt ggtagtttgt ggtttatgtg tatttgttta
 481 gggaattgtt ttagtgaaat ttgatttggg ttggaatttt tttgtagtat agtggttgtg
 541 tttattggaa tggaatgtta taagtgttga tttgtatttt ttttttagtt ttgataggga
 601 atatgtgttg tttttatgtt tatattgata tttggatttt tatttagttt ggtagagtt
 661 ttaggggtta gggattagtg tagggagaag gttttttatt ttagttttta ggatttttaa
 721 ttatagttta tttgttttta tttgttttg ttttaggttt agttgaattt atatgttttt
 781 gtagtgttga gtgttattat ttatagttgt tttttaaatt gtgattttta tttgggagat
 841 ttggaattat ttaggatttt ggtgtggggg gtagtatttt ttatatttgt ttttgaaaa
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 1801 tgtttttttt gttttgggtg ttttgtgttg gggtttgttt ttgtagtttt ttttagtttt

1861 ttttttagttt gggttttttt agttttgttt tagtttggtg tgtgttttgt ggggtgtttt
 1921 ttatatatgt tagtatattg gttattgggt gatttttttg gtttgtgatt ttgtgtgggt
 1981 gtagtttgta ggagtttatt ggtttgtgtt atgtatgggg gtttttagtg tatggatatg
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 2401 gtttgtaggt tgtagagatg ggggtatttt aaatgtgaaa gagtaatgaa ggaaaatgta
 2461 gatagagtga ggatgttgaa atttggttaa gttattgaga aggttataat atgtggaagt
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 3001 tgtttatttt atattgttta aagtaggttt atatagggtt tataaattat atatatgtat
 3061 aaattatata tatgtataaa ttatatgtat gatttgtaaa ttatttatta ttgtgtttat
 3121 gtatgtgtgt atatatatat atagtttttt atggttattt tttttttgta gttgagattt

SEQ ID NO. 20

Sequenza non metilata del gene ARHGAP20 (bottom strand), derivata da SEQ ID NO. 1

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1  ggggttttagt  tgtaaaaaga gagtagttat gaaaaattgt gtgtgtatat gtatatatat
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121 atagtgtgtg gtgatttata aagtttatgt aagtttattt taaatagtgt gaggtggata
181 aggttttaaaa tgggttgga tttttttttt ttattttttt tataataaat tttttttggg
241 tatgggtgtg atgtgtgtgt gtgtgagtgt gtgttgata gtattttttt tttggaatag
301 agttggttag agttttattt tttataaatt tgttttaata atagttaat ttggtaggaa
361 ttttgatttt ttttttttta ttataaaagt aaattaaatt tttttataa tttaatatta
421 tagtgtgtgt ttttttttta ttaatttgtt attgtttttt tagttttgat ttttaaggga
481 gaatgttatt tattgaatta tttgtattag ttaattagtt ttgtaaagt tagtaatatt
541 tagtttaatg tgggttagtt ttaaattttt tttttttgat ttttttttg tttttaaaat
601 atttttgttt ttatttgggt tgataggaag ttatgttttt ggtgtagata tttgataaat
661 atttttatat attgtagttt ttttaatagt ttagttaaat tttggtgttt ttgttttgtt
721 tgtatttttt tttattgttt ttttatgttt ggaatgtttt tgtttttgta gttttagat
781 agtggaatt gtgggtgtaa atgtgtaggg gttgttgata tgattggttg tagaagtta
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901 ggtttttaaa tttgtatagt tgtgatattt tgtgatgtg tattttattt ttagtgggt
961 ggggtggggg attttttttg tagtttgtg aaagtgaggt aggaattatt gtaattttt
1021 tgttttaggt gaggttgta ttgttttggt gatgtatgtg ttgtaggggt gttttttgtt
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1321 agggttgagg agggttgtgg ggggtgggtt tgggttaggg tgtttggagt ggagggggtg
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1381 gggttgagggt ggggtgggtt gtggtgttga tgggttgttg ttgttgtatt tgttttagt
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 1621 agattttttt tatggaagtg atgttttttt agtaggagat tttagggga tagttgggtt
 1681 gttttttttt tttgatagga gtgttttgggt ttgtgggagg tagttgtatt aagaagggtga
 1741 ggatgttgag tgggggtttg tgttttttgt tgtttagt ttatttgttg gtgtgtgttt
 1801 tttgtgtttg ttatagtagt gtgttaggtg gatgttgtgg gaattttagt tttagagttt
 1861 gtggttttta atgagagtgt tagaatattt tttgtttttg atggttagtg gtagtgtgtt
 1921 tgttttttgt agagtgtttg ttttttgtt tttagagt tttagttttt ttgagtattt
 1981 ttgtagtttt tttttgttt ttatttgttg ttggttttgt agtttggttt ttttttagt
 2041 tttagtgtgt gggttgtagt ggggtattgt tttttttga tttttgttg tgttttggg
 2101 ttttttgaag tggtttgggt gagtattgat tgttttttgg tgggttagt tttaaagtta
 2161 gggttggtga tgtttgttg gtagtggtag ttggtgttga agaaggtagg tagtgggggt
 2221 gtggtgttg ggggttgggt tttttattt gtttgttgag gtgtggttgt ttatagtag
 2281 tttttggggg gtagatatgg ggagtattgt ttttatatt agggtttttg atgattttg
 2341 gttttttagg tgggggttat agtttgagg gtgattgttg atgataatgt ttgatattat
 2401 ggggatattgt aggtttggtt gggtttagaa ttgagtaggg tgggggtggg tgggtgttg
 2461 ttgggggttt tgagggttga ggtggggat ttttttttg tattggtttt tggtttttg
 2521 gattttggtt gggttggata gggatttggg tgttgggtgt ggtgtgggg tagtgttgt
 2581 tttttgttaa agttgggaga gggatgtagg tgataattt tagtgtttta ttttgataaa
 2641 tatggttgtt gtgttgtggg aggattttga tttgggttag gttttgttg aatggttttt
 2701 tgagtaagtg tatgtgggtt gtgggttgtt ggttttttgt gttttgttt ttgaggaatt
 2761 gatttgggtg ttttagttt tgtttgtttg tttttgttt tttattttt gtttttagta
 2821 taagattttt tgatatattt ttttttttt ttttttgtt ttgttttagt ggtgtttttt

2881 tagttttttt ggaaataagt tgtgattaga ggtatttttt agtttttttt taagaaatat
 2941 ttttaagggat tgtatttggt ttattagaga tttaaagggg ttatgtaggt tttttgtttg
 3001 ttttgatttt attgtttttt ataaattttt ttattaggat tttaggttgg ttagaggtta
 3061 gttgaagaga ggtgattggt gtgttgagta tagaaatgtg tgggagtttt taaggatttt
 3121 gattgtgtta tggagttatt taggggtggt tgtgaatttg atgatgtatg ggttgtagt

SEQ ID NO. 21

Sequenza metilata del gene CDH11 (top strand), derivata da SEQ ID NO. 2

1 attttatatt ttttttagga ttacgtggaa ggggtgagaa aatttagga atagtttgta
 61 gttaaataag agtaaaattc gattattttt gagggaaagt cggatttttt gtttattttt
 121 ttttggtgaa gtaattttat ttataagttg aaatgaactt attagattat tttattatta
 181 ttattatggt ttattagagt ggggattttc ggcggtggtt tgggaagtat ttaaagtttt
 241 aggggttata gtagaggtta aaaaggtaga tagaggaagt agggtagagt tttgaaaagg
 301 tttagggtta gggatttata gggggaggta ggagtggtag gtattacgat ttgttttttg
 361 gcgttttata ggaaagtatc gggagttaat gttttcgccg gttttttcgc tagagtgtgg
 421 tgcgagggtg ggggggtatt ggagatttag ggggttatta ttttgatat ttatggtggg
 481 gggaagggtg aggagtaaga taatcgggta gttggaaatt tatagttttt ttttcgtagt
 541 ggaggaatga ggagtttaaa ggttacgttt atatagaggg tgatagaggt atttttttcg
 601 cgtaggacgc ggattggggg taggtacgta gcgttattcg gattttggag tcgttaagaa
 661 aaacgcgggc gcgtaggtcg aagagggtag gtttcggggt agtttcgtcg gtattcgttt
 721 tcgcgggcgt ttttttaagt cgtgtggaaa ttogggcgtg tgcgggcgtt cgggattcgc
 781 gggttggtga ttaggagttg gagggtaggg ttoggtcggt tttgttttag ttogtattg
 841 gggttttttt tttatcggtt taggatttta agtttttttt ttogttttcg gttttttttt
 901 tcgttaattt ttgggttcgt tttttttttt ttagtttttt taaattgttt ggttgtggcg

961 ttttagttttt ttttcgtagt tttttttttc gtttttttcg cgggtttatt tttttttttt
 1021 ttttagtttt attttcgttt ttttaggcgg ttttttttta gtttttattt attggcgttt
 1081 ttattttttt tcgttttttt ttttgttttt attttttatt ttgtaaattt gtttaagtta
 1141 ggggttttta tataggtatg gttgtttttt gttgggtgtg cggattttta cgtcgttttc
 1201 ggtatcgoga gcgtttcgtt tagtttttgg cgtgattttt aagtttcggt tttgtagtt
 1261 ttttttttcg gcgattcggg gagggagggt aggaagtagg ttcggggaat ttttacggt
 1321 gcgagtcgtt agtgagggga atagcggagg aaggagttag gatttcggcg ttgcgtttta
 1381 ttaggttttt ttttcgtag aaacgtatat tttatcgggt tttggcgggt ttgtagcgag
 1441 ggagtggtaa taagtatat tatcgcggg gggtattgat atttggttg ggtaggggtt
 1501 aaggtatttt tttaaaagt ggagcgaggt cgatttcggc gaagcgtttt tcgcgtattt
 1561 ttttcgagg cgttcgttg ggggtattag acgagaggag agttgagaga gaacggagat
 1621 tgggtttttt ttaagtttta agtttttttt ttcgttcgat ttattatta gagtattag
 1681 aagagtttgt aagggatggg agattgagag ggggtgggggt tgggtaggag tcgttaacgt
 1741 tgagggattt ttggaagtg ggggtgtgga gtgagaaaga atagaacgcg ttttgaatt
 1801 ttttaattgt ttttttattt ggacgatatt tttttttaat tattatttcg gttcgttagg
 1861 cgagagttta gtttggttag ttggagcgga tttgggggaa ggaggaaaat gggggttttt
 1921 aatttttttt tagttttttt tcgtcgtttt ttttgattgg ttgtcgtttt ttggagtta
 1981 attttagtcg ttttagattt tatttgagtt ttgagggagt cggagcgtcg cgttacggg
 2041 cgggaggggc ggttacgaat ttaggggtta gtatttttgg gtttttgggg ggaggggcgc
 2101 ggacggggtc ggttttcgta gtttttcga gggttatttc gttgttttc gtagtttcg
 2161 ttttttttag ttttcgtttt tttttttttt tatagcggta gttttttttt tttcgtttt
 2221 ttcgtttcgt attcgtttgt tcgttcgtta ttttttttcg gttttttatt tttgttatta
 2281 gcgcgttcgg cggtttattt cgcggtcgtc gttagttgag gggagcgtcg cgggtcgagg
 2341 agtagatgtc gcgggggtcg ttcgtagtcg tcgttgattt gtgaatggga tcgggattgg
 2401 ggtcgggatt gatatcgtag cgtttgtttt gcgttaggga ttggcgggtc ggaggttcg

2461 tttattttta agggtttttag gtgaggtgcg tgcgttagttt ttttttttcg tttggttggg
 2521 gtttttttga atggggggta ggattttttt aggaagagaa tgttttggcg gggcggggtg
 2581 gtgaggggga cgggtgtatt tgagtcgaga aggttttatt aacgtaaagt aaaaggagg
 2641 gagagatttg tttaaaaatt agaaaggag aaggagttta gttgtggcg cgggtaaagt
 2701 aggggaocga ggttttagat gtgcgtttta cgattttttt tggtttcggt tttttgtggg
 2761 gtttgcgtcg aggttatagt agagggggtt tgtatttggg tgggtaaga gattgtagag
 2821 tagatttttcg gatacgtcga ttgttttcgg ttatattttt ggggaaagtc gtttaocggc
 2881 cgggtgttcgt tagtttttcg tgcgtttttt aaagcggcga tatgatcgcg ttttgcggg
 2941 tttttatttt attttttcgg atttttgtcg aaagttttc ggggttttagt tttttagtc
 3001 gagattgtcg ggttaagtcg ggaacgga aagatttttag ttccggaagg agattgttcg
 3061 tattttaata gcgtgggttt ggggtcgtcg attgtggttt tgggtagta ggttgcggtg
 3121 cggtatagtt ttttagttcg agtttttcg gtagttttgg cgttcgtttg taagttttta
 3181 ttagcgtagg agtaggttta tgagcgttt agattcgggt tgcgtttttg tttgggattg
 3241 gcgaaagtgt ttagggttta cgttaatttt gagaattata ttttttcgaa atttgcgtcg
 3301 tttttcggag cgcgttaagt ttttttagtt ttccgtacgt acggtttttt tttttgcgtt
 3361 ttgtttcga acgcgagtcg ggaggtggga agtattgaga agttggttag atggggagga

SEQ ID NO. 22

Sequenza metilata del gene CDH11 (bottom strand), derivata da SEQ ID NO. 2

1 ttttttttat ttggttagtt ttttagtggt tttattttt cggttcgcgt ttccgggtag
 61 agcgtaggga gggaggtcgt gcgtgtcggg agttagagag gtttggcgcg ttccgagaag
 121 cggcgtaggt ttccgggaagg tgtggttttt aaagttaacg ttgatttttg tagttttcgt
 181 taattttaag ttagaggoga gttcaggttt gggtcgttta tggatttatt tttgcgttgg
 241 tgggagttta taaacgggcg ttagagtttt cgtagagatt cgggttgag ggtttagtcg

301 taticgtagtt tgttggttta gaattatagt cggcgggttt aaatttacgt tattaagtg
 361 cgggtaattt ttttcggag ttgggggttt ttcgtttttt cgggtttatt cggtagtttc
 421 gattgtaggg attaagtttc ggggagtttt cggtagggat tcgggaggat ggagtaagaa
 481 tttcgtagag cgcggttatg tcgtcgtttt ggggaagcgg cgtaggggtg gcgggtatcg
 541 cgtcgtgggc gatttttttt agagatatga tcggggatag tcggcgtgtt cggaggtttg
 601 tttttagttd ttttggttta gttaggtata aatttttttt gttgtgggtt cggcgtagat
 661 tttataggag gtcggagtta gggagagtcg tggagcgtat atttgaagtt ttcgtttttt
 721 gttttgttcg cgtttatagt tggttttttt tttttttttt gatttttaaa taaatttttt
 781 tttttttttt gttttgcgtt agtgaagttt tttcgattta gatattatcg ttttttttat
 841 tatttcgttt cgttaagata tttttttttt gagaaaattt tgttttttat ttaagaagt
 901 ttaattagg cagagaggaag ggattggcgg cgtattttat ttgggggttt tgagggtgga
 961 cgtaattttc gagtcgttag tttttggcgt agggtaagcg ttgcgggtgt agtttcgggt
 1021 ttagtttcgg ttttatttat aagtttagcg cggttgcgag cggttttcgc ggtatttgtt
 1081 tttcggttcg cgaagttttt tttagttggc ggcggtcgcg gaatgagtcg tcgagcgcgt
 1141 tagtggtagg aatgagaaat cggggggagg tggcgggcgg gtaggcgggt gcggggcggg
 1201 gggggcggga ggaggaggt tgcgttgtg agggaaggaa agggcggggg ttgagagaag
 1261 tcgaggttgc gagaggtagc gagatgggtt tcgtagaggt tcggggggtc gatttcgttc
 1321 gcgttttttt ttttaggggt ttagagatgt taatttttg attcgtggtc gtttttttcg
 1381 tttcgtggcg cggcgtttcg atttttttag ggttttagatg gagtttgag cgattgaagt
 1441 tgggttttag ggacgtatag ttaattaggg agggcggcgg agggaagttg gagaggggtt
 1501 gggagttttt attttttttt tttttttaa ttcgttttag ttggttaggt tgggttttcg
 1561 tttggcgggt cgggatggtg gttgggggaa ggtatcgttt aagtgagga agtaattggg
 1621 aattcgggag cgcgttttat ttttttttat tttattattt tattttttaa aaatttttta
 1681 acgttggcgg tttttgttta gtttttattt tttttaattt tttatttttt gtaaattttt
 1741 ttggtgggtt tgggtgtgaa gtcgggcggg gagggagatt taggatttgg gaagagtta

1801 gtttttcgttt ttttttagtt ttttttcgt ttagtgtttt ttacgtaacg tttcggagag
 1861 gggcgcgcg ggagcgtttc gtcggggtcg gtttcgtttt agtttttggg aggggtgttt
 1921 ggtttttatt ttagttaggt attagtggtt ttcgctcgta gtgttatttg ttgttatttt
 1981 ttcgttatag attcgttagg gttcggtgga gtgtcggttt ttacgggaga aagggtttaa
 2041 tggggcgtag cgtcggagtt ttagtttttt ttttcgttgt tttttttatt gacgattcgt
 2101 tatcgtgagg gtttttcggg tttgtttttt gttttttttt ttcgagtcgt cgggagaaa
 2161 ggttggtagg gtccgggttt aggaattacg ttaaggattg ggcggggcgt tcgcggtatc
 2221 gggaaacgcy tggggattcg tataatttagt aggaataat tatgtttgtg tggggatttt
 2281 tggtttgaat aagtttgtag ggtgggaggt ggaggttaaga gaggaggcgy aggaaggtgg
 2341 agacgttagt ggtgaaggt taaaaaggaa tcgtttaggg gacggggat gaggttggga
 2401 aaggagaaga gatggattcg cgaataagac ggggaaggag gttcggaggy gaaagttggg
 2461 cgttatagtt aagtagttt aaagggttag aggggaggag acgggtttag gaggtaacgy
 2521 aaaaagaggt cgaatacgya agagaaagtt tgggattttg agcgtatggg gaaggaattt
 2581 tagtcggggg ttaaggtaag agcggtcgag tttgttttt tagtttttgg ttattagttc
 2641 gcgggtttcg agcgttcgta gtcgttcggg tttttatacg gtttggggag acgttcgcyg
 2701 gggcggttgt cggcgaggtt gtttcgggat ttattttttt cggtttgcyg gttcgcgttt
 2761 tttttgacga ttttaggatt cgggtggcgt tgcgtgtttg ttttagttc gcgttttgcy
 2821 cggagaggat gtttttgta ttttttgtgt ggacgtggtt ttgaatttt ttattttttt
 2881 attcgggggy aagagttgta agtttttagt tgttcggtta tttattttt tagttttttt
 2941 tttattatag gtgtttaagg tgatagtttt ttgggttttt agtaatttt taatttcgta
 3001 ttatattttg cgaaggac gcgcgaggat attgattttc ggtgtttttt tgtagagcgt
 3061 tagagagtag atcgtggtgt ttgttatttt tgtttttttt tgtgggtttt tggtttgaa
 3121 tttttttaga gttttatttt gttttttttg tttgtttttt tggtttttgt tgtaattttt
 3181 aaaattttgg gtatttttta agttatcgtc gaaagttttt attttaatga ggtatggtga
 3241 tggtaatagg atgatttggg ggcgttattt tagtttataa atgaagttat ttatatagga

3301 gaggatggat aaggggttcg gttttttttt agaggatctc gagttttgtt ttgttttgg
3361 tataaattat tgtttggtt tttttaattt ttttacgtgg ttttagaggg agtgtgaagt

SEQ ID NO. 23

Sequenza non metilata del gene CDH11 (top strand), derivata da SEQ ID NO. 2

1 attttatatt ttttttagga ttatgtggaa ggggtgagaa aatttaggta atagtttgta
61 gttaaataag agtaaaattt gagtattttt gagggaaagt tggatttttt gttattttt
121 ttttgtgtaa gtaattttat ttataagttg aaatgatgtt attagattat tttattatta
181 ttattatggt ttattagagt ggggattttt ggtggtggtt tgggaagtat ttaaagtttt
241 aggggttata gtagaggta aaaaggtaga tagaggaagt agggtagagt ttgaaaagg
301 tttagggtta gggatttata gggggaggta ggagtggtag gtattatgat ttgtttttt
361 gtgttttata ggaagtattt gggagttaat gtttttgtgt gtttttgtg tagagtgtgg
421 tgtgaggttg gggggttatt ggagatttag ggggttatta ttttgatat ttatggtggg
481 ggaaggttg aggagtaaga taattgggta gttggaaatt tatagttttt ttttgtagt
541 ggaggaatga ggagtttaa gggtatgtt atatagagg tgatagaggt atttttttt
601 tgtaggatgt ggattggggg taggtatgta gtgttatttg gattttggag ttgttaagaa
661 aaatgtgggt gtgtaggttg aagaggtag gttttgggt agttttgttg gtatttgtt
721 ttgtgggtgt ttttttaagt tgtgtgaaa tttgggtggt tgtgggtgtt tgggatttgt
781 gggttggtga ttaggagttg gagggtaggg tttggtgtt tttgttttag ttttgtattg
841 gggttttttt ttatgtgtt taggatttta agttttttt tttgttttg gttttttt
901 ttgttaattt ttgggttgtt tttttttttt ttagttttt taaattgtt ggttgtggtg
961 tttagttttt ttttgtagt tttttttttt gtttttttg tgggtttatt ttttttttt
1021 ttttagtttt atttttgtt ttttaggtg ttttttttta gtttttatt attggtgtt
1081 ttattttttt ttgtttttt tttgttttt attttttatt ttgtaaattt gtttaagtta

1141 ggggttttta tataggtatg gttgtttttt gttgggtgtg tggattttta tgttgttttt
 1201 ggtattgtga gtgttttggt tagtttttgg tgtgattttt aagttttggt tttgttagtt
 1261 tttttttttg gtgatttggg gagggagggt aggaagtagg tttggggaat ttttatggta
 1321 gtgagttggt agtgagggga atagtggagg aaggagttag gattttgggt ttgtgtttta
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 1441 ggagtggtaa taagtatat tattgggtgg ggttattgat atttggttgg ggtagggggt
 1501 aaggtatttt tttaaaagt ggagttaggt tgattttggt gaagtgtttt ttgtgtattt
 1561 ttttttgagg tgttgtgtgg ggggtattag atgagaggag agttgagaga gaatggagat
 1621 tgggtttttt ttaagtttta agttttttt tttgtttgat tttattatta gagttattag
 1681 aagagtttgt aagggatggg agattgagag ggggtgggggt tgggtaggag ttgttaatgt
 1741 tgagggattt ttggaagggt ggggtgggtga gtgagaaaga atagaatgtg tttttgaatt
 1801 ttttaattgt ttttttattt ggatgatatt tttttttaat tattattttg gtttgttagg
 1861 tgagagttta gtttggtag ttggagtga tttgggggaa ggaggaaaat ggggtttttt
 1921 aatttttttt tagttttttt ttgttgtttt ttttgattgg ttgtgtgttt ttggagtta
 1981 attttagttg ttttagattt tatttgagtt ttgagggagt tggagtgttg tgttatgggg
 2041 tgggaggggt ggttatgaat ttgaggggta gtatttttgg gtttttgggg ggaggggtgt
 2101 ggatgggggt ggtttttgta gtttttgtga ggtttatttt gttgtttttt gtagttttgg
 2161 ttttttttag tttttgtttt tttttttttt tatagtggta gttttttttt ttttgttttt
 2221 tttgttttgt atttgtttgt ttgtttgta tttttttttg gttttttatt tttgttatta
 2281 gtgtgttttg tggtttattt tgtggttgtt gttagttag gggagtgttg tgggttaggg
 2341 agtagatgtt gtgggggttg ttgtagttag ttgttgattt gtgaatggga ttgggattgg
 2401 ggttgggatt gatatttag tgtttgtttt gtgttaggga ttggtggttt ggaggttgtg
 2461 tttattttta agggtttttag gtgaggtgtg ttgttagttt tttttttttg tttgggtggg
 2521 gttttttgga atggggggta ggattttttt aggaagagaa tgttttgggt ggggtgggggt
 2581 gtgaggggga tgggtgtatt tgagttgaga aggttttatt aatgtaaagt aaaagggagg

2641 gagagatttg tttaaaaatt agaaagggag aagggagtta gttgtgggtg tgggtaaagt
 2701 aggggatgga ggtttagat gtgtgttta tgattttttt tggtttgggt ttttgtggg
 2761 gtttgtgttg aggttatagt agagggggtt tgtatttgggt tgggtaaga gattgtagag
 2821 tagatttttg gatagtga ttgttttgg ttatatattt ggggaaagt gtttatggtg
 2881 tgggttttgt tagttttgtg ttgtttttt aaagtggga tatgattgtg ttttgtggg
 2941 tttttattt attttttgg attttgttg aaagttttt ggggtttagt tttttagtt
 3001 gagattgttg ggaagtgg ggaatgga aagatttag ttttgaagg agattgttg
 3061 tattttaata gtgtgggtt ggggtgttg attgtggtt tgggtagta ggtgtggtg
 3121 tgttatagt ttttagttg agtttttgg ggagtttgg tgttgttg taagtttta
 3181 ttagttagg agtaggtta tgagtgtt agatttgggt ttgttttgg tttggattg
 3241 gtgaaagtg ttagggtaa tgttaattt gagaattata ttttttgaa atttgtgtg
 3301 ttttttgag tgtgttaagt ttttttagt tttggtatgt atggttttt ttttgtgtt
 3361 ttgttttga atgtgagtg ggaggtgga agtattgaga agttggttag atggggagga

SEQ ID NO. 24

Sequenza non metilata del gene CDH11 (bottom strand), derivata da SEQ ID NO. 2

1 tttttttat ttggttagtt ttttagtgt ttttatttt tggtttgtg tttgggtag
 61 agtgtaggga gggaggtgt gtgtgttgg agttagagag gtttgggtg tttgagaag
 121 tgggttaggt tttgggaagg tgtggtttt aaagttaatg ttgatttgg tagttttgt
 181 taattttaag ttagaggtga gtttagtgg ggggtgtta tggatttatt tttgtgttg
 241 tgggagtta taaatgggtg ttagagttt ttagagatt tgggttggag ggtttagtg
 301 tatttagtt tgtgtttta gaattatagt tgggtgttt aaatttatgt tattaaagt
 361 tgggtaatt ttttttgag ttgggtttt tttgttttt tgggtttatt tggtagttt
 421 gatttaggg attaatgtt ggggagttt tggtagggat ttgggaggat ggagtaagaa

481 tttttagag tgtggttatg ttgttgtttt ggggaagtgg tgtagggttg gtgggtattg
 541 tgttgtgggt gatttttttt agagatatga ttgggatag ttggtgtgtt tggaggtttg
 601 tttttagttt ttttgtttta gttaggatata aatttttttt gttgtggttt tgggttagat
 661 tttataggag gttggagtta gggagagtgg tggagtgtat atttgaagt tttgtttttt
 721 gttttgtttg tgtttatagt tggttttttt tttttttttt gatttttaaa taaatttttt
 781 tttttttttt gttttgtgtt agtgaagttt ttttgattta gatattattg ttttttttat
 841 tattttgttt tgtaagata tttttttttt gagaaaattt tgttttttat tttagaagt
 901 ttttaattag tggaggaag ggattggtgg tgtattttat ttgggggttt tgggggtgga
 961 tgtaattttt gagtgttag ttttgggtt agggtaagt ttgtggtgtt agttttggtt
 1021 ttagttttgg ttttatttat aagttagtgg tggttgtgag tggtttttgt ggtatttgtt
 1081 ttttggtttg tgatgttttt tttagttggt ggtggttgtg gaatgagttg ttgagtgtgt
 1141 tagtggtagg aatgagaaat tggggggagg tgggggtgg gtaggtgggt gtgggtggg
 1201 ggggtggga ggaggaggt tgtgttgtg agggaggaa aggggtgggg ttgagagaag
 1261 ttgaggtgt gagaggtagt gagatgggt ttgtagaggt tgtgggggtt gattttgttt
 1321 gtgttttttt ttttaggggt ttagagatgt taatttttgg atttgtggtt gttttttttg
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SEQ ID NO. 25

Sequenza metilata del gene FLII1 (top strand), derivata da SEQ ID NO. 3

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7441 ttttaaggaaa agtgaagaaa

SEQ ID NO. 26

Sequenza metilata del gene FLII1 (bottom strand), derivata da SEQ ID NO. 3

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 3961 gtatatttta gttatattgt tttttattta gttagaaagg attttaattt tattattagg
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4141 taggtttttt tttttaattt ttgttggtt ggtaagtgat agattatttt tattatatta
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 4321 taattgtgga attttatcgt attttttgtt ttttaaagt tacggtaatt ttatggtttt
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 4681 attgttgttt ttttaaattt tgaaagggga tgggggaagc gttttaatta agtataatag
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 7261 tgtttttttt ttatttaaag cgtttttatg tgggtaatta ttttttttat ttttttgagg
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 7381 ttttagggg ttaggttggg tttttttttt atggggtttg ggcgtttggg ttgcggtgt
 7441 ttgttaataa tttttgagtt

SEQ ID NO. 27

Sequenza non metilata del gene FLI1 (top strand), derivata da SEQ ID NO. 3

1 ggtttaggag ttgttgataa atattgtagg ttaggtgtt taggtttat gagggaggag
 61 ttaggttgg ttttagggg ttaagggtgt tggttttatt ggggttatga ttgaatagt
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 241 ttggagata ttgatatgta gtagttgatg gataattgta atgatattta tagttatttt
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 781 agtgtgtaga gtatatattt gaaagtttt tgtttgttt ttgtttaata tttttagg
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 7381 tgaaggtttt ttttgattta gaagggtggg aagatggttt tagggttttg atgtggatat
 7441 ttttaaggaaa agtgaagaaa

SEQ ID NO. 28

Sequenza non metilata del gene FLI1 (bottom strand), derivata da SEQ ID NO. 3

1 tttttttatt tttttttagg gtgtttatat taagattttg aggttatttt attatttttt
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 121 ttagagggga gtattttatt attaaattta gaaatataga gatatttcta tgaatatatt
 181 aataggaagt agagaaatag gtataaaatg gtttaaatgat ttttattttt gggtttttgt
 241 aggaattttt ttttatttat tttttattta tttatttttg gtttgaggaa tttaggtttt
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 361 aagttttttt ggttgggtgt tttattttaa gttagtatat tttaaatttt tataaaaaaa
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 7381 tttttagggt ttaggttggg ttttttttt atggggtttg ggtgtttggg tttgtggtgt
 7441 ttgttaataa tttttgagtt

SEQ ID NO: 29

Sequenza metilata del gene FOSL2 (top strand), derivata da SEQ ID NO. 4

1 ggattgattc gttttgcgtt aaaggattgt atttatttag ttttgttgg agaggcgcgt
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 121 acggtcggcg cgcgcgttcg tttgtttat atttttttt tgggtttcg gagttgggga
 181 ttttgttag cgggtagtag cggaggtgcg aggagtttg ttggtttcgt ttcgtcgcgt
 241 acgcgcgcgc gtttttggg atagcgtta ggatagaatg tgttttatag ttgtaaataa
 301 tgatttcgag tattgtttgg gattatcgt ttttggggt tttggggcg ttagatgtcg
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421 gttttatttt tttttgttat taatattttt atttttaga taaggaaatt gaggatagaa
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SEQ ID NO: 30

Sequenza metilata del gene FOSL2 (bottom strand), derivata da SEQ ID NO. 4

1 gagtattatg ggaggtagag ggaagataga aaagtattt tggggattta ttaggtatag
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 3901 ttgtttatag ttataaaata tttttgttt tgaacgttat ttttaaggac gcgcgcgcgt
 3961 gcgcgacgag gcgaggttag ttagattttt cgtattttcg ttgttgttcg ttggatagag
 4021 tttttaattt cgtaggttta ggagaggggt gtggggtagg cggacgcgcg cgtcggtcgt
 4081 ggggtgtttg tttttttttt tttttttttt atttttgcgt tttggtttgt ttgggtgttt
 4141 acgcgttttt tttagtagga ttgagtaaatt gtagtttttt gacgtaaaac gaattagttt

SEQ ID NO: 31

Sequenza non metilata del gene FOXL2 (top strand), derivata da SEQ ID NO. 4

1 ggattgattt gttttgtgtt aaaggattgt atttatttag ttttgtggg agaggtgtgt
 61 aaatatttag gtaagttagg atgtagggat ggggaggggg aagaaaaag taaagtattt
 121 atgggtgggtg tgtgtgtttg tttgttttat attttttttt tgggtttgtg gagtgggga
 181 ttttgttttag tgggtagtag tggaggtgtg aggagtttg ttggttttgt tttgttgtgt
 241 atgtgtgtgt gtttttggg atagtgttta ggatagaatg tgttttatag ttgtaaataa
 301 tgattttgag tattgttttg gattattgta ttttggggtt tttgggttg ttgatgttg
 361 ttagttgttt tggaaatggt agtgttttat atagagtttt aggaaagttt tgtgttttg
 421 gttttatttt tttttgttat taatattttt atttttaga taaggaaatt gaggatagaa
 481 gttgtgtgat ggtgtatagt gagttgttag taatggattt ttaatatttt ttaattattg
 541 gtttttataa ggattttgtg gggtagat ggttgggtgt atttaagaat tgggtaaatt
 601 gaggttaata tagatttttg attaaaaatt aagttttttg atttttgtta tagtattttt

661 ttattttatat atattattat tttagtggaa ggattggagt tttagagtag agaagggttt
 721 aagggtatgt ttttaaattt tttatttta taggaggaaa ttgaggttta gagaggttaa
 781 ggaatttggt taagatttta tagtttgtaa atagtgtagt tgggtgtttt tgttttaagg
 841 tttgtgtttt gtattttgtg ttgtgttttt tttagttttg tttagtgagg gaggaggatt
 901 taaatgtttg gtaatttggt ttttgaattt tgttttaaaa tagttgaaga tgataatgtt
 961 ggggtatatt tttttgttgg tttttttttt ttttttttaa tttgtaatag tttggagttt
 1021 gtttataaat gtttgattat ttttattaga tgtgttttaa ttgtttggtg tatagggtgg
 1081 ttggaatgtt ttgattgggt aattttattt ttaaggttat ttttaatgaa ttaattgtag
 1141 gattgaaaat atgaaaaata aaaaaataaa agggaattgg taggtagatt gttatggagg
 1201 gaaaaatagg taggttagtt ttgtttggtg ttgtgttttg ttaatatattg gttgtagggt
 1261 ggtgtgggta ttttgtgtgt ttgggtgtt tgttgtattt ggtgggttg tggagggtgt
 1321 ttatgattgt gtgtagttgt gtttttttg tgagtgggtt tgtgtgttg gtttttggtt
 1381 ttttggtggt gttgtattga attgtttgtt ttgtgttag ggtgtgtatt attttttaa
 1441 atttggaggt gagatttggt tgggtgtttt tgggttttg ttttgagtt ttttttaggg
 1501 tgggggagag gttgtagtgt atttgggagt ggggtgagga atttttttt ttttatgtta
 1561 tttgaaagtg aggaaatttg tatttgtgtt ttttaatgta aatgattatt tttggtaatg
 1621 tgtgttaatg gaatagatta aggggtgttg gtttggggg tgagtggggg attggggagg
 1681 gttgggggtt ttttgggttt tttgaattgt gtgtggtgtt tgtttttgtt tgtgtatttg
 1741 tttggttttt ttgtgtgggg tgtgtggttg gtgttagtgt ggttgggagt tggggttggg
 1801 aggggagagt tgtgtttgtt tttttttttt ttgtgttttt ttttttttg tggttttttt
 1861 tttttgtttt tttgtgtgtt tttttttgta aggtggagtt tggggttgat gtgagtgaat
 1921 ttatatggta taggggttga gaataaagag tgtgagttga atttgtgtta ttgtagtgat
 1981 ttattttggg tagagtgtta gggttttgag tgaattagtg agtgagtga tgagtgggtg
 2041 ttggtgggga tagaaagagg gagagagaga gagagagaga gggagagggt tggttgggtg
 2101 aggtgggttt gtttgggagt gggttttggg gaagggtgtt gggtttgggt gttggagtgg

2161 ggagtggggt tgtgtttttt ttagtgtag ttttatttga gttttatgag ttgttgtttt
 2221 tttggtgtgt ttggggttgt gggatgggtg tatgttgttt ttttttagtt aagtatttga
 2281 gttgttttga aatttgggtg gtgagttggt tatgggaagt ttattttttg gttttttttt
 2341 taaaaggaag aaatagaagt ttttttagt ggatagtttt tttttttgtt tttttggttt
 2401 tgtttgaaat tgggggtttt tagggttggt aggttaggtt tgttgggttt ttaatttttt
 2461 ttttaatttt taatttttga ttgggttgtg ggtttttgtt gagtttttgt tgtgtgtggg
 2521 ggtgggaggg tgtgtgtagg ggagggattg agagatgtgt tgatttttta gagggaggga
 2581 ttgggtggat aatttggttt gtggtgtttg tagagttgga aagaagtgtt gtaagggatg
 2641 tttgggggat gttgtttttg aggtgttgtt gtttttttgt ttttgttttt tgtggtggg
 2701 gaaaaattta ggagtgaagt ttagagtttg tgggtgtggt ggtggatgaa tgagtgtgta
 2761 gtagttgtg tgtggttgtg gtgaggggtg gggaagaaaa atattttgtt ttttttttgt
 2821 tttttattgt ggattatgta ttaggattat tttgggaatt ttgatatttt gttttgggt
 2881 agtagtggtt tttttgtgta tgttgagttt tatttttagtg gtggtggtgg ttagtaggta
 2941 ggtgtgggtt ttggtgtatt tgggtgtgtg ggtggatttt tgtttttttt ttgttgttat
 3001 tgtttttttt gttttttttt tttttttttg gtgagaaaat atttatgggt tattgttgta
 3061 agttttggat ttttgttttt tttttttttt ttattttttt ttaaattagg ggattggaga
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 3181 tttggaattg taggtttttt attaggagtt tgttattttt ttttaagaat tatttttttt
 3241 ttttagtgtt tgtttttttt tttttatttt tgttttgtgt tttttttttg ggtggtggat
 3301 agataagaaa atttttgtat ttattggtat tttttgatat tttgggattt tattttttta
 3361 ggaaagtttt tttttttttt tttttgtttt ttattagtta taattttttt ttgaaagggg
 3421 ttggggattt agaaatatgg ttggattttt ttaagtaatt tggagtgagg gtgaggggtg
 3481 ttgttttggg aattaggtgt gaaggtagg aaggaagaag ttagtttttg ttggtttatg
 3541 ttgttttgtt gttttttgtt tgtttgtttg tttttttgtt gatttgtttt ttgtaaggat
 3601 tatggatagg aggttgtatt gttttttagg aatgaaggag tattttgagg gtttgggggt

3661 atttggagta aggagattgg tagaggggaag aggggggttg gtgggggaag agatattatg
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 3781 ttgtattgga gggattgtgt gtgtgatttt tgtgtttata aatattagga aggtgttggt
 3841 ggtggggggg tgttgatggg gtgtttgttt tttgtttag tttttttatt tgttttggtt
 3901 tgagagagag ttgggttaat gtaggtttaa tataatatga agtttattgt ggtagtatt
 3961 tgtggagttt agtatagttg gttgtagtaa gggatgttta tgttttataa ggtgggtggg
 4021 ttggttttta gaaggggtta ggggtgggtt ttagggaggg gtggatttag ttgaaagaa
 4081 ttttggaatg tgggtttttt ttggatttga tggggggggt tttgtttta aagtatttt
 4141 ttatatttgg tgagttttta aaatgggttt tttgttttt tttgttttt tatgggtttt

SEQ ID NO: 32

Sequenza non metilata del gene FOSL2 (bottom strand), derivata da SEQ ID NO. 4

1 gagtattatg ggaggtagag ggaagataga aaagtatttt tggggattta ttaggtatag
 61 ggaattattt tgggaataagg gattttttta ttagatttaa aagagagtta tgttttaaaa
 121 ttttttttag ttgagtttat ttttttttgg aagttatttt tagttttttt tagaggttaa
 181 ggttattggt ttatggagta tgagtatttt ttgtttagt taattatggt agattttata
 241 gatgttgatt atggtgggtt ttatgttgta ttgggtttgt gtttaatttag ttttttttg
 301 agatagagtg ggtgggggag ttgtagtaga gggtagatat gttattagta tttttttgtt
 361 aatagtattt ttttgggtatt tataaatata gagattatat gtataatttt tttagtgtaa
 421 attagtttgg ttgttttaga aataagttgt tttttgttt tagaattatt taggagtttg
 481 tgtgatgttt ttttttttat ttgatttttt tttttttttg ttgggttttt tgttttaggt
 541 atttttagat ttttaagggt tttttttgtt tttggggggt agttagtttt tttgtttgtg
 601 atttttatag aagatgggtt ggtggggggg taggtaggta ggtagggggg atatagggtg
 661 tatgagttaa ttaaggttgg tttttttttt tttagatttt gtatttgatt tttagagtgg
 721 tagtttttgt ttttgtttta gattatttga aggagtttaa ttatgttttt gggtttttaa

781 ttttttttag aaaggagtta tgattgatgg agaattggga ggagagagag agggtttttt
 841 tgaaggaata gggtttttagg atgttgagag gtgttagtgg gtgtaaagat ttttttgttt
 901 gtttattatt tagagagaag atgtggggtta ggggtggggg ggggggggta gatattgggg
 961 agggggagta gtttttgaa ggaggtaata ggtttttggt aggggggtta taattttagg
 1021 agttttattg ggtaaaatat aatgtgagag gaaaagggtta tgtgtttttt ttaagtttat
 1081 tttttaattt tttagtttaa aagggggtgg gggggaaggg gaggatgaaa atttagaatt
 1141 tataatggtg gttttaggtt attttttgt taagaaaag aaaagaaagt aaaagaggta
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 1261 tatttggttg ttgttgtgt tgttgagta ggatttggtg tgtgtaggag agttgttgtt
 1321 gttttgggat gaggtgttaa agtttttggg ataattttgg tatatgattt gtggtggggg
 1381 ttggagagga aatagggtgt ttttttttt ttgttttgt tgtggttgtg tattggttgt
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 1681 tttgtgtgta gttggagttt agtggggatt tatggtttta ttaaaaattg gaaattaaaa
 1741 aaaagattag gagtttagtg agtttggtt gttagtttg gggatttttg attttagata
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 1861 gaaaaggagt tggagaataa attttttggt gttgatttgt tgtttgagtt ttgggtggt
 1921 ttggatattt gattaggaga aggtggtgtg tgtttgtttt gtggttttga gtgtgttagg
 1981 gggatagtgg tttgtgggt ttaagtagag ttggtgttga gagggatgtg gttttgtttt
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 2101 tgtttgggtg tgtttttttt tttttttttt tttttttttt ttttttttg tttttgtga
 2161 gtgtgtttg tttgttgtt tgttggttg tttggagtt tagtgtttg tttgagatga
 2221 gttattataa tggataggt ttaattata ttttttatt tttagtttg tattatgtgg

2281 atttatttat gttaatttta gattttattt tgtagggagg agtgtatgag gaggtggggg
 2341 gaggaggttg tggaggagga agaggtgtgg gaggggagga ggtgggtgta gtttttttt
 2401 tttagttttg gtttttggtt gtgttgatgt taattgtgta ttttgtgta ggaagttagg
 2461 tgggtggtatg ggtgggagtg ggtgttatgt atggtttga ggtgttgagg tagttttggt
 2521 ttttttttagt tttttgttta tttttgggt ttagtgttt tggtttgtt tattggtgta
 2581 tgttgtaaa gatggttatt tgtgttagag gatgtgagt tgggttttt tgtttttggg
 2641 tgatgtggag ggagagggat tttttgttt gtttttgagt gtgttggtt ttttttttg
 2701 ttttggaag gggtttggg tgggttttg agagtgggtg tgtgggttt gtttttgat
 2761 tttagaaaat aattatagtt ttgatggtga gatgggtggt ttggtgtgtt gttattggga
 2821 ggttgggagt tgggtgtgta gagtgtttg tagggagggg gtggtgtgtt gtggtttag
 2881 gtgttttttg tgggtgtgtt gagtgtagt ggtgttttg gtgtgtaggg tgtttgtgtt
 2941 gttttgtgtt tgggtgttg tgggtatgg tgttgggtg ggttgggtt tttattttt
 3001 tttttgtgtt ggtttgttta ttggttttt tttgttttt tgttttttat gtttttggtt
 3061 ttatagttaa tttgttagga gtagtttga agatgaaatt aattagttaa gatattttg
 3121 ttgttttata tgttggtaa ttaggatgta ttaataaga gtaattgggt gttataagt
 3181 aaattttaga ttgttatgaa ttaaaaaaa aaaaaaaag ttagtgagag ggtgtgtttt
 3241 aatgttgttg tttttagtgt ttttgagtg aagtttaggg tgtgggtgtt tggatatttg
 3301 ggtttttttt tttgttggg tgggttggg aggggtgtg tgtagggtat agagtataga
 3361 ttttagagta ggaatgttg gttatgttat ttatgagttg tgagattttg gatgaatttt
 3421 ttaatttttt tgggttttag tttttttta taaagtgaag gagtttggag atatgatttt
 3481 aggttttttt ttgttttga gttttaattt tttgttgag atgatggtgt gtgtgaatgg
 3541 agaagtattg tagtggaagt tagggaattt aggttttgg ttagggtttg tgttagtttt
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 3661 ttaatgttaa gaggtgttga gagtttattg ttgataattt gttgtgtatt gttatataat
 3721 ttttgttttt agttttttta ttgttaaagt ggggtgttg gtagtagaga aaaatagagt

3781 tgggaatgtg aagttttttt ggggttttat ataaagtgtt ggtatttttg ggatggttgg
 3841 tggatatttg ttgttttaag ggttttaaga tatggtaatt ttaaataata ttgggggtta
 3901 ttgtttatag ttataaaata tattttgttt tgaatgttat ttttaaggat gtgtgtgtgt
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 4081 ggggttttg tttttttttt tttttttttt atttttgtgt ttgggttgt ttgggtgttt
 4141 atgtgttttt ttttagtaga ttgagtaaat gtagtttttt gatgtaaat gaattagttt

SEQ ID NO: 33

Sequenza metilata del gene HES2 (top strand), derivata da SEQ ID NO.5

1 tttttagttt gtctgttgtt ttttttttat ttgcggcga gaattttgaa ggaggagac
 61 gtggggttag cggtaggggt ggagttcgga agtggggttc ggggatagg gggttattt
 121 aatatttttg atagagtttt ttttggttc gttttatagg ggaatttttt ttggttggtt
 181 ttgtggattt ttttagttat tttttgttc ggtagttcgt agtgtggtc ggggcgttg
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 301 gttagtttgt cgtagtaacg gtaacggc gcgaaggcgg ttttggcgg gttattggg
 361 ttctatttta aaattgtttt gtctgcgct tataatgagt ttgattgttt tgcggcgag
 421 aattcggatt tttagtcgtt ggaatgaaa acgagtttc agggtttttag ggttgtttt
 481 gtttttttag gatttcgttt ttttatttaa agtttgagt gggtaatta aaagatttt
 541 aattaggtaa gtctogaag ggttttacgg gttttttaga gtcggcgtt tagcattgg
 601 ggtttttgtt taggttcgtt ttgttttag cgtcaggat tggagtaagt tacgatttt
 661 ttccgaatt cggatttttc gtttagttta gtttttatt cgataaagta gttgggggtg
 721 taagtttttt tegtgttgt ttttatggg agtttcgta atcgttgggt ttttgttc
 781 ggttagggc ggggttttaga gaagcgtt aattcagtt tggggaatga atgaaggta

841 gtattggaga ggagggatcg tagttttagt taggtaaggt ttggttttat ttggtttttt
 901 tgttttcggg gttacgtagc gaaggttttc gatggcgttt ttattatttt ttogtaggtg
 961 ttoggggaaa attgggggtc gttatttcgc ggtagatagg acgtaaaggc ggggagcggg
 1021 attttcgggg gcgtcgcggt ttttttttc ggttttattt tgcgtaggaa taaaggtagg
 1081 aggtgggatt agcgggcggt cggatttcgc gggcggggc gggcgggcg agtcgtttt
 1141 ttaaagtccg gtcgcggcg gggcgcgat tcytttgga ttagttcggg tcgcgttcgg
 1201 gattttattt cggatttcgg ttttttttg cgtggggttc gtagttgta togtttttc
 1261 gcggagtatg gggttgttc gtcggtagg ggacgcggcg gagtgcgta aggtgggtat
 1321 cggggattgg gggcggggtt ggggatttcg gggattcgtt taattatcg gtcgttcgtt
 1381 cgtagagttt gaagtcgttg ttggagaagc gtcggcgcg gcgtattaat tagagtttga
 1441 gttagttaa ggggtttatt ttgtcgttg tgggtcggga ggtgagcgcg ttcgggcgga
 1501 gggtagaggg ttttgggcg cggagcggg gtagggggac ggggtgtttt tgcgggagga
 1561 atttattagg gggtttcgc cggcgttcga ggcggagttt ggggtgggtg ggcgcgtcgc
 1621 agcggatttt tagtaggta cggcgcgttt tatatttagt ttcgattag agcaggggtg
 1681 cgtacgtag tcggttaaag tttgttttg gtggttttt gtcgttttt ttcgtggtcg
 1741 gcgtagaat ttaattgtt cgaagttaga gaaggtagac gttttgaaa tgatcgtgcg
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 1981 tttggttcgc gtgtgttcg tttgtcgtg ttggagttc gtcgtgagcg cgcgtttgtt
 2041 ggagtatttg tggcggagag cggttagcgt tattttggac ggcgggcgcg ttggggattt
 2101 tagtggttcg tttgttttcg ttttagcgtt cgcgtttgtt ttagagttcg tattcgttc
 2161 ggtgttttcg tcgttttcgt ttttttcgg ttttggttt tggcggcgt ggtagtttt
 2221 cggtcgattt atagattttg tcgattgtt gggattttg ggtattggat aggttgaagt

SEQ ID NO: 34

Sequenza metilata del gene HES2 (bottom strand), derivata da SEQ ID NO.5

```
1 gttttaattt gtttagtggt ttaaggtttt aagtagtcgg tagggtttgt ggatcggtcg
61 aggggttatt acggtcgta gaggttaggg tcgtagggag gcgagggcgg cgagggtatt
121 ggagcggatg cgggttttgg ggtagacgg ggcggtgggg cgggggtaga cgggttattg
181 gaatttttag cgcgttcgtt gtttaggggt gcgttggtcg ttttcgtta taggtgtttt
241 agtaggcgg cgtttacggt gggtttttag atacggtagg cgggtagtat gcgggttagg
301 cgcgttatat aggcgttgta gtttcgcgg tagttgtcgt aaggtattgt gggcggagag
361 tcgcgtgagg cgcggggtag ggtgtcgggt gcggggtgta gagcgcgg tagggtaggg
421 agggtttatt tacggggcgt tgcgtgggt tatgaggacg taggtagttt ttgtaggaa
481 cgtacggta ttttaggat gttgttttt ttagtttcg agtagttga gtttgcgtt
541 cgttacgag gaagagcgt agagaattat taagatagaa tttggtcgg ttatcgtcg
601 tattttcgtt ttagtcggga gttgggtgtg gggcgctcg tggtttgtg ggggttcgtt
661 tcgacgcgtt tattttattt aggtttcgtt tcgggcgtcg cgcggaattt tttggtgggt
721 ttttttcgta ggagtatttt gtttttttgt ttcogtttcg cgttttagga ttttttgtt
781 ttcgttcggg cgcgtttatt ttcggttta gtagcgtag gatgagtttt ttaagttggt
841 ttaggttttg gttgatcgt gcgcgtcgtt gtttttttag tagcgtttt aggttttcg
901 gacggcggt gcggtggtta gacgggtttt cggagtttt agtttcgtt ttagtttcg
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1321 tatttcggg agagtggtaa aggcgttatt ggggtttttt gttcgtgat ttcgaggga
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1381 ggagggttag gtggggttag gttttgtttg attggagtta cggttttttt tttttaatgt
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 1621 aaaggtcgtg atttgtttta gttttcgacg ttgggaatag gtcgagtttg gataagggtt
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 1981 tggcgttttt cgtttatttg tttcgggttt ttttttttcg atcggttggt ggggtaacgg
 2041 ttacgttcgt gaattatatt gcgaattggt gggtagagag atgattggag ggatttatag
 2101 agttagttag gaggagtttt tttatggggg ggggttaagg agggttttgt ttaggggttt
 2161 ggatgaattt tttgtttttt gaattttatt ttcgagtttt atttttgtcg ttagttttat
 2221 gttttttttt tttagggttt tcgtcgtagg gtggaagaag gttagcgaat atattgaggg

SEQ ID NO: 35

Sequenza non metilata del gene HES2 (top strand), derivata da SEQ ID NO.5

1 tttttagtggt gtttggtggg ttttttttat tttgtggtga gaattttgaa ggaggagat
 61 gtgggggttag tggtaggggt ggagtttgga agtgggggtt ggggatagg gggtttattt
 121 aatatttttg atagagtttt ttttggtttt gttttatagg ggaatttttt ttggttggtt
 181 ttgtggattt ttttagttat tttttgtttt ggtagtttgt agtgtgggtt gtgggtgtgg
 241 ttgttgtttt gttagttggt tgggggaggg gagtttgag tagatgggtg ggggatgta
 301 gttagtttgt tgtagtaatg gttatgtggt gtgaagggtg ttttggtggt gttattgggg

361 tttgtattta aaattgtttt gtttgtgtgt tatatgagtt ttgattgttt tgtgggtgag
 421 aatttggatt tttagtgtgt gggaatgaaa atgagttttg agggtttttag ggttgttttt
 481 gtttttttag gattttgttt ttttatttaa agtttggagt ggggtaatta aaagattttt
 541 aattaggtaa gttgttgaag ggttttatgg gttttttaga gttgggtgtt tagtgattgg
 601 ggtttttgtt taggtttgtt ttgtttttag tgttgaggat tggagtaagt tatgattttt
 661 ttttgggaatt tggatttttt gtttagttta gttttttatt tgataaagta gttgggggtg
 721 taagtttttt ttgttgttgt ttttatggg agtttttgta attgttgggt tttttgttgt
 781 ggttttaggtt ggggtttaga gaagatgttg aatttgagtt tggggaatga atgaagggtg
 841 gtattggaga ggagggttg tagttttagt taggtaaggt ttggttttat ttggtttttt
 901 tgtttttggg gttatgtagt gaaggttttt gatgggtgtt ttattatttt ttgtaggtg
 961 tttggggaaa attgggggtt gttattttgt ggtagatagg atgtaaaggt ggggagtggg
 1021 atttttggg gtgttgttgt tttttttttt ggtttttttt tgtgtaggaa taaaggtagg
 1081 aggtgggatt agtgggttgt tggattttgt ggggtgggtt ggggtgggtg agttgttttt
 1141 ttaaagtttg gttgtgggtg ggggtgtgtat ttgttttgta ttagtttggg ttgtgtttgg
 1201 gattttattt tggatttttg tttttttttt tgtgggtttt gtagttgtta ttgttttttt
 1261 gtggagtatg gggttgtttt gttgggtagg ggtgtgtgtg gagtgtgtga aggtgggtat
 1321 tggggatttg ggggtgggtt ggggattttg gggatttgtt taattattgt gttgtttgtt
 1381 tgtagagttt gaagtgttg ttggagaagt gttggttgtt gtgtattaat tagagtttga
 1441 gttagtttaa ggggtttatt ttgttgttgt tgggttggga ggtgagtgtg tttgggtgga
 1501 gggtagaggg ttttgggggt tggagtggg gtaggggat ggggtgtttt tgtgggagga
 1561 atttattagg gggttttgtg tgggttttga ggtggagttt ggggtgggtg ggtgtgttg
 1621 agtggatttt tagtaggtta tgggtgtttt tatatttagt ttttgattag agtgagggtg
 1681 tgtatggtag ttggttaaag ttttgttttg gtggtttttt gttgtttttt tttgtggtg
 1741 ggtgtagaat ttttaattgt tgaagttaga gaaggtagat gttttggaaa tgattgtgtg
 1801 tttttttag gagttgttg tgtttttatg gtttatggta gtgttttgtg agtgagtttt

1861 ttttgttttg ttgtgtgttt tgtattttgt atttgggtatt ttattttgtg ttttatgtgg
 1921 ttttttgttt gtagtgtttt gtgatagtta ttgtgagggg tatagtgttt gtgtgggtg
 1981 tttggtttgt gtgttgtttg tttgttgtgt tttggagttt gttgtgagtg tgtgtttgtt
 2041 ggagtatttg tggaggagag tggtagtgt tattttggat ggtgggtgtg ttggggattt
 2101 tagtggtttg tttgtttttg ttttagtgtt tgtgtttgtt ttagagtttg tatttgtttt
 2161 ggtgtttttg ttgtttttgt tttttgtgg ttttggtttt tgggtggtgt ggtagttttt
 2221 tggttgattt atagattttg ttgattgttt gggatttttg ggtattggat aggttgaagt

SEQ ID NO: 36

Sequenza non metilata del gene HES2 (bottom strand), derivata da SEQ ID NO.5

1 gttttaattt gtttagtgtt ttaaggtttt aagtagttgg tagggtttgt ggattggttg
 61 aggggttatt atggttgta gaggttaggg ttgtaggag gtgaggggtg tgagggtatt
 121 ggagtggatg tgggttttgg ggtagatgtg ggtgttgggg tgggggtaga tgggttattg
 181 gaatttttag tgtgtttgtt gtttagggg gtgttggttg tttttgtta taggtgtttt
 241 agtaggtgtg tgtttatggt gggttttagg atatggtagg tgggtagtat gtgggttagg
 301 tgtgttatat aggtgttgta gttttgttg tagttgtgt aaggtattgt ggtggagag
 361 ttgtgtgagg tgtgggtag ggtgttgggt gtgggtgta gagtgtgtg tagggtaggg
 421 agggtttatt tatggggtgt tgtgtgggt tatgaggatg taggtagttt ttgtaggaag
 481 tgtatggtta ttttaggat gtttgttttt tttagttttg agtagttga gttttgtgtt
 541 tggttatgag gaagagtgat agagaattat taagatagaa ttttggtttg ttattgtgtg
 601 tatttttgtt ttagttggga gttgggtgtg ggtgtgttg tgggttgtg ggggtttgtt
 661 ttgatgtgtt tattttattt aggttttgtt ttgggtgttg tgtggaattt tttggtgggt
 721 ttttttgta ggagtatttt gttttttgt tttgttttg tgttttagga tttttgttt
 781 tttgtttggg tgtgtttatt ttttggttta gtagtgtag gatgagtttt ttaagttggt

841 ttagggttttg gttgatgtgt gtgtgttggg gtttttttag tagtggtttt aggttttgtg
 901 gatgggtggg gtgggtggta gatgggtttt tggagttttt agttttgttt ttagtttttg
 961 gtattttatt tgtgtagtgt tgttgtgttt tttgtttggg gaggtagtgt tatgttttgt
 1021 ggggaagtgg tggtagttgt gagttttatg taaagggaaa ttgaggtttg aaatgaggtt
 1081 ttgggtgtgg tttgggttgg tgttagatga gtgtgtgttt tgtttgtggg tgagttttaa
 1141 gggagtggtt tgtttgtttt gttttgtttt gtggagtttg gttgtttgtt ggttttattt
 1201 tttgtttttg tttttgtgta ggggtggagt gggaggggag attgtgatgt ttttggggat
 1261 tttgtttttt gtttttgtgt tttgtttatt gtgggttggg ggtttttagt tttttttgag
 1321 tatttgtggg agagtggtaa aggtgttatt ggggtttttt gttgtgtgat ttgagggta
 1381 ggagggtagt gtgggttagt gttttgtttg attggagtta tggttttttt tttttaatgt
 1441 tgttttttat ttatttttta ggtttgggtt tagtgttttt tttgagtttt gttttgggtt
 1501 gtagtagggg atttagtggt tatgggagt tttatgaggg atagtagtgg gagggatttg
 1561 tatttttagt tgttttattg ggtgaagggt tgagttggat gggaaatttg agttttggag
 1621 aaaggttgg atttgtttta gtttttgatg ttgggaatag gttgagtttg gataagggtt
 1681 ttagttgttg gatgtttggg ttttaaggagt ttgtagaatt ttttgggtgg ttgtttagtt
 1741 aagagttttt tgggtatttt attttagggt ttgggtgggg aaatggaatt ttagagaagt
 1801 agaggtagt ttggagtttt tggagtttgt ttttattttt attggttagg ggtttgggtt
 1861 tttgtttgta agatagttag ggtttatgtg atgtgtgggt aggatagttt tgggtgtggg
 1921 ttttagtggt ttgttttaga ttgtttttgt gttgtgtggg tgttgttggg gtaaattggg
 1981 tgggtttttt tgtttatttg ttttgggttt tttttttttg attggttggg ggggtaatgg
 2041 ttatgtttgt gaattatatt gtgaattgtt gggtagagag atgattggag ggatttatag
 2101 agttagttag gaggagtttt tttatggggg ggggttaagg agggttttgt ttaggggtgt
 2161 ggatgaattt tttgtttttt gaattttatt tttgagtttt atttttgttg ttagttttat
 2221 gttttttttt tttagggttt ttgtttagg gtggaagaag gttagtgaat atattgaggg

SEQ ID NO: 37

Sequenza metilata del gene HTR6 (top strand), derivata da SEQ ID NO.6

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1  tatttagtgg atgcgtttta aaagatgtat tgaagtattt gttaaataaa tgaatgaata
61  atagtattaa ttgtatagt agtgtaggt agagattttt ttagttaga ggggagacgt
121 atagaggag gttatattta ggggaaatta tattttacgt tttgtttgt agcgattttt
181 aatatatttg gtttgggat ttttaaattt gtttacgttt tgtagatta ggagcgtaa
241 tagtttaggg attttatttt tagtatttgg ttttttggg gatcgggatg gttttgcgg
301 gaaaggtttt ggggaagggt agttttttgt ttaaattaac ggtgaagaat gtttagaatt
361 attaatattt tttatagata tgtaattga ggttagagg ggtgtaggc gatttgttta
421 atatttttta atttttggtt tttttgaaag ttcggtgatt tcgttgtgag tggtaggta
481 tttattagag agtagttttt ggataagggt aggttatagt ttttgtttt tagtttcgtt
541 tgcgtcgtcg ttaagtgtgg gttgggagg gtatttgagg gtgtgggggt tgttatagt
601 cgggaggtga tttttcgtag ttggggcggt ttgattttcg gtttataggt tcggggtgtc
661 gggatttcgt tttttttagt ggttaggggt cgtttttttt cgtttatcgc gaggcggggc
721 gtacgtttcg cggcgcgggg atcgcgcgtt ttagggtgta ttcggttttt ttttcgcgcg
781 tcggggtttt tcgcgcggtt tttcgggttc gggagattcg gtttcgtcgt tcgttcggtt
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901 agttagagcg ttttaggtat tagtgccggc gggagacgga ggcgattttg ttgtcgggtg
961 gggagggggc gtcgcgcggt cgttggtttt tttttttcgc ggggtttggc ggtttcggcg
1021 aattttcgcg tcgtataggt cgtgtcgcgc ggatttcggt gttttcgcgt tagttgagat
1081 ttgttttttt taggggcggt ttgtttcgg tttttaggtt tcgttttgg tattttatac
1141 gtttatcggc cgcggggagt ttgtttcggc tcgagagcgt ttatttattt tttttattta
1201 ttttttcgcg tttttatttt ttcgtatttt gattcggtcg gacgtttttt ttttattttg
1261 tcgttcgttt tttttagggg gttttgtttt tattttaggg agtttattcg atttttgttt
1321 gatttttcgt cgtttttttt aggggtttcg gtttatcggg tgtttttttt taaattttta
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1381 attcgtttgt tttaggagt tttgttttat ttccgagggc gtttaaataag ttatatgtg
1441 tttttttgta gtcgttggtt tttgatttag ccgatttag cgttttcgtt tatgttttt
1501 tatttttttt ttccgggggg cgtggtgagt ccggtttgt tttacggac ggttttcgtt
1561 tagtttgctt ttccgggggg tttttatttg ttttttcgtt attttattat tttttgtcg
1621 tttattttcg gtttttatgg ttttagagtc gggtttaatc gttaatagta ttccggttg
1681 gggggtaggg tcgtcgctcg ttccgggggg tagcgttggt gtggcggtcg cgttggtcgt
1741 ggttatccg ttgacggcgg ccgttaattc gttgttgatc ccgtttattt gtatttagtt
1801 ccgttgctt aatacgttta attttttttt ggtgtcgtt tttaohttg atttgatggt
1861 ggggttggtg gtgatgtcgt ccgttatgtt gaacgcgttg tacgggcgtt ggggttggtc
1921 ggcgggtttt tgtttgtttt ggatcgtttt ccacgtgatg tgttgtagcg tttttatttt
1981 taatttttgt tttattagtt tggatcgtta tttgtttatt ttttcgtcgt tgcgttataa
2041 gttcgctatg acgttttttc gttttttggt tttagtttg gccgtttgga gtttcgtcgt
2101 tttcgttttt tttttgtttt tgttggtggg ttggtacgag ttgggttacg tacggttatt
2161 cgtttttggt tagtgctgtt tgttggttag tttgtttttt gtttttgtgg cgtccgggtt
2221 tatttttttt ttgttttcgg gtgttatatg tttatttat tgtaggattt tgttagttgt
2281 tcgtaagtag gtcgtgtagg tggttttttt tattatccgt atggttagtt aggtttcgga
2341 gacgttgtag gtatttgggg tgcgtaggga gattccgggt gtgggataga gaggaatgag
2401 tagtttttgg ggattttttg ggtattttta tttagtatat atttgtttat ggttttcgtt
2461 ggttggttg agcgtttatt tttttttga attttagagt taatgttga tttatttat
2521 ataggatagt ttccgttagga tttgggggta ggtttttttt aggtattatg tataataggg
2581 aatttatggt ggtttaattt tttttatttt tgttttttgg gtttttttta ttatggtaaa
2641 tggattatt ccggtattat atgttaggaa tttagggaata tttttttttt ttatttttat
2701 gttatttat agcagattt gttggcgttg ttttaaatag gtgtattttt tttgttatt
2761 tttatccgg gaggttggt agattttttt tgggtttttt gttttgtcg tagatttagt

SEQ ID NO: 38

Sequenza metilata del gene HTR6(bottom strand), derivata da SEQ ID NO.6

```
1 attgggtttg cggtagaagt aggggagtta ggagaagttt atatagtttt ttoggttagga
61 agtggttaggg gagatggtat ttgttttagag tagcgttaat aggtttcgtt aatgaatggt
121 atgaggggtga gggagaaaag tatttttaag tttttggtat gtagtgctgt aatgggtgta
181 tttgttatga tggggaagat tagggaggtg aagatgggga gagttgggtt attataaatt
241 ttttgttgta tatggtattt gggagaagtt tgtttttaaa ttttgacgga gttattttgt
301 ggtgggtggg ttaggtattg gttttggagt ttagaagaaa ggtgggcgtt tataatagtt
361 acgtagggtt atgagtaaatt gtgtgttaag tgggatggt taggggggtt ttaggggttg
421 tttatttttt tttattttat agttcgggtt tttttgcgta ttttaggtat ttgtagcgtt
481 ttogaggttt gattggttat gtcggtggtg agggaggtta tttgtacggt ttgtttgogg
541 gtagttagta ggattttgta gtaggtgaag tataatggtat tggagggtag gaagaagggt
601 aggttcgaag ttataaggat aaaaggtagg ttggttagta ggcggtattg gttagggacg
661 ggtggtcgtg cgtggttttag ttctgttttag ttttagtagta ggggtaggaa ggaggcgaga
721 gcggcgaggt tttaggcgtt taggattagg gttagggtac gtaggggcgt tatgcgtagt
781 ttgtagcgta gcggcgagag gatgagtagg tagcgtttta ggttgatgag gtagagggtg
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901 gttagtattt agcgttcgta tagcgcgttt agtatggtcg gcggtattat tattagtatt
961 attattaggt tagacgtgaa gagcgatatt aggaagaagt tggacgtgtt gcgtagcgcg
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1261 gacggggatc gttcgtgaga atagatcgcg atttattacg ttttcgggg gaggtgagtg
1321 gggggatatg ggcggggcgc ttgggtcgcg ttaggttagg gggtagcgat tataggagga
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1381 tatagtgtgg ttatttgggc gttttcgggg atggggtagg aatttttga gtaaacgggt
 1441 tggaggtttg gggaggggta ttogatgagt cgagggtttt gaaggaagcg gcgggaagtt
 1501 aagtagaggt cggatgggtt ttttgggtg ggagtagagt tttttggagg ggcggggcgg
 1561 taagataggg gaggggcgtt cggtcgggtt agagtgcggg gaagtgggaa cgcggggagg
 1621 tgggtgaggg gggggaatgg gcgttttcgg gtcggagtag gtttttcgog gtcgggtggc
 1681 gtgtggggta ttagggcggg ggtttagggg tcggagtaaa gtcgtttttg ggaaaggtag
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 1981 ggtcgggcgg gcggcgggat cgggtttttc gatttcggga ggcgtcgcga ggggttcgta
 2041 cgcgcggagg agaggtcggg tctagtttgg agcgcgggt tttcgcgtcg cggagcgtgc
 2101 gtttcgtttc gcgggtggcg gggagagtcg agttttggtt ttgtaggagg gcggggtttc
 2161 ggtatttcgg gtttgtgggt cgaagattag agcgttttag ttgcgagggg ttatttttcg
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 2401 tggataaatc gtttgatatt tttttgggtt ttagttgtta tatttgtaa atgggttagt
 2461 aattttgggt attttttatc gttagtttga gtaagaagtt aatttttttt agggtttttt
 2521 tcgtagaaat tatttcgatt tttaaagggg ttaggtatta aggatgaagt ttttgagttg
 2581 ttggcgtttt tagtttaata gagcgtgaat agatttgaga atttttaggt taggtgtgtt
 2641 aagagtcgtt gtaggtagag gcgtgggggt tggttttttt tgggtgtgat tttttttgt
 2701 acgttttttt tttggttgag aagagttttt gtttaatttt gttgtgtagg ttaatatgt
 2761 tatttattta tttattgaat agatatttta atgtattttt taaggcgtat ttattagatg

SEQ ID NO: 39

Sequenza non metilata del gene HTR6 (top strand), derivata da SEQ ID NO.6

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1  tatttagtgg atgtgtttta aaagatgtat tgaagtattt gtttaatgaa tgaatgaata
61  atagtattaa ttgtatagt agtgtaggt agagattttt ttagttaga ggggagatgt
121 atagaggagg gttatattta ggggaaatta tattttatgt tttgtttgt agtgattttt
181 aatatatttg gtttgggat ttttaaattt gtttatgttt tgtagatta ggagtgttaa
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301 gaaaggtttt ggggaagggt agttttttgt ttaaattaat ggtgaagaat gtttagaatt
361 attaatatat ttatagata tgtaattga ggttagagg ggtgtaggt gatttgttta
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661 gggattttgt tttttttag ggttaggggt tggttttttt tgtttattgt gaggtgggtt
721 gtatgttttg tgggtgagg attgtgtgtt ttaggttgta tttggtttt tttttgtgtg
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1261 ttgtttgttt tttttagggg gttttgtttt tatttttagg agtttatttg atttttgttt
1321 gattttttgt tgtttttttt aggggttttg gtttattggg tgtttttttt taaattttta
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1381 atttgtttgt tttaggagt tttgttttat ttttgagggt gtttaaatag ttatattgtg
1441 tttttttgta gttgttgttt tttgatttag tgtgatttag tgtttttgtt tatgtttttt
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1561 tagtttgtgt tttgttgggg tttttatttg tttttttgtt attttattat ttttttgttg
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1981 taatttttgt tttattagt tggattgtta tttgtttatt tttttgtgt tgtgtataa
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2101 ttttgtttt tttttgtttt tgttgttgg ttggtatgag ttgggttatg tatggttatt
2161 tgtttttgg tagtgttgt tgttggttag tttgtttttt gtttttgttg tgttgggtt
2221 tatttttttt ttgttttttg gtgttatatg tttatttat ttaggattt tgttagttgt
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2341 gatgtttag gtatttggg tgtgtaggga gatttgggtt gtgggataga gaggaatgag
2401 tagtttttgg ggattttttg ggtattttta tttagtatat atttgtttat ggttttgtgt
2461 ggttgttgt agtgtttatt tttttttga attttagagt taatgttga tttatttat
2521 ataggatagt tttgttagga tttgggggta ggtttttttt aggtattatg tataataggg
2581 aatttatggt ggtttaattt tttttattt tgttttttg gttttttta ttatggtaaa
2641 tggattatt gtggtattat atgttaggaa tttaggata ttttttttt ttatttttat
2701 gttatttatt agtgagattt gttggtgtt ttttaaatag gtgttattt ttttgttatt
2761 ttttattggg gaggttgtgt agattttttt tggttttttt gtttttgttg tagatttagt

SEQ ID NO: 40

Sequenza non metilata del gene HTR6 (bottom strand), derivata da SEQ ID NO.6

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1 attgggtttg tggtagaagt aggggagtta ggagaagttt atatagtttt tttgtagga
61 agtggtaggg gagatggtat ttgttttagag tagtgtaaat aggttttggt aatgaatggt
121 atgaggggtga gggagaaaag tttttttaag ttttggtat gtgatgttgt aatggtgtta
181 tttgttatga tggggaagat tagggaggtta aagatgggga gagttgggtt attataaatt
241 tttgttgta tatggtattt gggagaagtt tgtttttaaa tttgatgga gttattttgt
301 ggtgggtggg ttaggtattg gttttggagt ttagaagaaa ggtgggtgtt tataatagtt
361 atgtagggtt atgagtaaatt gtgtgttaag tgggatgtt tagggggtt ttagggttg
421 tttattttt tttattttat agtttgggtt ttttgtgta ttttaggtat ttgtagtgtt
481 tttgaggtt gatttggtat gttggtgtg agggaggtta tttgatggt ttgtttgtg
541 gtagttagta ggattttgta gtagggtgaag tatatggtat ttgagggtag gaagaagggt
601 aggtttgatg ttataaggat aaaaggtagg ttggttagta ggtggtattg gttagggtg
661 ggtggttgtg tgtggtttag tttgtgttag ttttagtagta ggggtaggaa ggaggtgaga
721 gtggtgaggt tttaggtgtt taggattagg gttagggtat gtagggtgt tatgttagt
781 ttgtagtgt gtggtgagag gatgagtagg tagtggtta ggtgatgag gttaggttg
841 aggatggagg tgtttagta tattatgtt aaggtggtt agagtaggt gaggttgtgt
901 gttagtattt agtgtttgta tagtgtgtt agtatggtt gtggtattat tattagtatt
961 attattaggt tagatgtgaa gagtgatatt aggaagaagt tggatgtgtt gtgtagtgt
1021 ggttgagtgt agatgagtgt gatttagtgt gagttggtt ttgttgttag tgtgatgatt
1081 atgtatagt tggttgttat ttagttgtt tttttggg ttgatggtg tttgtttt
1141 taggttggg tgttattgt ggttgggtt ggttttggga ttataggat tgagggtgga
1201 tggtaaggga gtgatagggt ggtgggaaag tagatgaggg ttttggtaa gtgtaggtt
1261 gatggggatt gtttgtgaga atagattgtg atttattatg tttttggg gaggtgagt
1321 ggggatatg ggtgggggtg ttgggttgtg ttaggttagg ggttagtgat tataggagga
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1381 tatagtgtgg ttatttgggt gttttgggg atgggtagg aatttttga gtaaattggg
 1441 tggaaagtgg gggaggggta ttgatgagt tgaggttttt gaaggaagtg gtgggaagtt
 1501 aagtagaggt tggatgggtt ttttgggtg ggagtagagt ttttggagg ggggtgggtg
 1561 taagataggg gaggggtgtt tggttgggtt agagtgtggg gaagtgggaa tgtggggagg
 1621 tgggtgaggg gggggaatgg gtgtttttg gttggagtag gttttttgt gttgggtggg
 1681 gtgtgggta ttaggggtgg ggtttagggt ttggagtaa gttgttttg ggaaaggtag
 1741 gttttagtgg gtgtggaggt attgggattt ggtgtatatg gtttgtgtgg tgtgggggtt
 1801 tgttgggggt gttaggtttt gtgggaagag gagggtagtg gttgtgtggt gtttttttt
 1861 tatttgtag taggggtgtt tttgtttttt gttgtattg gtatttgggg tgttttgggt
 1921 gttttgttgt ttgtgattgt ggtaatgtt gtgggggtgt gagaggaaga ggtggttgtg
 1981 ggttgggtgg gtggtgggat tgggtttttt gaggttggga ggtgttgtga ggggtttgta
 2041 tgtgtggagg agaggttggg ttagtttgg agtgtgtggt ttttgtgtg tggagtgtgt
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 2161 ggtattttgg gtttgtgggt tgaagattag agtgttttag ttgtagggg ttattttttg
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 2401 tggataaatt gtttgatatt ttttgggtt ttagttgtta tatttgtaa atgggttagt
 2461 aattttgggt attttttatt gttagtttga gtaagaagtt aattttttt agggttttt
 2521 ttgtagaaat tattttgatt tttaaagggg ttaggtatta aggatgaagt tttgagttg
 2581 ttggtgtttt tagtttaata gagtgtgaat agatttgaga atttttaggt taggtgtgtt
 2641 aagagttgtt gtaggtagag gtgtgggtg tggttttttt tgggtgtgat tttttttgt
 2701 atgtttttt tttggttag aagagttttt gtttaatat gttgtgtagg ttaatatgt
 2761 tatttattta ttattgaat agatatttta atgtattttt taagggtgat ttattagatg

SEQ ID NO: 41

Sequenza metilata del gene LHX3 (top strand), derivata da SEQ ID NO.7

```
1  ttcggtagga aatatagga aacgggtttt tattattatt tggagttggg gtattttatt
61  gggttttttt tatgttaagt gttatgggta ttttttttag ggatttttcg taaatgtggt
121 tgttttgttt ggtggttttg tttgtagggt ttcggggtaa atattaatgt tttttttatt
181 attgggtagt cgtaaaatta tttatgagtg gattggataa gtcgatttat tgtttttgtg
241 ttaggcgtgg gtgtttttta tatcgttaga gttattttaa cgtttgggtt ttcgttggtt
301 ttgtttttta tattttattt cggatttgta ggttttttgg aggaattata ttggggaggt
361 ttaaggggtg tttgtgggag tttcagttt gtgagcgggt tttttagggt ttaaggggtg
421 aggatttttt ttttatttag aaaaagtttt tggagagag gagtgttcgt tgaagggatt
481 gggattttatt gatatttgt attcgttttt ttggttggtg atttcgtcgg ttttagttta
541 ttttttagtg ggtgagagat attaggaagg ggttttttcg attttcggcg gaaaaaattg
601 ggttcggttt ttttacgtag tggcgggaaa tcgcgatga atgcgtttcg tattcggtaa
661 aatcgtagtt tcgggtgcgg agcgtcgagg attcgttcg cgttcggggt ttttatcgtg
721 ggtagcgatt gtaggcgagg attcgttcg gagcggggcg gttcgatagg tcgatatagt
781 gcgatttag tatcgcggat cggatagcgt ttcggtcgta gttcgtcgtt ggcgttcgcg
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901 atgcgattt tagttttggt ggggtttttt gtgttaggga tggcgggggt ggcggagttt
961 ggacgttagt tcgttcgttt cggtagttt tttcagagct gggcgcgtag tttttttttt
1021 tttttttttt ttttcgtttt ttagttttcg cggttaattt tttttaggaa tcgtcgaaaa
1081 ataaataaat aagtagggaa tcgcgagttt ttatagtttg gatgtaattt ttttttcgtt
1141 ggtcgtttt ttttattttt tattggtttt ggggtttttt tttttattt gcggttttag
1201 ttggttcggg agtcgaggag aattgttttag gttttttaag aattaaagt ttgggagtta
1261 gagtgggttt attaggaagt tggggggttt ggagaagaga ggtttttttt tatagacggg
1321 ttttgagcgg ggataaatcg agcgggtggt tgtgggcgta gacgttgaaa tttgatttcg
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1381 gggagatcga cggcggaggt ttagttcgat ttgggttttt gtatttgatt ttgtttcgtt
 1441 ggaacgtgga aagagttcgg ttggggcggg ttttttggg atttttttgt ttcgtgggta
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 1561 gggtttttta gtttattttg gattttcgag agttttttgg tcggagtagt gtaggttat
 1621 aattttattt attttttgat aatttaggtt aggggttttg taataaatat aggttaggtt
 1681 gtttagcgtt ggaacgttcg gggttttcgt gtttattttt gtttagattt tttagttttt
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 2581 gagagagaat aggttttgtt ttttgatat gtagttaaga tttcgggtcg tgagggtcgt
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 2821 gttagtatta gttttgggta gttattcggg gaagaatata gtagtgggtg gttttcggta

2881 gtataggatt tggtaaaggt aggggtgttt tggtagtgcg tagaaatata taggaaggg
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4381 tttagtttag ggtttattgg ggtatttttt tgtagggtgt ttgttggtta gggaattttt
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 4921 tgtgtagttg atatgtattt tagttgtttt ttaatttggt taaaattaag ggttttggtt
 4981 tgtgagtttt gtttagatta gtttaggga gatgatttat tattgttttt tattttttat

SEQ ID NO: 42

Sequenza metilata del gene LHX3 (bottom strand), derivata da SEQ ID NO.7

1 gtagaagatg gaaagtagtg atagattatt tttttggagt tgatttggac gagatttata
 61 ggataagatt tttagtttta tataggtaa agggtagttg agatgtatgt tagttatata
 121 ttttaaagag tacgcgcggt agtttagttt gagggtatat tagaggattt ttagtttgtt
 181 tgagtgggta tttttttgtt ttttgggtgt gagtgttttg ttaaggttgt ttgtggtgtt
 241 ttgtggggtg tttttgattt cgtgttggtt ttgtttttt ttttattttt gttgtgttag
 301 tgggggtagg gtagtgggta atagttttgt ttgtggttgt ggaggaagtc ggttggattt
 361 tttttgggta ggttggttag aggttggttag taatttagtt attcgttagg tatcgagtag
 421 atattagttt ggggtgtgtat tgggcgattt ttttaggttt tgtttatgtt taaggttttg
 481 agtttttagt agtgtttttg ttatagggga ttgtagggtt tttttttttt ggtagttcgg
 541 aggggtgcgg gttgagtttt ttttagaagt tgggggttga gtttaaggag gtttaagagt
 601 gaaagttttt tgattagtaa aatatttgta ggagagtgtt ttagtgagtt ttgggttggg

661 gttgattacg tatggggttg ttccggggta cggtttgsgt attgtttttt agagggttga
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 781 aattcggcga attttagcgt tttagtaggg tttggagttt agggaggagc gggtagcgtt
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2161 tgtcaggggt tatttattgt tgtgtttttt ttcgggtggt tgtttagggt tgggtgtggt
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3661 cgaagttagg ttttagcgtt tgcgtttata gatattcgtt cggtttattt tcgtttaggg
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 4021 ggaaggagga ttgcgcgttc gcgttcggga gagttggtcg gagcgggagg gttggcgttt
 4081 aggtttcgtc gatttcgtta ttttgatat aggagtttcc gttagggttg gagtcgttat
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 4201 ccggggcgtc ggcggcgagt tgcggtcgag gcgttggtcg gttccgggtg ttgaattcgc
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 4561 ggttttttta gcgggtattt ttttttttta gagatttttt ttaagtgaag agggagtttt
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 4681 atttttttag tgtggttttt ttagggggtt tgtagtatcg aagtggggtg tggggggtag
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 4861 gatggggaag gtattgatat ttatttcgga ggtttgtaga tagggttatt aggtagggtta
 4921 gttatatttg ccaggagttt ttagaaagag tggttatgac gtttaatatg aaggagattc
 4981 gatgggggtg tttagtttta ggtgatggtg aagattcgtt ttttatgtt tttgtcggg

SEQ ID NO: 43

Sequenza non metilata del gene LHX3 (top strand), derivata da SEQ ID NO.7

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1 tttggttagga aatataggga aatgggtttt tattattatt tggagtggg gtattttatt
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SEQ ID NO: 44

Sequenza non metilata del gene LHX3 (bottom strand), derivata da SEQ ID NO.7

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SEQ ID NO: 45

Sequenza metilata del gene LOC51149 (top strand), derivata da SEQ ID NO.8

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 2641 aaaaattgag agataatatg ttaatagata atggttagat aacgaatgat aataaattga

SEQ ID NO: 46

Sequenza metilata del gene LOC51149 (bottom strand), derivata da SEQ ID NO.8

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721 ttgtatttta gtttgggcga ttgagcgaga ttgtttttta aaataaaaaa taaaaaaaaa
781 atatttcgtt tttttggtga tagttattgt gtaaaagttg gaaaaaaat taaaattata
841 attttagata tcgaggggtt tacggtggga ggtaatttta atattttttg tattttattt
901 tttacgagg ttataatttt aagttatata ggggtgcggc gtgagcgtcg ggttcgggg
961 gcgtttttat ttttcgtagg gtgggttttg gacgttttcg ggggtgtagg gggatcgggt
1021 tcgcgttcgg cggtcgcgcg ttttcgtcgt ttttttcggg aagcgtgggt gtggtgagtt
1081 ttttcgtttt ttcgtatttt atttcgggtt tcggtttaaa ggtaattgt tcgttggtat
1141 ttaaaagtac ggtagcgtag gtttggtagg gcggtttttt agtttcgttt cgcgttggtt
1201 ttaaggattg gttagcggag gttttgtcgt ttttaatttta gtttttttag ggtcgggaatt
1261 agtgtttttag gaagatgcgg gtacggtttt ggttagacga cgagtcgggt attaggaatt
1321 tcgtatttag gatttttttc gaggtcggag gggcgtagat gattagcgag aggcgcggt
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1381 ggtagagagg attttagtgc gtagggggcg ggtcgggcg gtcggagcga agagtataag
 1441 cgtatgcgag acggcgtagg ggattagagg gttcggagcg cgtgcgtggg gcggggtcgc
 1501 ggcgggataa atgtagagcg tacgcgtttg gttgtttggc gattgtataa gtagggatgg
 1561 cgtcgtttta gcgttttcgg gtgttacgtt gttgtagttg tcgttttttt taggcgtatt
 1621 aggtttggcg ggtgttagtt tttttttttt ttttcggcgc ggggatagcg gacggggagt
 1681 ggcggggctg tgggtgttgt ttccaatggt ttcgggatgt atcgggttcg aaggagtgt
 1741 gggatcgttg agggcgggtt ttattggggt cgttttcgta taacgttttg agttttttgt
 1801 ttggtttttg tataaattag aggtaatggt tttcggagg tgggtttttg tgaattgtag
 1861 taggtagtgg gagaattcgg ttgagtatag tattttttac gtagagtta ttttacgaag
 1921 tagcgttgtc gtagtttttag tgagaggggg aggacgggtt ttagagatcg agcgcgtcgc
 1981 ggcggcggtt ttgttttata tttggcggtt ttttcgtcgc tttcgcgtt ttgtcgtcgt
 2041 tcgttttcgc ggggttaggg atttgatatg gttgttcgtc gacgtataaa ttaogggtt
 2101 cggagtttta aagatagata atttgtgtt ttaggatata tttgtttttt taatttttag
 2161 cgtgttagat agagaatggt atttaatttt ttcggatcg tatttggttt ttgtttgat
 2221 attatttaat attgtagtta tcgtatttgt tttgatagt tttttttttt taattattgg
 2281 taatttgta tgttttgaga aagaatagta ttagattttt tttttttttt tttttttttt
 2341 tgagacggag tttcgttttt gttgtttagg ttggagtgt atggcgcgat ttcggtttat
 2401 cgtaattttc gtttttttagg ttttaagtaat ttttttgtt tagtttttcg agtagttgga
 2461 ttataggat gcgttattat gtttagtta tttgtgttt ttaatagaga tagggttttt
 2521 ttatgttgg taggtcgggt tcgaattttt gattttaggt gattcgtttg tttcggtttt
 2581 ttaaagtgtt gggattatag gcgagagtta ttgtgttcgg cgtggattag atttgtttaa
 2641 gaggtatgtt aaaaagttag taagatgttg agtatgtgt tgtaagtttg tatttaattg

SBQ ID NO: 47

Sequenza non metilata del gene LOC51149 (top strand), derivata da SBQ ID NO.8

```
1 gtattaaatg taagtttata gatatatatt tagtattttg ttgatttttt aatatatttt
61 ttaaaataagt ttgatttatg ttgggtataa tggtttttgt ttgtaatttt agtattttgg
121 gaggttgagg taggtgggtt atttgagggt aggagtttga gattgggttg attaatatgg
181 agaaattttg tttttattaa aaatataaaa ttagttgggt atggtggtgt atgtttgtaa
241 tttagttatt tgggaggttg aggtaggaga attgtttgaa tttgggaggt ggaggttgtg
301 gtgagttgag attgtgttat tgtattttag tttgggtaat aagagtgaat ttttgtttta
361 aaaaaaaaaa aaaaagaaga agaagtttga tgttattttt ttttagggta tagtagatta
421 ttaataatta ggaggagggt attattagaa gtagatatgg tgattgtagt gtaagtgtat
481 attaatgagg gagatagggt tgatttggaa aagggttaagt ggtatttttt atttggtagt
541 ttgaaagtta gggagggttaa tatgttttag aaatatagat tatttgtttt taagattttg
601 gggtttgtgg tttatgtgtt ggtgaatagt tatattaagt ttttggtttt gtggaaatgg
661 atggtggtag aggtgtgggg tgatggagag ggtgtttagg tgtggagtag ggatgttgtt
721 gtggtgtgtt tggtttttaa gaattgtttt ttttttttta ttgaaattgt gatagtgtta
781 ttttgtgggg taggttttgt gtaaaggatg ttatatttaa ttggattttt ttattatttg
841 ttataattta taagagggtta tttttgtaga attattattt ttggtttgta taagaattaa
901 ataaaaagtt tagaatgtta tgtgggggtg attttaatga gatttgtttt tagtggtttt
961 tgtatttttt tgggttttgt gtattttgga gttatttgag ataattttta tagttttgtt
1021 attttttgtt tgttgttttt gtgttggagg aggaggaggg ggttgggtatt tgtagattt
1081 ggtgtgtttg gaagaggtgg tagttgtagt agtgtagtat ttgagaatgt tgaagtgatg
1141 ttatttttgt ttgtgtagtt gttaggtagt taagtgtgtg tgttttgat ttgttttgtt
1201 gtggttttgt tttatgtatg tgttttgaat ttttagttt tttatgttgt ttgtatgtg
1261 tttatatttt ttgttttgtt tgttgggtt ttgttttgtt gtattgggat ttttttagtt
1321 tgttgtgttt tttgttggtt atttgtgttt ttttgatttt ggaaagagtt ttgggtgtgg
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1381 gatttttggg agttgatttg ttgtttgatt aggggtgtgt ttgtattttt ttaaggatt
 1441 ggttttggtt ttggggagat tggaattgag atgatagggt tttgttgat tagtttttg
 1501 atataatgtg gagtggggtt gaggggttgt tttgttaggt ttgtgttgtt gtgttttag
 1561 gtagtagtga atagttagtt tttgaattgg agtttgggtt ggaatatggg gagatggagg
 1621 ggtttattat atttatgttt tttggagagg gtggtggagg tgtgtggttg ttgagtgtga
 1681 agttggtttt tttgtagttt tgggagtgtt ttaggtttat tttatggagg gtggagggt
 1741 tttgtagttt tgatgtttat gttgtaattt tgtgtggttt aggggtgtta tttgttgga
 1801 aaataaaata taaaaaatat taaaattatt ttttattgta taatttttgg tgtttagggt
 1861 tgtaatttta attttttttt taatttttat atagtgatta ttattaaaa agtgagggtt
 1921 ttttttttg tttttgttt ttggagatag tttgttttag ttgtttagggt tggagttag
 1981 tgggtgtgatt tttttgtttt agttttttta gtagttggga ttatggatgt ttgttattat
 2041 gtttagttta tttttgtatt ttttagtagag atggtgtttt tttatgttgg ttaggttgg
 2101 tttgaatttt tgattttagg tgattttatt gttttggttt tttaaagtat tgggattata
 2161 gatgtgagtt attgtatttg gttgatattt gtttttaata gtagaaatta tttgttgaa
 2221 gaaaatattt aattttgata aggggttagg gagggttatt ttttgatag ggtgttgga
 2281 gaatggtaa gtgtaaaatt gtggaaagta atttggtaat attgttattt taagaaagga
 2341 atttttttat ttaggtgatt tattatttat ttttagtgtt ttttgaaga atattaggaa
 2401 gaaatggaaa ttagtgtttt gaagaatggt atggattttt aggtagtatt attagtaaga
 2461 atttgagttt gaagtataa tgtgtgttg agaggtaagg ttatagaatt atagtattt
 2521 gtttgatttt tgtgatattg gtattatttt ttggtgtgtg tgtgtgtgtg tgtggttaag
 2581 gttgtaggta atgttaattt ttaaattttt ttaatttttg tatagtaagt agttagaaaa
 2641 aaaaattgag agataaatg ttaatagata atggtagat aatgaatgat aataaattga

SEQ ID NO: 48

Sequenza non metilata del gene LOC51149 (bottom strand), derivata da SEQ ID NO.8

```
1  ttatgtttatt gttatttgtt atttgattat tgtttattgg tatattgttt ttttaatttt
61  ttttttaatt atttattgta taaaagttag aaaaatttaa aaattagtat tatttatgat
121 tttagtata tatatatata tatatgttag aaaataatgt tgggtgtata gaagttaa
181 gatgtattgt aattttgtaa ttttgttttt ttatagtatg ttgttatttt aaatttaggt
241 ttttgttgat ggaattgttt aagagttagt gttgtttttt agaattattga tttttatttt
301 tttttagtat tttttaggga atattaggga atgaataata aattatttag gtgaagggat
361 tttttttttg gggtagtagt attgttaggt tgttttttat ggttttgtat ttgattgttt
421 ttttagtatt ttgttagagg ggtagttttt tttgtatttt tgttaggatt ggggtttttt
481 ttaaatggga tgggttttgt tgttaaaagt gagtgttggg tgggtgtagt ggtttatggt
541 tgtaatttta gtattttggg aagttgaggt ggggtggatta tttgaggta ggagttagg
601 attagttagg ttaatatgga gaaatattgt ttttattaaa aatataaaaa ttagttgggt
661 gtggtggtgg gtatttgtaa ttttagttat tggagagggt gaggtaggag aattatgta
721 ttgtatttta gtttgggtga ttgagtgaga ttgtttttaa aaataaaaaa taaaaaaa
781 atattttgtt ttttgggtga tagttattgt gtaaaagttg gaaaaaaat taaaattata
841 attttagata ttgaggggtg tatggtggga ggttaattta atattttttg tattttattt
901 ttaaatgagg ttataatttt aagttatata gggttgtggt gtgagtgttg ggttgtggg
961 gtgtttttat tttttgtagg gtgggttttg gatgtttttg gggttgtagg gggattggtt
1021 ttgtgttttg tggttgtgtg tttttgttgt tttttttggg aagtgtgggt gtggtgaggt
1081 tttttgtttt tttgtatttt attttgggtt ttggttttaa ggttaattgt ttgttgttat
1141 ttaaaagtat ggtagtgtag gtttggtagg gtggtttttt agttttgttt tgtgttgtgt
1201 ttaaggattg gttagtggag gttttgttgt ttaatttta gtttttttag gtttgggaatt
1261 agtgttttag gaagatgttg gtatggtttt ggtagatga tgagttaggt attaggaatt
1321 ttgtatttag gatttttttt gaggttggag ggggttagat gattagttag aggtgtggta
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1381 ggtagagggg atttttagtgt gtaggggtgg ggttggtgtg gttggagtga agagtataag
 1441 tgtatgtgag atggtgtagg ggattagagg gtttggtgtg tgtgtgtggg gtggggttgt
 1501 ggtgggataa atgtagagtg tatgtgtttg gttgttttgt gattgtataa gtagggatgg
 1561 tgttgtttta gtgttttttg gtgttatgtt gttgtagttg ttgttttttt taggtgtatt
 1621 aggtttgttg ggtgttagtt tttttttttt tttttgtgtt ggggatagtg gatggggagt
 1681 ggtggggttg tgggtgttgt tttgaatggt tttgggatgt attgggtttg aaggagtga
 1741 gggattgttg aggggtgggt ttattggggt tgtttttgta taatgttttg agttttttgt
 1801 ttggtttttg tataaattag aggtaatggt tttgtggagg tgggtttttg tgaattgtag
 1861 taggtagtgg gagaatttggt ttgagtatag tattttttat gtagagtta ttttatgaag
 1921 tagtgttgtt gtagttttag tgagaggggg aggatgggtt ttagagattg agtgtgttgt
 1981 ggtggtgttt ttgttttata tttgggtgtt tttttgttg ttttgtgtt ttgtgttgt
 2041 ttgtttttgt ggggttaggg atttgatatg gttgttttgt gatgtataaa ttatgggttt
 2101 tggagtttta aagatagata atttgtgttt ttaggatata ttgttttttt taatttttag
 2161 tgtgttagat agagaatggt atttaatttt ttttggattg tatttgtttt ttgttttgat
 2221 attatttaat attgtagtta ttgtatttgt ttttgatagt tttttttttt taattattgg
 2281 taatttgta tgttttgaga aagaatagta ttagattttt tttttttttt tttttttttt
 2341 tgagatggag ttttgttttt gttgtttagg ttggagtga atggtgtgat ttgggtttat
 2401 tgtaattttt gttttttagg ttttaagtaat tttttgttt tagttttttg agtagttgga
 2461 ttataggat gtgttattat gtttagtta ttttgtgttt ttaatagaga taggggtttt
 2521 ttatgttgtt taggttggtt ttgaattttt gattttagggt gatttgtttg ttttggtttt
 2581 ttaaagtgtt gggattatag gtgagagtta ttgtgttttg tgtggattag atttgtttta
 2641 gaggtatgtt aaaaagttag taagatgttg agtatgtgtt tgtaagtttg tatttaatgt

SEQ ID NO: 49

Sequenza metilata del gene MAP1B (top strand), derivata da SEQ ID NO.9

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1 atagggtgag ggtgaggagt gggtagtggg tgtgtacgtg gtgggtggtg taggttgaga
61 gcgttttttt tttttacggt tgtagtagga gtttagcggg cgttttagtt ttttggttcg
121 cggttttggt togattattg ttcgtatatt tcgttttttt agttttcggg tcgcgggcga
181 gatgatttgt tgtagatgat attagtttcg ggttaacggt tggagagcgc gaggtagtta
241 tcgcgtgagg atgtgtcggg tggttttttt tttttttttt tttttttttt ttocggtttt
301 tgtttagttt ttatataaaa gcggcgtcgt ttttcgttt tttttattt ttocgttttt
361 ttocgcgcgt atttttcgc gcgttgggag agggcggagg gggaggcggc gcgcggcgtt
421 agaggagggg ggacgtaggg ggccgagcgc agatagtatt ttccgagata atttttttt
481 ttgtcgtagt ggagaggagc ggtccgagcgc agatatttcg tcgaggtata gtagtcggta
541 ggatggcgat cgtggtggtg gaagttagc agtcggagtc gttcggtagt atcgtaatt
601 cggcggcgtt tatttcgttt agtttgctgt atcgtttttt tgatagtaag ttttatttgt
661 tggtagtcgt cggcgagatc gtgacgcagg agtatttcgc gcgtgttacc ggtaatatcg
721 agttcggtaa gtggtttcgc gtttttagag acgcgcgttg ggagacgcgt aaatacgatt
781 ttatttaggg cgcgacggtt attgcgtttt tttcgcgcgt ttocgtattt tgttttttt
841 cgttattttt tatatttggt ttagattttt tttgggttaa ttaagaataa ttogaattat
901 tagatatgag atttagaggg agagttttta ataattttga gggatttggt attacgttga
961 gttcgtagtt tgtgttgagt tggttatcgt ttttttcgtt aagtgaatg taggtgtag
1021 gggagtagag gttataataa agtcgtaac gtaggaggta gaagggtggg ggagatttga
1081 tgtaattatt ttttttagtt ttttttgggt tttaggaaaa ggttgggatt tttattatcg
1141 tagatttggg gtcgaagttt atgtgttagg gttcgcgtgg gatttatttt tattacggtt
1201 attttagttt ttgagaaacg ttttttttga ttttaaattt ttocattttt tttttttta
1261 gaatgattag gttagtttta gggttacgtt cgtttttttc gttttttttt ttccggggag
1321 atgttgggat gtagaatcgt ttgcgttttc ttattagata gatttcgttt cgttatcgtt
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1381 tttggggttt tggttgtagt ttttagaaa gataatggga ttttaagttg cggggtgggg
1441 ttgttgtttt tagaagtttt agtttcggga gtggtagttt gaagggggtc ggtgaggag
1501 acgttagcgg gtagggtagt ttttcgttc ggtgttcgta ttagtggcgc gttttcgga
1561 ggtogaatag cggtaacgct gggatttttg gcggggtcgt gagggttcgg cgggtatagt
1621 ttggggcgta tagagagatc gtttttagtt ttattcgagt tgcgtagtg ttttcggatc
1681 gttcgttata tttgttttt tatattgcgg cgttttcgtc gggtaagggt ggttgggttt
1741 gcgtttcgtt cgggtttcgg gttggcgggg gtcgcgcggt tttatttttt agtttgtttg
1801 gttttgttgt tttgggagtt tttgggtggg tagttttggt tttgttttt tttttattt
1861 ttggcgtttc ggtttttttt tcgtttttga tagaggtcgt cgggtttttt cgtagtttta
1921 gttcgcgttt tatttttttg ggggtgtgtt gaagcgtttt ttcgggagat atcggttggt
1981 gggcgtgggt tagttcgat tgcggttttt acggtagttc gaggcggata aagggcgttt
2041 acgtagtttt cgttttttat ttttttttt taataaaaaga cgaaagaaaa attttgtttt

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SEQ ID NO: 50

Sequenza metilata del gene MAP1B (bottom strand), derivata da SEQ ID NO.9

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1 aaaataaggt ttttttttcg ttttttattg gggaggggga gtggggaacg agggttgcgt
61 gaacgttttt tgttcgtttc gggttgtcgt agagatcgta gtgcggattg tattaogttt
121 attaatcggg gtttttcgga gaaacgtttt agtattattt taggagaata gagcgcgggt
181 tggggttgcg gagggattcg gcgatttttg ttaggagcga ggggagggtc gggacgttag
241 ggataaaggg aaaggtagag attagagttg tttatttagg gatttttagg gtaataaagt
301 taggtaaatt gagaggtggg ggcgcgcggt tttcgttagt tcgaggttcg ggcggagcgt
361 aagtttagtt agtcgtgttc gacgggggcy tcgtagtgtg ggggggtagg tgtggcgggc
421 ggttcggagg tattgcggta gttcgggtgg ggttgggggc ggtttttttg tgcgttcgag
481 gttgtgttcg tcggattttt acggtttcgt ttagggtttt cggcgatatc ttattcgttt

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541 ttcgtagagc gcgttattgg tgcgagtatc gggcgaggag ttgattttat tcgttgacgt
 601 tttttttatc gatttttttt aagttattat tttcgaggtt gggattttta aaagtagtag
 661 ttttatttcg taatttgggg ttttattgtt ttttttgaga gttgtagtta aggttttaag
 721 ggcggtagcg aggcgggttt tgtttggtgg cgaagcgtag gcggttttgt attttagtat
 781 tttttcggg aggggggggc ggggggagcg gcggtggttt taggattagt ttagttattt
 841 tgaggaaaga aaggatcggg aggtttgaaa ttagaaaagg cgttttttag gggttgaggt
 901 agtcgtggtg aggatgaatt ttacgcgggt tttggtatat gggtttcggt tttaggttg
 961 cgggtggtggg ggttttagtt ttttttgag gttagaagag gattgaaagg agtggttgta
 1021 ttaggttttt tttatttttt tgttttttgc ggttcgggtt ttattgtggt ttttgttttt
 1081 ttgatatttg tattttattt agcgggagag gcggtggtta atttagtata ggttcgggat
 1141 ttagcgtggt gatagatttt ttaaggttat tggagatttt tttttgggt tttatattta
 1201 ataattcgga ttatttttaa ttagtttaga aagggtttgg attaagtatg agaggtgacg
 1261 aggagaggtg tgggtgcggg gcgcgcggga ggagcgtagt gatcgtcgcg ttttgggtgg
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 1381 cgatgttgtc gatggtacgt cgtaggtgtt ttccggttac gatttcgtcg acgattatta
 1441 gtaagtagaa tttgttgta aggaagcggg gcgatagggt aggcgaggtg gacgtcgtcg
 1501 ggttggcgat gttgtcggac ggtttcgggt cggtggtttt tattattacg gtcgttattt
 1561 tgcggttgt tgtgttcgg cgaagtgtt cgttcggtc gttttttttt attgcggtag
 1621 gagaaaggat tattttcgaa ggtattgtt tcgtttcgtt ttttgcgtt ttttttttt
 1681 ggcgtcgcgc gtcgtttttt ttttcgtttt ttttagcgt ccgggagagt gcgcggcgga
 1741 gaggagcggg gagtgagaga gggcggggag gcggcgtcgt ttttatatgg agattaggtg
 1801 gggagtcggg aggaggagga agaggaggag gaaaggatta ttccgtatat ttttacgcg
 1861 tgggtgtttt cgttttttta gtcgttggtt cggggttgat gttatttgta gtaaattatt
 1921 tcgttcgcgg ttccgaagtt ggagggacga ggtgtcggga taatggtcgg ggtagggtcg
 1981 cgagttaagg ggttggggcg ttcgttgagt tttgttgta gtcgtgaagg gggaagacgt

2041 ttttaattta tattatttat tacgtatata tttattgttt attttttatt tttattttgt

SEQ ID NO: 51

Sequenza non metilata del gene MAP1B (top strand), derivata da SEQ ID NO.9

1 atagggtagg ggtgaggagt gggtagtggg tgtgtatgtg gtgggtggtg taggttgaga
61 gtgttttttt tttttatggt tgtagtagga gtttagtggg tgttttagtt ttttggtttg
121 tggttttggt ttgattattg tttgtatatt ttgttttttt agtttttggg ttgtgggtga
181 gatgatttgt tgtagatgat attagttttg ggttaatggt tggaagagtg gaggtagtta
241 ttgtgtgagg atgtgttggg tggttttttt tttttttttt tttttttttt tttggttttt
301 tgttttagtt ttatataaaa gtggtgttgt ttttttggtt ttttttattt tttgtttttt
361 tttgttgtgt attttttgtg gtgttgggag aggggtggagg gggagggtgt gtgtggtgtt
421 agaggagggg ggatgtaggg ggtggagtgg agatagtatt tttggagata attttttttt
481 ttgttgtagt ggagaggagt ggttggagtg agatattttg ttgaggtata gtagttagga
541 ggatggtgat tgtggtggtg gaagttattg agttggagt ttgtgtagt attgttaatt
601 tgggtggtgt tattttgttt agtttgttgt attgtttttt tgatagtaag ttttatttgt
661 tgggtggtgt tggtagatt gtgattgagg agtatttgtg gtgtgttatt ggtaaatattg
721 agtttggtaa gtggttttgt gtttttagag atgtgtgttg ggagatgtgt aaatatgatt
781 ttatttaggg tgtgatggtt attgtgtttt ttttgttgtt tttgtattta tgtttttttt
841 tgttattttt tataatttgg tttagatttt tttgggttaa ttaagaataa tttgaattat
901 tagatatgag atttagaggg agagttttta ataattttga gggatttggt attatggtga
961 gttttagtgt tgtgttagt tggttattgt tttttttggt aagtgaatg taggtgtag
1021 gggagtagag gttataataa agttgtaatt gtaggaggta gaagggtggg ggagatttga
1081 tgtaattatt ttttttagtt tttttttggt tttaggaaaa ggttgggatt tttattattg
1141 tagatttggg gttgaagttt atgtgttagg gtttgtgtgg gatttatttt tattatggtt

1201 attttagttt ttgagaaatg ttttttttga ttttaaattt tttgattttt tttttttta
 1261 gaatgattag gttagtttta gggttatgtt tgtttttttt gttttttttt ttttggggag
 1321 atgttgggat gtagaattgt ttgtgttttg ttattagata gagtttgttt tgttattgtt
 1381 tttggggttt tggttgtagt ttttagaaag gataatggga ttttaagttg tgggtgggg
 1441 ttgttgtttt tagaagtttt agttttggga gtggtagttt gaaggggggtt ggtgagggag
 1501 atgttagtgg gtagggttag ttttttgttt ggtgtttgta ttagtgggtt gttttgtgga
 1561 ggttgaatag tggtagttg gggatttttg gtgggtttgt gagggtttg tgggtatagt
 1621 tttgggtgta tagagagatt gtttttagtt ttatttgagt tgtttagtg tttttggatt
 1681 gtttgttata tttgtttttt tatattgttg tgtttttgtt gggtaggtt ggttgggttt
 1741 gtgttttgtt tgggttttg gttggtgggg gttgtgtgtt tttatttttt agtttgtttg
 1801 gttttgttgt tttgggagtt tttgggtggg tagttttggt tttgttttt ttttttattt
 1861 ttggtgtttt ggtttttttt ttgtttttga tagaggttgt tgggtttttt tgtagtttta
 1921 gtttgtgttt tatttttttg ggggtggttt gaagtgtttt tttgggagat attggttggt
 1981 ggggtgtggt tagtttgtat tgtggttttt atggtagttt gaggtggata aaggtgtttt
 2041 atgtagtttt tgttttttat tttttttttt taataaaaga tgaagaaaa attttgttt

SEQ ID NO: 52

Sequenza non metilata del gene MAP1B (bottom strand), derivata da SEQ ID NO.9

1 aaaataaggt tttttttttg ttttttattg gggaggggga gtggggaatg agggtttgtt
 61 gaatgttttt tgtttgtttt gggttgttgt agagattgta gtgtggattg tattatgttt
 121 attaatgggt gttttttgga gaaatgtttt agtattattt taggagaata gagtgtgggt
 181 tggggttggt gagggatttg gtgatttttg ttaggagtga ggggaggggt gggatgttag
 241 ggataaaggg aaaggtagag attagagtgt tttatttagg gatttttagg gtaataaagt
 301 taggtaaatt gagaggtggg ggtgtgtggt tttgttagt ttgaggtttg ggtggagtgt

361 aagtttagtt agttgtgttt gatgggggtg ttgtagtggt ggggggtagg tgtggtgggt
 421 ggtttgagg tattgtgta gtttgggtgg ggttgggggt ggtttttttg tgtgtttgag
 481 gttgtgtttg ttggattttt atggttttgt ttagggtttt tgggtattg ttatttggtt
 541 ttgttagagt gtgttattgg tgtgagtatt gggtagaggag ttgattttat ttgttgatgt
 601 tttttttatt gatttttttt aagttattat ttttgagggt gggattttta aaagtagtag
 661 ttttattttg taatttgggg ttttattgtt ttttttgaga gttgtagtta aggttttaag
 721 ggtggtagt aggtgggttt tgtttgggtg tgaagtgtag gtggttttgt attttagtat
 781 ttttttggg aggggggggt ggggggagt ggtgtggttt taggattagt ttagttattt
 841 tgaggaaaga aaggattggg aggtttgaaa ttagaaaagg tgttttttag gggttgaggt
 901 agttgtggtg aggatgaatt ttatgtgggt tttggatat gggtttttgt ttaggtttg
 961 tgggtggtgg gggttttagt ttttttgag gttagaagag gattgaaagg agtggttga
 1021 ttaggttttt tttatttttt tgtttttgt ggtgtggtt ttattgtggt tttgttttt
 1081 ttgatatttg tattttattt agtgggagag gtggtggtta atttagtata ggtgtggat
 1141 ttagtgtgtt gatagatttt ttaaggttat tggagatttt tttttgggt tttatattta
 1201 ataatttga ttatttttaa ttagtttaga aagggtttgg attaatgat agaggtagt
 1261 aggagagga tgggtgtggg gtgtgtggga ggagtgtagt gattgttgtg tttgggtgg
 1321 ggtgtgttt gtgtgttttt tagtgttgt ttttgggggt gtggggttat ttattgagtt
 1381 tgatgttgt gatggtatgt ttaggtgtt ttttgggtat gatttgttg atgattatta
 1441 gtaagtagaa tttgtgtta aggaagtgt gtgatagggt aggtgaggtg gatgttgtg
 1501 ggtggtgat gttgttggat ggttttgggt tgggtggttt tattattatg gttgttattt
 1561 tgttggttgt tgtgttttgg tgaagtgtt tgttttgggt gtttttttt attgtggtg
 1621 gagaaaggat tatttttgaa ggtattgtt ttgtttgtt ttttgtgtt ttttttttt
 1681 ggtgttgtgt gttgtttttt tttttgttt tttttagtgt tgtggagagt gtgtggtgga
 1741 gaggagtggg gagtgagaga ggggtgggag gtggtgttgt ttttatatgg agattaggta
 1801 gggagtggg aggaggagga agaggaggag gaaaggatta tttgtatat tttatgtgg

1861 tggttggtttt tggtttttta gttgttggtt tggggttgat gttatttgta gtaaattatt
 1921 ttgtttgtgg tttggaagt ggagggatga ggtgtgtgga taatggttgg ggtaggggtg
 1981 tgagttaagg ggttgggtg tttgttgagt tttgttgta gttgtgaagg gggaagatgt
 2041 ttttaattta tattatttat tatgtatata tttattgttt attttttatt tttattttgt

SEQ ID NO: 53

Sequenza metilata del gene MDM2 (top strand), derivata da SEQ ID NO.10

1 tagagaaaa gtggcgtgc ttcgtgttta taggtttatt ttttaatcgt tattgaatat
 61 agttgggaaa atgtatggtt taaatagttt tagttggaga taagttagga ttttaatttt
 121 tttattgtag tttcggaacg tgtttgaatt tgattagttt aagaggaaaa gttgagttaa
 181 tttgtttatt gaatcggttt aatttcgttt agattacgcg tagcgtttat attagtgatt
 241 cgataggtat ttgcgattat tcggattttt cgcgtcgaag cggtttcgta gttttcggtt
 301 ttcgtgattt ttattttgaa ttttcgcgga gattttcgaa ttatttttat ttttatcgtc
 361 gcgagagtcg ttcgaaattt cgtttttttt tttggcggcg attgtttagt tttagttaa
 421 taaaattttc gtaaagtac gtgttttatg tttcgcgttt cgcgtttcga gtttttagtt
 481 acgaatcgta taaaggttc gaacgggtag aggttgggaa ttagcgatag aggggatatc
 541 gttagagttt agatttaaaa gtgacgttc gttgtcgggt tagtatttgt tttttattat
 601 tcggggtttt cgcgtttgga gtcgggggtt ttttaagatt ttttagtttt ttttacgggg
 661 cgcgcggaag tacgacgttt tgggtttcgg ggattatttt attttcggg ttagggtatt
 721 gggcgttcgt acgtattaat tcggggaggg acggtgtttt tggttgcgaa agtagtagga
 781 tttcggttag aggggtcgcg gtctgttttc gggttcgggt tttgtttta tttttcgcg
 841 atatagggtt atataggttt tagaagtagt taagtctgc gcggtgttc ggtgcgcgtt
 901 ttttatcgtt cgaggggagc gcgcgggtcg tcgcggcgta ttcgggtatt tgtgcgcgcg
 961 tatataatcg gtttcgtttt cgttaattgg gttcgggggt cggtcgtatt attttcggga
 1021 tgatggagtg gggggtgtcg tttcgcggc gcgcggggtt gtgaggcggg gtgggggtgt

1081 tggtcgcgag ttgagagggg ggggttcggg ttggcgcgga gttagtaagg tttggcgttg
1141 tgataaaaaa ttagtcgttg cgttatgttt gtatattttg tgtttatatt ttcgttcgc
1201 ggtggaaatt gcgataaatg cggattttcg tgcgttggtt attaaaaa aattaaaatt

SEQ ID NO: 54

Sequenza metilata del gene MDM2 (bottom strand), derivata da SEQ ID NO.10

1 aattttggtt ttttttggg aatagcgata cggagattcg tatttgcgt agttttatc
61 gggggcggga agtgtaata taagaaatat aaatatagcg taacggtaa aggagtgtta
121 tagcgtaaa tttgttggg ttcgcgttag gtcgagtttt attttttag ttcgcgtta
181 atatttttat ttcgttttat agttcgtgc gttcgcgggg cgataatttt tattttatta
241 tttcggaggg ggtgcggtcg agtttcggat ttaattggcg gaagcggggg cggttgtgtg
301 cgcgcgtata aatgttcgga tgcgtcgcga cgattcgcg gtttttttcg ggcggtaggg
361 ggcgcgtatc gaggtatcgc ggcgagtttg gttgtttttg gggtttgtgt ggttttgtgt
421 gtcggaaaga tggagtaaga agtcgagttc gaggggcggg cgcgattttt ttgatcgaga
481 tttgttgttt ttcgtagtta ggagtatcgt tttttttcgg attagtgcgt acgagcgttt
541 agtgtttttg ttcggagagt ggaatgattt tcgaggttta gggcgtcgtg ttttcgcgcg
601 tttcgtgaag gaaattgggg agttttgagg gattttcgat ttaagcgcg aaaatttcgg
661 atggtgagga gtaggtattg gttcggtagc gacggttat ttttgggttt gggttttgac
721 ggtgtttttt ttatcgttgg ttttagttt ttgttcgttc gtagtttttg tgcggttcgt
781 ggttgggggt tcggggcgcg gggcgcgggg tatggggtac gtggttttgc ggaggtttg
841 ttggattggg gttaggtagt cgtcgttagg gaggagggcg ggatttcgga cggttttcgc
901 ggcgggtggg gtgggggttg ttcggaggtt ttcgcgggag tttagggtta aggttacggg
961 ggtcgggggt tcgggggtcg ttcggcgcg ggaggttcgg atgacgtag gtgtttgtcg
1021 ggttattagt gtgaacgttg cgcgtagttt gggcgggatt ggtcgggttt agtgggtagg

1081 ttgatttagt tttttttttt gagttggtta agtttagata cgtttogaaa ttgtagtaaa
 1141 aggagttaag ttttgatttg ttttagttg gggttattta aattatgtat ttttttagtt
 1201 gtgttttagtg gogattggag ggtagatttg tgggtacgga cgtacgttat tttttttttg

SEQ ID NO: 55

Sequenza non metilata del gene MDM2 (top strand), derivata da SEQ ID NO.10

1 tagagaaaa gtggtgtgtg tttgtgttta taggtttatt ttttaattgt tattgaatat
 61 agttgggaaa atgtatggtt taaatagttt tagttggaga taagttagga ttttaatttt
 121 tttattgtag ttttggaatg tgtttgaatt tgattagttt aagaggaaaa gttgagttaa
 181 tttgtttatt gaattgggtt aattttgttt agattatgtg tagtgtttat attagtgatt
 241 tgataggat ttgtgattat ttggattttt tgtgttgaag tggttttgta gtttttggtt
 301 tttgtgattt ttattttgaa tttttgtgga gatttttgaa ttatttttat ttttattggt
 361 gtgagagtgt tttgaaattt tgtttttttt ttgggtggtg attgtttagt ttaggttaa
 421 taaaattttt gtaaagtatt gtgttttatg ttttgtgttt tgtgttttga gtttttagtt
 481 atgaattgta taaaggttgt gaatggtag aggttgggaa ttagtgatag aggggatatt
 541 gttagagttt agatttaaaa gtgattgttt gttgttgggt tagtatttgt tttttattat
 601 ttggggtttt tgtgtttgga gttgggggtt ttttaagatt ttttagtttt ttttatgggg
 661 tgtgtggaag tatgatgttt tgggttttgg ggattatttt attttttggg ttagggattt
 721 ggggttttgt atgtattaat ttggggaggg atggtgtttt tggttgtgaa agtagtagga
 781 ttttggttag aggggttgtg gttgtttttt gggtttgggt ttttgtttta ttttttgat
 841 atatagggtt atatagggtt tagaagtagt taagtttgtt gtggtgtttt ggtgtgtgtt
 901 ttttattggt tgaggggagt gtgtgggttg ttgtggtgta tttgggtatt tgtgtgtgtg
 961 tatataattg gttttgtttt tgtaattgg gtttgggggt tggttgtatt atttttggga
 1021 tgatggagtg ggggtgtgtg ttttgtgggt gtggtgggtt gtgaggtggg gtgggggtgt

1081 tgggtgtgag ttgagagggg ggggtttggg ttgggtgga gtagtaagg tttggtgtg
1141 tgatattttt ttagttgttg tgatatgtt gtattttttg tgtttatatt ttttgtttg
1201 ggtggaaatt gtgataaatg tggatttttg tgtgtgtgt attaaaaaga aattaaaatt

SEQ ID NO: 56

Sequenza non metilata del gene MDM2 (bottom strand), derivata da SEQ ID NO.10

1 aattttggtt ttttttggg aatagtata tggagatttg tatttgtgt agtttttatt
61 gtgggtggga agtgtaaata taagaaatat aaatatagt taatggtaa aggagtgtta
121 tagtgtaaa ttttgttgg tttgtgttag gttgagttt attttttag tttgtggtta
181 atatttttat tttgtttat agtttgtgt gtttgtggg tgatatttt tattttatta
241 ttttggagg ggtgtggtg agttttgat ttaattggtg gaagtgggg tgggtgtgtg
301 tgtgtgtata aatgtttgga tgtgtgtga tgatttgtgt gtttttttg ggtgtaggg
361 ggtgtgtatt gaggtattgt ggtgagttt gtgtttttt gggtttgtgt ggttttgtt
421 gttggaaaga tggagtaaga agttgagtt gaggggtgt tgtgatttt ttgattgaga
481 ttttgttgtt tttgtagtta ggagtattgt ttttttttg attagtgtgt atgagtgtt
541 agtgttttg tttggagagt ggaatgatt ttgaggttta ggtgttgtg ttttgtgtg
601 ttttgtgaag gaaattggg agttttgagg gatttttgat ttaagtgtg aaaattttg
661 atggtgagga gtaggtattg gtttggtagt gagggttat ttttgggtt gggttttgat
721 ggtgttttt ttattgttg ttttagttt ttgtttgtt gtagttttt tgtggtttg
781 ggttggggg ttgggtgtg ggtgtgggg tatgggtat gtggtttgt ggaggtttg
841 ttggattggg gttaggtagt tgtgttagg gaggaggtg ggattttga tggttttgt
901 ggtggtggg gtgggggtg tttggaggt tttgtggag tttaggtaa aggttatgg
961 ggttggggg tgtgggttg ttttgggtg ggaggtttg atgatttag gtgtttgtg
1021 ggttattagt gtgaatgtg tgtgtagtt ggtgggatt ggttgggtt agtgggtag
1081 ttgatttagt ttttttttt gagttggtta agtttagata tgttttgaat ttgtagtaa

1141 aggagttaag ttttgatttg ttttagttg gggttattta aattatgtat ttttttagtt
1201 gtgttttagtg gtgattggag ggtagatttg tgggtatgga tgtatgttat tttttttttg

SEQ ID NO: 57

Sequenza metilata del gene NID1 (top strand), derivata da SEQ ID NO.11

1 gtaggatagg ttgtagtcgt tgcgtttgta gttttaattt ttttttttcg gtttaatttt
61 tatatttttg gaatgtatat aagttttata tgaaatttat atggtgggag gtogaggaag
121 gtagcgttac gaaagatttt taataagttg atagcgattt taggttcggt tagttacggg
181 gaggatttag ggagttgtag gttatttggg ttcgtttttc gtttgggggt ttcggtgtga
241 taatgttttg ttataggaaa tgggattatt gggagttttg tgtttttcgt tttggatttt
301 ggattttgaa acgagtttaa ttggaaagta gtattattgt taagatatat tcggagttaa
361 tatataaata taggaggttg tcggcgaaat ttttcgtag ttataagagt ttcggggttc
421 gcgcgtagat tcgagtttag tttcggtttt tgttttgcgg aggtttcgcg agagaatttg
481 gttttattcg ggatcgggta ggttttagtt tcgaagggat tggatagtcg agggacgcgg
541 attgattttt ttgcggcgat gtagtttata gtgcgcgggg aggaagtttc gcggggttta
601 tgggtgtcgg ggttacggtt cggggcgcg cggagtattt agatttcgag attcgttttt
661 cggatagtag ggatcgggtc gggaagattt tcgcggattt tgtagaggcg ggagattttg
721 cgtcgtgttc ggtgtttcgg cggtagcgg gttcgggttt tcgtttgtta cgtttaagtt
781 cgttcgggtt tacgggcggt ttcggttcgt cgcgttttgt agtttttcgt tcgttttttc
841 ggggtttatt tacgtagatt gcgtcgatgt cggatttgc gtagaagcgg agcgttttat
901 ttagttttag gtaggagag acgaagttat tttcgttttt tagtttttag tttttttggt
961 cggggtcgaa gggaaagagt ttttggcgg ttaggtagtt tataggtttc gttagtagta
1021 gcggtagtag tagcgttcgc gtttacgtag ttoggattcg gttgttcgag gttaatatgt
1081 tttcgaattg cgttttcgta aattcgtttt cgcggttagg atagaggaag gcggggatgt

1141 aatcggaagt ttttggtagt tttttttttt ttctgttttc ggctgtttta tttcgggaaa
 1201 taggggaggg gagcgagggg gagagcggag ggtttcgttt cgttttagcg gcgcgtcgcg
 1261 gggtagttta atggtcgca gggggagggc gagggcgaa gtcaattttt tcttttggg
 1321 cgtcgtgtt tgcgattttc gaaattagt cgttttttag cgaacggcgt tttcgggagg
 1381 gggagtagag cgcgggattc gtatcgtggt tttttgatta gggttgggtc gtggagagtc
 1441 ggcgagctgg aaacgtttcg gatttaggaa cggcgtttat tttattgtcg ttcggtcgcg
 1501 ttcggggttt aattcgtttg attttgtag gaagacgggg tgggagttgg gaattagtta
 1561 agggatagag ttattaatac gtttatgggt ttattttttt atttattgcg cgttttttga
 1621 gtgtttgatt ttgtgtttt tattgtggag gtctgttagg aaacgggggt ttatttttcg
 1681 aggtaaagt attagtgtat aatataagt agtgtttagt gggggtttta agttattaaa
 1741 gatattaggg ttggaaaaat tggcggggaa agttgtaggt gggacggcgg gaattaattc
 1801 ggggtttttg gaaggaatgg gatgttatta ggcggtagag aagggaggtg gaggatcgag

SEQ ID NO: 58

Sequenza metilata del gene NID1 (bottom strand), derivata da SEQ ID NO.11

1 ttcggttttt tatttttttt ttttgcgtt tcatgatatt ttattttttt tagagtattc
 61 gggttgattt tctcgtttt attttagtt ttttcgtta gtttttttag ttttaattgtt
 121 tttgatgatt tggggttttt attgatatt ggtttgtgtt gtatattggt gattttgttt
 181 cggaggggtga gatttcgttt tttggcgaat ttttataata gggagtatag gattaggtat
 241 ttaaaaaacg cgtaatgaat ggggtgatga gtttatgaac gtgttggtgg tttgttttt
 301 tggttgattt ttagttttta tttcgttttt ttattaggggt taagcgaatt ggatttcgga
 361 cgcggtcgag cgttaatggg gtgggcgtcg tttttgaatt cggagcgttt ttacgtcgtc
 421 ggttttttac gatttaattt taattagagg attacgggtc gggtttcgcg tttgttttt
 481 ttttcgggag gcgtcgttcg ttgggagtcg ggttggtttc gagaatcgta ggtatcggcg

541 ttttaaggcgg gaggttcggt ttcgtttttc gttttttttt tcgcggttat tgggttcgtt
601 cgcggcgcgt tcgttggaag ggcgggggtt ttcgtttttt ttttcggtt tttttttta
661 tttttcgggg tgggaacgtc gggaggcggg aggagagggg gttgttaggg gcgttcggtt
721 atattttcgt ttttttttgt tttggtcgcg ggatcgggtt tcggggatcg tagttcggga
781 atatgttggt ttcgagtagt cggattcggg ttgcgtggac gcgggcgttg ttgttgctgt
841 tgttgttggc ggggtttgtg ggttgtttga gtcgttagga gttttttttt tcoggtttog
901 gataggggga tttggagttg gaggacggg atgatttcgt tttttttgtt ttggagtga
961 gtggggcgtt tcgtttttac gatagattcg atacgacgt agtttacgtg agtgagttc
1021 gggagggcgg gcgaggggtt gtagggcggc gcgggtcggg ggcgttcgtg gagtccgacg
1081 gatttgggcg tagtaggcgg ggattcggat tcgttggtcg tcggggtatc gggtaacggc
1141 tagggttttt cgtttttgta gggttcgcga aggttttttc gattcgggtt ttgttattcg
1201 aagagcgggt cgcgggggtt ggggtgttcc gcgcgtttcg ggtcgtgatt tcggtattta
1261 tggatttcgc ggagtttttt tttcggcgtt tgtgggttgt atcgtcgtag ggaggttagt
1321 tcgcgttttt cgggtgttta gttttttcgg ggttaggatt tggtcgggtt cgggtggagt
1381 taggttttcg cgcggagttt tcgtagggtta agagtcggag ttggatcgta gtttgcgcgc
1441 gggtttcggg atttttgtgg ttgcgggaga gtttcgtcgg tagttttttg tatttggtg
1501 tggatttcgg atgtgttttg gtagtgatgt tgttttttag ttgggttcgt tttagagttt
1561 agagttaga gcgggaaata tagggttttt agtgatttta ttttttgtg ttaggtattg
1621 ttattacgga ggttttaaac gaggagcggg attagatgat ttatagtttt ttggattttt
1681 ttcgtgattg gtcgggtttg gggtcgttgt taatttggtg aagtttttc gtgtcgttgt
1741 ttttttcggt cgtttattat gtggatttta tataagggtt gtgtgtattt tagaagtgtg
1801 gggggttggt cgggggaagg gggttggaat tgtaaacgta gcgggtgtag tttgttttgt

SEQ ID NO: 59

Sequenza non metilata del gene NID1 (top strand), derivata da SEQ ID NO.11

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1 gtaggatagg ttgtagtgtg tgtgtttgta gttttaattt ttttttttg gtttaatttt
61 tatatttttg gaatgtatat aagttttata tgaaatttat atgggtgggtg gttgaggaag
121 gtagtgggtat gaaaggattt taataagttg atagtattt taggtttggt tagttatggg
181 gaggatttag ggagtgtag gttatttggg tttgtttttt gtttggggtt tttgtggtga
241 taatgttttg ttataggaaa tgggattatt gggagttttg tgtttttgt tttggatttt
301 ggattttgaa atgagtttaa ttggaaagta gtattattgt taagatatat ttggagtta
361 tatataaata taggaggttg ttggtgaaat tttttgtag ttataagagt tttggggttt
421 gtgtgtagat tgtgatttag ttttggtttt tgtttgtgg aggtttgtg tgagaatttg
481 gttttatttg ggattggta ggttttagtt ttgaaggat tggatagttg agggatgtgg
541 attgattttt ttgtggtgat gtagtttata gttgttggg aggaagtttt gtggggttta
601 tgggtgttg gggtatggtt tggggtgtgt ggagttattt agattttgtg atttgttttt
661 tggatagtag ggattgggtt ggaagattt ttgtggattt tgtagagggt ggagattttg
721 tgttgtgttt ggtgttttg tggtagtgg gtttgggttt ttgtttgta tgtttaagtt
781 tgtttgttt tatgggtgtt tttggttgt tgtgtttgt agtttttgt ttgtttttt
841 ggggtttatt tatgtagatt gtgtgatgt tggatttgt gtagaagtgg agtgttttat
901 ttagttttag gtaggagag atgaagttat tttgttttt tagttttagg ttttttgtt
961 tggggttgaa ggaagagt tttggtggt ttaggtagtt tataggtttt gttagtagta
1021 gtgtagtag tagtgtttgt gtttatgtag tttggatttg gttgtttgag gttaatatgt
1081 ttttgaattg tggttttgta aatttgggtt tgtggttagg atagaggaag gtggggatgt
1141 aattggatgt ttttgtagt ttttttttt tttgttttt ggtgttttta tttgggaaa
1201 taggggaggg gaggaggag gagagtggg ggtttgttt tgttagtgg gtgtgtgtg
1261 gggtagttta atggttgtga ggggagggt gaggggtgaa gttgaatttt ttgttttggg
1321 tgttgggtgt tgtgattttt gaaattagtt tgatttttag tgaatggtgt tttgggagg
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1381 gggagtagag tgtgggattt gtattgtggt tttttgatta gggttgggtt gtggagagtt
 1441 ggtgatgtgg aaatgttttg gatttaggaa tgggtgttat tttattgttg tttggtgtg
 1501 tttgggtttt aatttgtttg attttggtag gaagatgggg tgggagttgg gaattagtta
 1561 agggatagag ttattaatat gtttatgggt ttatttattt atttattgtg tgttttttga
 1621 gtgtttgatt ttgtgttttt tattgtggag gtttgtagg aaatggggtt ttattttttg
 1681 aggtaaagtt attagtgtat aatataagtt agtgtagat gggggtttta agttattaaa
 1741 gatattaggg ttggaaaaat tgggtgggaa agttgtaggt gggatgggtg gaattaattt
 1801 ggggtgtttg gaaggaatgg gatgttatta ggtgtagag aaggaggtg gaggattgag

SEQ ID NO: 60

Sequenza non metilata del gene NID1 (bottom strand), derivata da SEQ ID NO.11

1 tttggttttt tatttttttt ttttgtgtt tgatgatatt ttattttttt tagagtattt
 61 gggttgattt ttgttgtttt attttagttt ttttttgta gtttttttag ttttaagtgt
 121 tttgatgatt tggggttttt atttgatatt ggtttgtgtt gtatattggt gattttgttt
 181 tggaggggta gattttgttt tttggtgaat ttttataata gggagtatag gattaggtat
 241 ttaaaaaatg tgtaatgaat gggtagatga gtttatgaat gtgttgggtg ttttgttttt
 301 tggttgattt ttagttttta ttttgttttt ttattagggt taagtgaatt ggatttttga
 361 tgtggttgag tggtaatggg gtgggtgttg tttttgaatt tggagtgttt ttatgttgtt
 421 ggttttttat gatttaattt taattagagg attatggtgt gggttttgtg ttttgttttt
 481 ttttttggag gtgttgtttg ttgggagttg ggttggtttt gagaattgta ggtattggtg
 541 ttttaagggtg gaggtttggt tttgtttttt gttttttttt ttgtggttat tgggttgttt
 601 tgtggtgtgt ttgttgatg ggggtgggtt ttttgttttt ttttttgttt ttttttttta
 661 ttttttggg tgggaatgtt gggaggtggg aggagagggg gttgttaggg gtgtttggtt
 721 atatttttgt ttttttttgt tttggtgtg ggattgggtt tgtgggattg tagtttggga

781 atatgttggg tttgagtagt tggatttggg ttgtgtggat gtgggtgttg ttgttgttg
 841 tggtgttggg ggggtttgtg ggttgtttga gttgttagga gttttttttt ttgggttttg
 901 gataggggga tttggagtgt gaggatgggg atgattttgt tttttttgtt ttggagtga
 961 gtgggtgtt ttgtttttat gatagatttg atattgatgt agtttatgt agtgagttt
 1021 gggaggggtg gtgaggggtt gtaggggtg gtgggttggg ggtgtttgtg gagttggatg
 1081 gatttgggtg tagtaggtgg ggatttggat ttgttgggtg ttgggttatt gggatatggg
 1141 tagggttttt tgtttttgta gggttttgta aggttttttt gatttgggtt ttgttatttg
 1201 aagagtgggt tgtgggggtt ggggtgtttt gtgtgttttg ggttgtgatt ttggtattta
 1261 tggattttgt ggagtttttt ttttgggtgt tgtgggttgt attgtttag ggaggttagt
 1321 ttgtgtttt tggttgttta gtttttttgg ggttaggatt tggttgggtt tgggtggagt
 1381 taggtttttg tgtggagtgt ttgtagggtg agagtggag ttggattgta gtttgtgtgt
 1441 gggttttggg atttttggg ttgtgggaga gttttgttgg tagttttttg tatttgtgtg
 1501 tggatttttg atgtgttttg gtagtgatgt tgttttttag ttgggtttgt tttagagttt
 1561 agagttaga gtgggaaata tagggttttt agtgatttta tttttgttg ttaggtattg
 1621 ttattatgga ggttttaaat gaggagtggg attagatgat ttatagtttt ttggattttt
 1681 tttgtgattg gttaggtttg gggttgttgt taatttgttg aagttttttt gtgttgtgt
 1741 ttttttgggt tgtttattat gtggatttta tataagggtt gtgtgtatt tagaagtgtg
 1801 ggggttgggt tgggggaagg gggttggaat tgtaaatgta gtggtttag ttgttttgt

SEQ ID NO: 61

Sequenza metilata del gene NID2 (top strand), derivata da SEQ ID NO.12

1 atttttaagt tatttttagt ttgttgttt taaggtagg tttagcgtaa gagtaggtt
 61 agaaataatt tcaggttagt ttttgggtcg ttgttttaga atttaagttt attttttaat
 121 ttttttagta gttaaatatt tttggttatt tatttttttc gaggttagcg tttcgcgtt

181 gatttttttcg taagcgttta tttgttttta ggtgggttagg aaggcgtggg tgggggtaaa
 241 gcgcgtagag cgcgggaagt tagcgcgtat atagcgggcg gttaggttta gtattgcggg
 301 ggagggtgtt tttcgtata ggattcgggt tttgtcgtgg ttcgtgtcga tgttcgttag
 361 aaaaggggcg atggtcggga agtcgggtggg gaaattatag tttatatatt gcgttttttt
 421 ggggaagttt tgagtggaga tgatgtcgtt ggtgtttatt tgggagagga gagggataaa
 481 aagggtgatag tcgtttaagt ttaaggacgt tatttttttcg cgtagggagg gaagggaatt
 541 gatttaggta aaaagttttt tttttttttt ttattgggta gggagtgttg atttagggaa
 601 ataagcgtaa tttttcgat tgttttagtt tcgcgttgta gtaggtttag gggtttttaa
 661 attcgtttat ttattttttt atttttttta taatttcgga gttttatgtt ttcggagagg
 721 aagtttttag gtttgaagag ggaatatttt agtttcgtag acgggtatag ttttttcgcg
 781 gttttaattg taaagttcgt tggtcgtttt agtaacgtta ttttttttgt ttgggaacgcg
 841 tacgtggttg cgaataattt ttgttttttt ttttaggtta tttttgtttt tttatagtag
 901 cggggttaggt agcgggtatcg ttttttggtc ggggtattatc gtaagggtgt tggggggttt
 961 taggagtggg gtttgttttt ttttttttgg aggtagggtt ttcgtgagat cgatttttagg
 1021 gaagaagttg cgggaaaagt gttaggaggg ggttgaattt acgtagaggt tgttgaatcg
 1081 ggtttcgtag aagtgtaggg gattcgttag ttttattacg gttgagtttt cgtcgtcgtt
 1141 tttttgtagg agttggtttt tttacgattt ttcgtgtggg aagagttcgt ttgggtgtag
 1201 cgtcgcgggt cgtaatatta gtaacggtag tagtagtagt attggtaacg acgatagtat
 1261 cggtcgttcg gttattcgtt ttttttttat gttcgttcgg tcgtgcgttt attcgttgta
 1321 taacgcgttt cgtttcgggt tttagtttat ttttcgcgtc gcgttagttt cgaatttgga
 1381 ttttcgcggg cgtttgggcg gggcgggatt ttaggtttat ttagtaagtt aattggttga
 1441 ggttttcggt tggggattaa ttatcgggtt tgagaaagtt cggtagtggt tattatatatt
 1501 ggttttcgtt aattttttta aggtagcgtt cgttggagta gcggggttg cggggtaaaa
 1561 gtttttggtt aggggtgttt ggagttgttt tttttatttc gtttttaggg agttttcggg
 1621 ttattttttt attcgggttg tttcgcgtt ttaaggagt tttatttttc ggattaaatg

1681 gttcgttaagg tttagggtag cggcgttgta ggagatgagt ttagcgtaaa gggaatttcg
 1741 tagcggcgag tcoggttggt ggtttcgcgc ttgtggtttt aataggttg tagggcgcg
 1801 gcgggtggcg gggttgcggt atgagttttg ttttttggtt tggggtttcg gcggttttg
 1861 gttttggagg ttgtgtatc ggttcgaaaa gtaaagggat attgtcgtgg ttttttcggt
 1921 cgtttcgttt tatttagaga cgttttgagg agaagcgagt tttgtacga aggtagagg
 1981 ttgattttta agttttggtt ttttttcgaa ggtcggtcgt tagggaagat ttggtattt
 2041 tttggaagta ttttttttcg ggaaaatcgt agtaggaaag attatgaaat attatttgt
 2101 gtgattcgtt tcgtttgggg agtaggatga ggtatttcgt ttggttatta ggtagaaagg
 2161 ggcgagtcgc ggggatggga agattttgat tttttgttca ttgttcggt cgtcggagat
 2221 gttttttttc gcggttacgg aggcggtaat ttgagttgtt tcgtaggatt ggaaatcgta
 2281 taatttcgaa attagttgcg taggagaagg ggaattttat ttattataaa ttttttttt

SEQ ID NO: 62

Sequenza metilata del gene NID2 (bottom strand), derivata da SEQ ID NO.12

1 agaggggatg tttatggtg atggggtttt tttttttttg cgtagttggt ttcgaggttg
 61 tcoggttttt agttttgcgg agtagtttag gttatcgttt togtggtcgc gggggagggt
 121 attttcgacg gtcgtagtaa tgggtaagag attagggttt tttatttttc gcgattcgtt
 181 tttttttggt tggttaattaa gcgggatgtt ttattttatt ttttaaocgg agcggattat
 241 atatagtagt attttatggt tttttttggt gcggtttttt cgggggaagg tatttttaga
 301 ggggtggttaa gtttttttta gcggtcgttt ttcgggaggg ggatagaatt taggagttag
 361 ttttttggtt tcgtataaag gttcgttttt ttttagggcg tttttgggtg gagcgaagcg
 421 gtogagggga ttacgataat gtttttttgt ttttcggatc gatggttagg ttttagagt
 481 taggagcgtt cgggatttta gggtagggag taaagtttat atcgtaattt cgttattcgt
 541 tcgcgttttg ttagtttggt ggggttatag cgcgtaggtt agtagtcgta ttcgtcgttg

601 cgggggttttt tttgcgttga gtttattttt tgtaacgtcg ttgttttaaa ttttgcgggt
 661 tatttggttt cgggggtggg gttttttggg ggtcgcgggg tagttcggat gagaggatga
 721 ttcgggagtt ttttgggggc ggagtgaag gggtagtttt aggtagtttt ggtaggagt
 781 ttttatttcg ttagtttcgt tgtttttagcg gtogttgttt tagaaaagtt aacgagaatt
 841 agatgtggtg gttattgtcg aattttttta gagtcgggtga ttggttttta gtcgagggtt
 901 ttagttaatt agtttgttg gtgggtttgg agtttcgttt cgtttaggcg ttocgggaga
 961 tttaggttcg aggttgccgc ggcgcggaga gtgggttga ggtcggggcg ggacgcgtg
 1021 tgtagcgggt aagcgtaagg tcgagcgagt atggaggggg atcgggtggt cgggcggtcg
 1081 gtgttgcgt cgttattagt gttattgttg ttgtcgttgt taatgttcg ggtcgcggcg
 1141 ttgtatttag acgagttttt tttatacggg gagtcgtggg gggattagt tttgtaggaa
 1201 ggcgacgac aaagttagt cgtggtgaag ttggcgaatt ttttgtattt ttacgaagtt
 1261 cgatttagta atttttacgt aagttagtt tttttttggt atttttttcg tagttttttt
 1321 tttggggtcg gttttacgga aattttgttt ttagagggga ggaaatagat tttatttttg
 1381 gagtttttta gtatttttgc ggtggtattc ggttagagag cgatgtcgtt gttgtttcg
 1441 ttgttgtagg ggagtaagaa tgatttgag gggagagtaa gaattgttcg tagttacgta
 1501 cgcgttttag gtagaaaagg tggcgttgtt agggcgggta gcgggttttg tagttaggat
 1561 cgcgagaagg ttgtgttcgt ttgoggagt ggggtgtttt ttttttagat ttggaggttt
 1621 ttttttcgag gatatggggt ttcggggttg tgaggggagt gagaagatag gtgaacgagt
 1681 ttagagggtt ttggatttat tgtagccgg agttgggata gtogtaaaag ttgcgtttgt
 1741 ttttttgaat ttagattttt tggtagtggt ggaaggagag agaggttttt tgtttaagtt
 1801 agtttttttt tttttttcg cgaaagggt gogtttttgg gtttgagcga ttgtattttt
 1861 ttgttttttt ttttttttta ggtgggtatt aacggtatta tttttattta ggattttttt
 1921 agggaaacgt agtatgtgga ttatgatttt tttatcgatt tttcggttat cgtttttttt
 1981 ttggcggata tcgatacgag ttacggtaga ggtcagtttt tgtatcgaga ggatattttt
 2041 ttcgtagtgt tgggtttggt cgttcgttat gtgcgcgttg gtttttcgcg ttttcgcgtt

2101 tttattttta ttacgtttt ttggttatt tgggagtagg taggcgttta cgaggagggt
 2161 aagcgcgggg cgttggtttt gggagaggta agtgattagg gatatttgat tgttgaggaa
 2221 attgaaggat gggtttaaatt ttggggtag cgatttaggg attggttcgg agttgttttt
 2281 gagttttatt ttgcgttgaa ttgattttg gaggtagtag ggtaggagtg gtttgggagt

SEQ ID NO: 63

Sequenza non metilata del gene NID2 (top strand), derivata da SEQ ID NO.12

1 atttttaagt tatttttagtt ttgtgtttt taaggtagg tttagtgtaa gagtaggttt
 61 agaaataatt ttgagtagt tttgggttg ttgttttaga atttaagttt attttttaat
 121 ttttttagta gttaaatatt ttggttatt ttttttttt gagggtagtg tttgtgttt
 181 gatttttttg taagtgttta ttgttttta ggtggttagg aagggtgagg tgggggtaaa
 241 gtgtgtagag tgtgggaagt tagtgtgtat atagtgggtg gttaggttta gtattgtggg
 301 ggagggtgtt ttttggata ggatttggtt ttgttgttg tttgtgtga tgtttgttag
 361 aaaaggggtg atggttgga agttggtgg gaaattatag tttatatatt gtgttttttt
 421 ggggaagttt tgagtggaga tgatgtgtt ggtgtttatt tgggagagga gagggataaa
 481 aaggtagatg ttgtttaagt ttaaggatgt ttttttttg ttagggagg gaagggaatt
 541 gatthagga aaaagttttt ttttttttt ttattggta gggagtttg atttagggaa
 601 ataagtgtaa tttttgtgat tgttttagt ttgtgttga gtaggttag gggttttaaa
 661 atttgttat ttattttttt attttttta taattttga gttttatgtt tttggagagg
 721 aagtttttag gtttgaagag ggaatatttt agtttttag atgggtatag ttttttgtg
 781 gttttaattg taaagtttgt tgggtgttt agtaatgta tttttttgt tgggatgtg
 841 tatgtggtg tgaataattt ttgtttttt ttttaggta ttttgtttt tttatagtag
 901 tgggtaggt agtggattg ttttttggt gggattatt gtaagggtg tgggggggtt
 961 taggagtggt gtttgtttt ttttttttg aggtagggtt ttgtgagat tgattttagg

1021 gaagaagttg tgggaaaagt gttaggaggg gggtgaattt atgtagaggt tgttgaattg
 1081 ggttttgtag aagtgtaggg gatttgtag ttttattatg gttgagtttt tgttgttgtt
 1141 tttttgtagg agttggtttt tttatgattt tttgtgtggg aagagtttgt ttgggtgtag
 1201 tgttgtggtt tgtaatatta gtaatgtag tagtagtagt attggtaatg atgatatgat
 1261 tgggtgtttg gttatttggg ttttttttat gtttgtttgg ttgtgtgttt atttgttgta
 1321 taatgtgttt tgttttgggt tttagtttat tttttgtgtt gtgttagttt tgaatttggg
 1381 tttttgtggg tgtttgggtg ggggtggatt ttaggtttat ttagtaagtt aattggttga
 1441 ggtttttggg tggggattaa ttattgggtt tgagaaagt ttgtagtggt tattatattt
 1501 ggtttttgtt aattttttta aggtagtggg tgttggagta gtgggttgg tggggtaaaa
 1561 gtttttgggt agggttgttt ggagttgttt tttttatttt gtttttaggg agtttttggg
 1621 ttattttttt atttgggttg ttttgggtt tttaaggagt tttatttttg ggattaaatg
 1681 gtttgaagg tttgggtag tgggtgtgta ggagatgagt ttagtgtaaa gggaaatttg
 1741 tagtggtag tgtggtgtt gggttgtgtg ttgtggtttt aataggttgg taggggtgtg
 1801 gtgggtgggt ggggtgtggt atgagttttg ttttttgttt tggggttttg ggtgtttttg
 1861 gttttggagg tttggttatt gggttgaaaa gtaaagggat attgttgtgg ttttttggg
 1921 tgttttgttt tatttagaga tgttttgagg agaagtgagt ttttgtatga aggtagaggg
 1981 ttgattttta agttttgttt ttttttgaa gggtgggtgt tagggaagat ttggttattt
 2041 tttggaagta tttttttttg ggaaaattgt agtaggaaag attatgaaat attatttgtt
 2101 gtgatttgtt ttgtttgggg agtaggatga ggtattttgt ttggttatta ggtagaaagg
 2161 ggtgagttgt ggggatggga agattttgat tttttgttta ttgttgtggt tgttggagat
 2221 gttttttttt gtggttatgg aggtggtaat ttgagttgtt ttgtaggatt ggaaattgta
 2281 taattttgaa attagttgtg taggagaagg ggaattttat ttattataaa tttttttttt

SEQ ID NO: 64

Sequenza non metilata del gene NID2 (bottom strand), derivata da SEQ ID NO.12

```
1 agaggggatg tttatggtgg atggggtttt ttttttttg ttagttggt tttgaggttg
61 tgtggttttt agttttgtgg agtagtttag gttattgttt ttgtggttgt gggggagggg
121 atttttgatg gttgtagtaa tgggtaagag attagggttt tttattttt gtgatttgtt
181 tttttttgtt tggtaattaa gtgggatggt ttattttatt ttttaaatgg agtggattat
241 atatagtagt attttatggt tttttttgtt gtggtttttt tgggggaagg tatttttaga
301 ggggtggttaa gtttttttta gtggttggtt tttgggaggg ggatagaatt taggagttag
361 ttttttgttt ttgtataaag gtttgttttt ttttaggggtg tttttgggtg gagtgaagtg
421 gttgagggga ttatgataat gtttttttgt tttttggatt gatggttagg ttttagagt
481 taggagtgtt tgggatttta gggtagggag taaagtttat attgtaattt tgttatttgt
541 ttgtgttttg ttagtttgtt ggggttatag tgtgtaggtt agtagttgta tttgttgtt
601 tggggttttt tttgtgttga gttattttt tgtaatgttg ttgttttaa tttgtgggt
661 tatttggttt tgggggtggg gttttttggg ggttggtggg tagtttgat gagaggatga
721 tttgggagtt ttttgggggt ggagtgaag gggtagtttt aggtagtttt ggttaggagt
781 tttatttttg ttagttttgt tgttttagtg gttgtgttt tagaaaagtt aatgagaatt
841 agatgtggtg gttattgttg aattttttta gagtgtgtga ttggttttta gttgaggggt
901 ttagttaatt agtttggttg gtgggttttg agttttgttt tgtttagggtg tttgtggaga
961 tttaggtttg aggttggtgt ggtgtggaga gtgggttggg ggttgggtg ggatgtgttg
1021 ttagtggtt aagtgtatgg ttgagtgagt atggaggggg attgggtggt tgggtggttg
1081 gtgtgttgtt tgttattagt gttattgttg ttgttgttgt taatgttgtt ggttgtggtg
1141 ttgtatttag atgagttttt tttatatggg gagtgtggg gggattagtt tttgtaggaa
1201 ggtgatgatg aaagtttagt tgtggtgaag ttggtgaatt tttgtattt ttatgaagtt
1261 tgatttagta atttttatgt aagtttagtt tttttttggt attttttttg tagttttttt
1321 tttggggttg gttttatgga aattttgttt ttagagggga ggaaatagat tttatttttg
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1381 gagtttttta gtatttttgt ggtggtattt ggtagagag tgatgttgtt gtttgttttg
 1441 ttgtttagg ggagtaagaa tgatttgag gggagagtaa gaattgttg tagttatga
 1501 tgtgttttag gtagaaaagg tgggtgtgtt aggggtggtta gtgggttttg tagttaggat
 1561 tgtgagaagg ttgtgtttgt ttgtggagtt ggggtgtttt ttttttagat ttggaggttt
 1621 tttttttgag gatattgggt tttgggttg tgaggggagt gagaagatag gtgaatgagt
 1681 tttagggttt ttggatttat tgtagtgttg agttgggata gttgtaaaag ttgtgtttgt
 1741 ttttttgaat ttagattttt tggtagtggt ggaaggagag agagggtttt tgtttaagtt
 1801 agtttttttt tttttttgtg tgaaagggtta gtgttttttg gtttgagtga ttgttatttt
 1861 ttgtttttt ttttttttta ggtgggtatt aatggtatta tttttattta ggattttttt
 1921 agggaaatgt agtatgtgga ttatgatttt ttattgatt ttttggttat tgtttttttt
 1981 ttggtggata ttgatatgag ttatggtaga ggttgagttt tgtattgaga ggatattttt
 2041 tttgtagtgt tgggttttgt tgtttgttat gtgtgtgttg gttttttgtg ttttgtgtgt
 2101 tttattttta tttatgtttt tttggttatt tgggagtagg taggtgttta tgaggaggtt
 2161 aagtgtgggg tgttgttttt gggagaggta agtgattagg gatatttgat tgttgaggaa
 2221 attgaaggat gggtttaaat tttgggtag tgatttaggg attggttttg agttgttttt
 2281 gagtttattt ttgtgttgaa ttgattttg gaggtagtag ggttggagtg gtttgggagt

SEQ ID NO: 65

Sequenza metilata del gene PNU2L2 (top strand), derivata da SEQ ID NO.13

1 tgggggggtt tttttattg atttttaaag tagttaggat attgattttt tttgataaag
 61 agatttttat agaggagttt gatttgaatt agttagtta agaatttggg tggtttgagg
 121 gtaggggttt gaggatgggg attttggtga tgggtgttg ggtggagggg ggtgtgtttt
 181 taattagaga agaatagtgt ggtttcggat aagtcgaaag tattaagatt ttagttgaat
 241 tgaagttagt gtgtggtaga aaaagttttt ttagtttttg ttgggttttg tattggggat

301 aattagtgtt ttttaggtt tttatttta gaataattag tttatttatt tattatgtg
 361 ggagaagtgg gggaaaggaa taaggatagg ttttttttag gaattttcgt tgggggaagg
 421 ttataggggtt attaagattt tttggttaag gtttgggtt ttgtttggat atagtttgag
 481 agataagagt ttaaaagggtt ggttttatta aatttgaaag tttttgattt taggggggtt
 541 agggagtttt tttttggagg ttgtttatag ttaatatattt gttttatagg ttggttagtg
 601 attttttttt gttgtaaata gtttgtgtt tttaatgtag agggtaaagg ttgtgggtt
 661 tttagattga gaggagagga cgggtgtgtg tttagagggt ttgatattt tacgttatt
 721 gtggtagggt ttggttaata tgttaggaga agagattata ttttagagt taagtattaa
 781 aaatttttta tttgggtatt tttaggagg ttggttggg ttattgttt ttttttatt
 841 ataggtaggt ggtagggatg ggtgttttta tttttatata ttgtagagg atttgggtg
 901 tggggaggga gcgggtagat gtagtaggag gaagttttt tatggtttt gtttagggg
 961 tagaaggata tagttaattt tatcggtag gatggtgggt tgggttttt ttttttggg
 1021 gtttttttg gaaagggtta gggattgtt tttgttaggt tgagggaagg aggggttaag
 1081 cgttttatta ttttttttg tgaggtaggt agtgtttg ggttttttt gcgttttta
 1141 aatgaagtgt gtattggtt ttgtgttag ggtagggtgg tgaggaggg ttatttaggt
 1201 aaaagttgat ttaggcgagg atgggattt ttattttcgt ttattattga tgcgttttt
 1261 ttagtttaat aagcgcgtt ttattagcgg gtatttttt tagtacggat ttatttttt
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 1381 aaatttggga gtagcgagt atcgtcgtt ggtagtagtg ttagtttg ttgggggtg
 1441 gcgacgggt tttttattt gtatagtcgt ggttcgggt tcgagggtt tttgtagtt
 1501 gttcgggagt gatcggttt gogtatttta gttttgttt gcgttcgtt gttgtttgt
 1561 ttgttttatt atggtttag ttggggcgg gtoggtttc tttgtagt gttagagga
 1621 ttgcggcgg agttgcggt cgatttcgta gtatcgtcgt tattttttc tttttcga
 1681 tgcggatcgt tgcgggagg gttcggcgt gggggcggag cagtcggtt tggggcggg
 1741 gtttgtatt tagttgttag cgggtcgt gcgaagtgg tcgggtgt tagttgggg

1801 tcggtttcgt agttcgcgat tttcggatgt gtagagtatg tagagttatt taggatagag
 1861 cggggagttt tagtttttcg ttttcgggtt gtattggata tttggttttt ttttatttag
 1921 ttttagaagt atcgcggggg tttgagttag tttttaaaga aaaaggaacg gtttatttga
 1981 tattttttaga aggagacgtt tttggaaggg agggggagtt gttgtatgag ttggagagaa
 2041 attattagtt atcgtaggga ttttaataagg tttttataaa gtgaattcgg ttgatgttta
 2101 agttattgat tattatattt tttaaagggg aatgtagat attttttatt tttattcgag
 2161 ttgtgaaggg gtaggttaga gtaggtttt ttttatgtag tatttttagat tatagattaa
 2221 agaggatttg ttgtataaat tatttaggga ttatttggtg gaaggataga agggagaggt
 2281 tgagtgggtt taatagggcg gtgtagtttt gtttggtggt gaggatagtg gggaggggtt
 2341 taggagaggt taatttaggt gtgatttagg tttagttggg ttattttttt tttgataagt
 2401 aggtgagatg tcgaggggat agatgtttta gaagtttttag aggtattaga ggtttagaaa
 2461 ggtttagagta gtagttaggg gaaggtagat gtttggtagg tgggggtgtg gtgagggatt
 2521 ttttgagtta agtaggggtt gagttgggtt gggttttggt gaagttttta gaagtatgtt
 2581 tttttttgat tcgtaagatt ttttttttaa tggtaggttg attgggtttt gtttgaatat
 2641 attttggata aaattgagat

SEQ ID NO: 66

Sequenza metilata del gene PNU2L2 (bottom strand), derivata da SEQ ID NO.13

1 gtttttagttt tgtttagagt gtatttaggt agaagttagt tagtttgta ttgagagagg
 61 ggttttgcgg gtttaggaagg gatatgtttt tggaaatttt tataggaggt tgattagttt
 121 agattttatt tagtttaggg aattttttat taatatttta tttattaagt atttgttttt
 181 ttttagttgt tgttttgatt ttttgagtt tttaatgttt ttaaagtttt tggggatatt
 241 gttttttcgg tattttattt gtttggttaga ggaagagtgg tttagttggg tttgggttac
 301 gtttgggttg gttttttttg aggttttttt tattgttttt agttataggt aaggttatat

361 cgttttgtta aagttattta gttttttttt tttatttttt tagtagatga tttttggata
 421 atttgtgtag taaatttttt ttaatttgta atttggggta ttgtatgaag ggaatttggt
 481 tttaatttgt ttttttatag ttccgggtgga ggtggagaat atttgatatt ttttttagg
 541 aggtgtagtg attagtaatt tgggtattag tcggatttat ttgtgaaaa tttgttgaa
 601 tttttcggtt aattaatggt ttttttttaa tttatgtagt aatttttttt ttttttaaa
 661 ggcgtttttt tttgggatg tttagtggtt cgtttttttt tttttgggaa ttggtttaag
 721 ttttcgggtt gtttttgag ttgagtaaaa aagagttagg tgttagtgt agttcgggga
 781 cgaggagttg aggtttttcg tttgttttg ggtgatttg tatattttgc gtattcggg
 841 gtccgggtt gcgagtcgg ttttagttg ggtatttcga tttatttcgc gtcggtatcg
 901 ttagtagttg aggtataggt ttctgttcgg ggtcgattcg ttctgttttc gtcgctgggt
 961 ttttttcgta gcggttcgta ttccggggagg cgggaggggt acggcggtgt tgcgagtcg
 1021 gcgctagtt tcgtccggg tcgttcgggc gttgtttagg cggagtcggt ttcttcggg
 1081 ttgtagttat ggtaaggtag gtaggtaggc gggcgggcgc ggggtagggt tggggtcgt
 1141 agggtcggtc gttttcgggc ggtgttaagg ggattccgg tatcgtagtc gcggttgtgt
 1201 aggggtggag gcgtcgtcgt cggtttcggg tataggttgg tattgtgttc gggcggcggt
 1261 gcgtcgttgt ttttaagttt tttttttga gtagttacgg agtgggcgtt aatttttggg
 1321 tgatgtttgc gttttaggac gaaggggtgg gttcgtgttg agggaggtgt tcgttggtgg
 1381 agacgcgttt gttgggttg ggaaggcgta ttagtaataa gcggaggtga gggtttttat
 1441 ttctgtttgg gttagttttt atttgagtaa tttttttta tttatttatt ttgggtatag
 1501 gggtagtat taattttatt tggaaaacgt agaggaggtt tataaatatt gttgtttta
 1561 ttaggagggg tggtaaagac tttgggtttt tttttttta gtttgataag gggtagtttt
 1621 tggttttttt ttaaagggtt tttagagagg gggaggttta gtttattatt ttgttcggtg
 1681 ggattagtta ttttttttg ttttgggat aggaattatg gaaagtgtt ttttgttgt
 1741 atttattcgt tttttttta ttagttaggt tttttgtag tgtgtggggg tgggggtatt
 1801 ttttttgtt atttgttgt agtgggaaga gaaatagtaa ttttagttag ttttttggg

1861 ggtgttttagg taggaagttt ttgatgtttg gttttgaaga tgtaattttt ttttttgata
 1921 ttgttgtag agtttgttat aaataacgta aggggttag gatttttagg ttatatatcg
 1981 tttttttttt ttagtttga agttttatag tttttgtttt ttgtattggg ggatataaat
 2041 tgtttatagt agggggggat tattgattag ttgtggggc gggatgttg ttgtggtag
 2101 tttttagaag ggagttttt ggttttttg ggattagaag ttttaggtt tggtagggtt
 2161 aatttttttg gttttgttt ttttaagttg ttttaggtag aggtttaagt tttggttagg
 2221 aagttttggt gattttgtga tttttttta acgggggtt ttgagagagg tttgtttta
 2281 tttttttttt ttattttttt ttatatggtg gatggatgga ttgattgtt tagggatgga
 2341 agtttaggga agtattgatt gtttttagtg ttaagtttag taggggttag aggggtttt
 2401 ttgtttatat attaatttta gtttagtga ggttttggtg ttttgggtt gttcgaggtt
 2461 atattgtttt tttttaatta aagatatatt tttttttatt ttaattatta ttattaaagt
 2521 ttttattttt aggtttttgt ttttaagtta gtttaagttt taggttgatt ggttagatt
 2581 agattttttt atgagggtt tttgttaaa ggaggtagt gttttagtg ttttgggaat
 2641 tagtggggga gattttttta

SEQ ID NO: 67

Sequenza non metilata del gene PNU2L2 (top strand), derivata da SEQ ID NO.13

1 tgggggggtt tttttattg atttttaag tagtaggat attgatttt tttgataaag
 61 agatttttat agaggagttt gatttgaatt agttagtta agaatttggg tggtttgagg
 121 gtaggggtt gaggatggg attttggga tgggtgttg ggtggaggg ggtgtgttt
 181 taattagaga agaatagtgt ggttttgat aagttgaaag tattaagatt ttagttgaat
 241 tgaagtagt gtgtgtaga aaaagtttt ttagttttg ttgggtttg tattggggat
 301 aattagtgtt ttttaggtt tttattttta gaataattag tttatttatt tattatgtg
 361 ggagaagtgg gggaaaggaa taaggatagg ttttttttag gaattttgt tgggggaagg

421 ttatagggtt attaagattt ttgggtaag gttggggtt ttgtttggat atagtttgag
 481 agataagagt ttaaaagggt gggtttatta aatttgaaag tttttgattt taggggggtt
 541 agggaggttt tttttggagg ttgtttatag ttaatatatt gttttatagg ttggttagtg
 601 attttttttt gttgtaata gtttgtgtt tttaatgtag agggtaaagg ttgtggggtt
 661 tttagattga gaggagagga tgggtgtgtg tttagagggt ttgatattt tatgtattt
 721 gtggtagggt ttggttaata tgttaggaga agagattata tttttagagt taagtattaa
 781 aaatttttta ttgggtatt tttaggagg ttggtgggg ttattgttt tttttttatt
 841 ataggtagggt gtaggggatg ggtgttttta tttttatata ttgtagaggg atttgggttg
 901 tggggagggg gtgggtagat gtagtaggag gaagttttt tatggtttt gttttagggg
 961 tagaaggata tagttaattt tattgggtag gatgggtggg tgggttttt ttttttggg
 1021 gtttttttgg gaaagggtta gggattgtt ttgttaggt tgagggaagg aggggttaag
 1081 tgttttatta ttttttttgg tgaggtaggt agtgtttgt gggtttttt gtgttttta
 1141 aatgaagtgt gtattggtt ttgtgttag ggtagggtgg tgaggaggg ttatttaggt
 1201 aaaagtgtat ttaggtgagg atggggattt ttatttttgt ttattattga tgtgttttt
 1261 ttagtttaat aagtgtgtt ttattagtgg gtatttttt tagtatggat ttatttttt
 1321 gtttttagagt gtaggtatta tttagggtt ggtgtttatt ttgtggtgt ttagagggaa
 1381 aaatttggga gtagtgatgt attgtgttt ggtagtagtg ttagtttgt ttgggggtg
 1441 gtgatgggtt tttttattt gtatagttgt ggtgtgtgt ttgtgggtt tttgtagt
 1501 gtttgggagt gattggttt gtgtatttta gttttgttt gtgtttgtt gttgtttgt
 1561 ttgttttatt atggtttag tttgggtgg gttggtttt ttggatagt gtttgagtga
 1621 tttgtgtgt agttgtgtt tgattttgta gtattgtgt tattttttt ttttttgag
 1681 tgtggattgt tgtgggagg gtttgggtt ggggtggag tgagttggt ttgggtggg
 1741 gtttgtatt tagttgttag tgggtgtgt gtgaagtgg ttgggtgtt tagttgggg
 1801 ttggttttgt agttgtgat tttggatgt gtagagtat tagagttatt taggatagag
 1861 tggggagtt tagtttttt ttttgggtt gtattggata ttggttttt tttatttag

1921 ttttagaagt attgtggggg tttaggttag tttttaaga aaaaggaatg gtttatttga
 1981 tttttttaga aggagatggt ttggaaggg agggggaggt gttgtatgag ttggagagaa
 2041 attattagtt attgtagggg ttaataagg tttttataaa gtgaatttgg ttgatgttta
 2101 agttattgat tattatattt ttaaaagggg aatgttagat attttttatt tttatttgag
 2161 ttgtgaaggg gtaggttaga ggtaggtttt tttatgtag tatttttagat tatagattaa
 2221 agaggatttg ttgtataaat tatttagggg ttatttgttg gaaggataga agggagaggt
 2281 tgagtgggtt taatagggtg gtgtagtttt gtttgggtt gaggatagtg gggaggggtt
 2341 taggagaggt taatttaggt gtgatttagg tttagttggg ttattttttt ttgataagt
 2401 aggtgagatg ttgaggggat agatgtttta gaagtttttag aggtattaga ggtttagaaa
 2461 ggtttagagta gtagttaggg gaaggtagat gtttggtag tggggtgttg gtgagggatt
 2521 ttttgagtta agtaggggtt gagttggta ggttttgtg gaagttttta gaagtatgtt
 2581 ttttttgat ttgtaagatt ttttttttaa tggtaggttg attggttttt gtttgaatat
 2641 attttggata aaattgagat

SEQ ID NO: 68

Sequenza non metilata del gene PNU2L2 (bottom strand), derivata da SEQ ID NO.13

1 gtttttagtt tgtttagagt gtatttaggt agaagttagt tagtttgta ttgagagagg
 61 ggttttgttg gttaggaagg gatatgtttt tggaaatttt tataggagtt tgattagttt
 121 agattttatt tagtttaggg aattttttat taatatttta tttattaagt atttgttttt
 181 ttttagttgt tgttttgatt ttttgagtt ttaatgttt ttaaagtttt tggggtattt
 241 gtttttttgg tattttattt gtttgttaga ggaagagtgg tttagttggg tttgggttat
 301 gtttgggttg gtttttttgg aggttttttt tattgttttt agttataggt aaggttatat
 361 tgttttgta aagttattta gttttttttt tttatttttt tagtagatga ttttggata
 421 atttgttag taaatttttt ttaatttgta atttggggtt ttgtatgaag ggaatttgtt

481 ttttaatttgt ttttttatag tttgggtgga ggtggagaat atttgatatt ttttttagg
 541 aggtgtagtg attagtaatt tgggtattag ttggatttat tttgtaaaa tttgttgaa
 601 tttttgtggt aattaatggt ttttttttaa tttatgtagt aatttttttt tttttttaa
 661 ggtgtttttt tttgggatg ttaggtgggt tgtttttttt ttttgggaa ttggttaag
 721 tttttgtggt gtttttgag ttgagtaaaa aagagttagg tgttagtgt agtttggga
 781 tgaggagtgt aggtttttt tttgttttg ggtattttg tatatttgt gtatttggg
 841 gttgtgggtt gtgaggttg ttttagttg ggtattttga tttatttgt gttggtattg
 901 ttagtagttg aggtataggt tttgttttg ggttgatttg tttgttttt gttgtgggt
 961 ttttttgtta gtggtttgta tttggggagg tgggagggtg atggtggtgt tgtgaggtg
 1021 gtgtgtagtt ttgttggg ttgtttgggt gttgttagg tggagtgggt tttgttggg
 1081 ttgtagttat ggtaaggtag gtaggtaggt ggtgggtgt gggtaggggt tgggtgtgt
 1141 aggggtgggt gttttgggt ggttgaagg ggaattgtg tattgtagt gtggttgtgt
 1201 aggggtgggag gtgttgtgt tggtttggg tataggttg tattgtgtt ggggtgggt
 1261 gtgttgtgt ttttaagttt tttttttga gtagttagg agtgggtgt aatttttgg
 1321 tgatgttgtt gtttaggat gaaggggtg gttgtgttg agggaggtgt ttgttgggt
 1381 agatgtgttt gttgggttg ggaagggtga ttagtaataa gtggaggtga gggttttat
 1441 tttgttttg gttagtttt atttgagtaa tttttttta tttatttatt ttgggtatag
 1501 gggtagtat taattttatt tggaaaatgt agaggaggt tataaatatt gttgtttta
 1561 ttaggagga tggaagatg tttgttttt tttttttta gttgataag gggtagttt
 1621 tggtttttt ttaaagggt tttagagag gggaggtta gttattatt ttgttgggt
 1681 ggattagta ttttttttg ttttgggat aggaattat ggaagtttt ttttgtgt
 1741 atttatttgt tttttttta ttagttagg tttttgtag tgtgtgggg tgggggtatt
 1801 ttttttgtt atttgttgt agtgggaaga gaaatagtaa ttttagttag ttttttggg
 1861 ggtgttagg taggaagtt ttgatgttg gttttgaaga tgtaatttt tttttgata
 1921 ttgtttagg agtttgtat aaataatga aggtgttag gatttttagg ttatatattg

1981 tttttttttt ttagtttga agttttatag tttttgtttt ttgtattggg ggatataaat
 2041 tgtttatagt agggggggat tattgattag ttgtgggggt gggatgttg ttgtgggtag
 2101 tttttagaag ggagtttttt gggttttttg ggattagaag tttttagggt tggtaggggt
 2161 aatttttttg gttttgttt ttttaagttgt gtttaggtag aggtttaagt tttgggttag
 2221 aagttttggt gattttgtga ttttttttta atgggggttt ttgagagagg tttgttttta
 2281 tttttttttt ttattttttt ttatatggtg gatggatgga ttgattgttt tagggatgga
 2341 agtttaggga agtattgatt gtttttagtg ttaagtttag taggggttag aggggttttt
 2401 tttgttatat attaatTTTA gtttagttga ggttttggtg tttttggttt gtttgaggtt
 2461 atattgtttt tttttaatta aagatatatt tttttttatt ttaattatta ttattaaagt
 2521 ttttattttt aggtttttgt ttttaagtta gtttagtttt taggttgatt ggtttagatt
 2581 agattttttt atgagggttt ttttgtaaa ggaggtagt gtttagttg tttgggaat
 2641 tagtggggga gattttttta

SEQ ID NO: 69

Sequenza metilata del gene PRPH (top strand), derivata da SEQ ID NO.14

1 aggtataggt tgtaagttag atttattagt cgtttttata ttttaaggagg taaaagaatg
 61 gacgggtacg gagatttttag aggogaagta agttgttagc gtttttggtt aggtttcgtt
 121 ttgttcggtt tagtttcgat ttogttttgt ttogtttttag tagttttatt ttatocggtt
 181 tttttcgttt ttttagtagtt tcoggttaggt ggogatttcg atgtttaggg ttattttgac
 241 gttgaggagt ttttggtatt ttttaggtg tcoggttatt ttttttttta gttgtcgtag
 301 ttttttttcg agtcgcgtag cgttcgtttg gtagtttttc gtttttaggg ogaattgttt
 361 ttttagtttt ttttaattgtt tgagtagcgt ttogtttttg ggtaggagag tgggaaggggt
 421 tagttgtaga atattttatc gttcgttttt cgggttcgag cgcgtagttt cgtatttatc
 481 gtgtcogta gttcgtttat ttogtaogtt agattttgga tttggcgtcg ggatttcgtt

541 attttttggt tggtttggcg tagggtttcg tggtttcggt tggtagcgtc ggatagggtc
 601 gcgtattgag aagtgggggt aatttaggtt ttagtcggtt gggacgcgcg atattatatt
 661 agcgtttcgt ttcgtagggt ttttcgggtt ttgtattttg gatttgtatt attttttcgt
 721 tttttgtagg tttttcgcgc cgatgttttc gtattgcgcg cggatgtttt ttagcgttgt
 781 cgttagttcg ggttttatcg tggtttttat tttattttgt tgtatttgtt ggttttttat
 841 atttatttgt aggtttcgta gtttttacgc tcgggagtag gtagaggatg gatagcggcg
 901 taaattttac gcgggttacg tagttcgtgt atagaaaaga gaagaaacgt ttgaacgaat
 961 agaagtgggc gttagggagg gtagggcgta tagttttcgc ttttcgcggg cgcgagatta
 1021 gaggttaggt ttcggaggta tagtttcgtt gttcgtcgtt aggtggcgta agggtagggg
 1081 ttttaattatt tgtagattag ggtggagggg ttgcgtttat ttagtatcgt tttgattttt
 1141 agggcgatgt ttcgttttta ttcgttaggt ttagcgagat tattttataa ttttagaaat
 1201 cgtttttgat atcgggttta tttatttttt cgtgtagttt tttgaggaat ttaattttat
 1261 ttattagaga ttaatttttg cgttttaggt ttaggcggga tagagtggta tcgtttacgt
 1321 ttttcgaggg gtggtagtgg aggtttaaga taagttaggg gttgcgtaga ttaaggaagg
 1381 attagggttt tttgtttgt tttaggaggt atttgggtta tttttttttt ttocggttta
 1441 tcgatgttat ttttgatat tgagatcggg ggtagcggtg gggaggttga attcggagag
 1501 gggttcggat ttattttcgc gaagagtacg aggttggtt tcgcgttttt tcgtttgcgc
 1561 gttttttttt ttaatttgac ggggaagagc tgtagaggtt gaattgcggg gtcgtcgttt
 1621 agttcgtatt ttagatcgta cgttttttag gattcgggtta gaggttggtt tgttggttag
 1681 gattttaaat ggagggttga ggttggttaa tgggaattgt tcgtattgtt ttaacggat
 1741 tgggagttga aaagggggtt tttttattat ttaggggagg tatagatatt tatttttttt
 1801 atttttttaa atatttagag taaaggggta gcggggggtt tttggagttc gtgggtaggg
 1861 atgttggtcg tatatatttg ggttggttaag gggagttata tttttgggtt gttgatggag
 1921 aggggaagcg aggggaggtt agagtagtcg tttcgacggt cgtttcgatt tcgtttcgac
 1981 ggtagcgggt tagttttgtt ttttgatttt tgtttgagcg tcgttaggtt ttcgttagt

2041 tcgtcgcggtt ttatttgtat tcggttaoct tcgcggttta atagttttag ttttcgctgt
 2101 agttcgcgta gtttttgttg gtatagttag tcggcgcgcg tcggtttttg gtttcgggtt
 2161 tggtttagtt ttttcgctag ggtcgcggtt tgttgttta gaaagcgat ttttcgatg
 2221 aagttggcga agcggtcggt gagtttttgt agtttttgtt tttcgttgtt gcgcgtgggt
 2281 aggaattttt ggttgagggt ttcggttatg gagaagtcga ggcgtttcga gggtaggcgt
 2341 aggagggcgt tcgttttcgt tcgggggtta cggaagtgt ttaggcgtat cgaggagttc
 2401 ggggacgcgg agtttagtag gcggttgttg gagaagcggg agttggacga gtaggagaag
 2461 gtttcggggg atagtgggg cggtggatcg aaggtacggc ggtatgaggt ggagttgaag
 2521 tcggttcgga ggttcgacgg gtggtggtt attcggtta aggatgggt gttatcgttc
 2581 gtagagttag gtcgggggtt ggaaggagt cgtagatcgt tcgagggcgg ttttatagtt

SEQ ID NO: 70

Sequenza metilata del gene PRPH (bottom strand), derivata da SEQ ID NO.14

1 ggtataaag tcgtttcgta gcggtttcgg gttttttttt agttttcggg ttagttttgc
 61 gaacggtgat tgtttatttt tggtcgtaat gagttattat tcgtcgggtt ttcgggtcgg
 121 ttttagtttt attttatatc gtctattttt cggtttatcg tttttattat ttttcggggg
 181 ttttttttat tcgttttagtt ttcgtttttt tagtagtcgt ttgttggggt tcgcgttttc
 241 gagtttttcg gtgcgttttg gtagtttttc tagttttcga gcgggagcgg gcgttttttt
 301 gcgtttgttt tcggagcggt tcgatttttt tatggtcgag gtttttaatt aggagttttt
 361 ggttacgcgt agtaacgaga agtaggagtt gtaggagttt aacgacggt tcgttaattt
 421 tatcgagaag gtacgttttt tggagtagta gaacgcgggt ttgcgcgggg agttgagtta
 481 agttcggggg taggagtcgg cgcgcgtcga ttagttgtgt tagtaggagt tcgcgaggtt
 541 gcgcgagag ttggagttgt tgggtcgcga gcgtgatcgg gtgtaggtgg agcgcgaagg
 601 gttgcccggg gatttggcgg cgtttaagta gaggttaggg gtaggggttg ggtcgttgc

661 gtcgaggcga ggtcgaagcg gtcgtcgagg cgggtgtttt tgttttttt cgttttttt
 721 ttttattagt agtttaaggg tgtggtttt tttattaatt taggtgtgtg cgggtagtat
 781 ttttgtttac gggttttaag tgttttctg ttttttttg ttttgagtgt ttggggaggt
 841 gggagaagtg ggtatttgtg tttttttga gtaatgagga aattttttt ttagtttta
 901 gtctgttaga gataatgcgg ggttaattta ttagatagtt ttagttttt atttagagtt
 961 ttgggtagta gaatagttt taatcgatt ttgggggcg tgcggttggt ggtgcagtt
 1021 gggcgcgcat ttctagttt agtttttga cgttttttc gttaggttg aggaggagac
 1081 gcgtaacggg gaggaocgg agtataatt cgtgttttt cgttaaggtga gttcagttt
 1141 ttttctagt ttagttttt tatcttatt ttctattta gtatttagag gtggtatcgg
 1201 tgggcgcggg gagaagggg taatttagat gtttttgag gtagatagg aaggtttggt
 1261 ttttttttg tttcgtagt ttttaattt tttgaattt ttattgttat ttttgaagg
 1321 acgtggacga tgtattttg tttcttttg aattagagcg taagattgag ttttgatgg
 1381 atgagattga gttttttaag aagttgtacg aggaggttaag tgggttcggt attagggcg
 1441 gtttttgagg ttgtgggtg gttctgttg agttggcggg tggagcggag gtatcgttt
 1501 ggggattagg acgatgttg gtagacgtg tttttttatt ttagtttata ggtggttaga
 1561 tttttattt tgcgttatt ggcgggcggg agcggggttg tttttcgaa atttggttt
 1621 tggtttcgcg ttccggggg cgtagggtg tacgtttgt ttttttggc gttattttt
 1681 gttcgtttaa cgttttttt tttttttgt gtacgaattg cgtggttcgc gtggaattg
 1741 cgtcgttgtt tttttttgt ttgttttcg tctaggagt tgcgagattt gtaggtgagt
 1801 gtggagagtt agtaggtgta gtaggtggag gtggaagtta cgggaagtt caggttgacg
 1861 gtagcgttga gggatattcg ccgtagtac gagagtatcg tgcgaagaa tttgtaggag
 1921 gcggaggagt ggtataagtt taaggtgtaa ggtcgggag ggtttcgag gcgggacgtt
 1981 ggggtggtgt ccgcggttt agtcgattaa agtttgggtt atttttatt tttagtaocg
 2041 ggatttgttc gacgttgta atcggaatta caggttttg cgttaggtta agtaggagat
 2101 gaacgagttt ccacgttaga tttagagtt aacgtgcgag gtggacgggt tgcgcgtac

2161 ggtgagtacg aagttgcgcg ttccgggttcg gggagcggac gatgaaatgt tttgtaattg
 2221 gtttttttta tttttttatt ttagaacgag gcgttggtta ggtagttgag agagttggag
 2281 gagtagttcg ttttggaggc ggggggttat taggcggcgc ttgcgcggtt cgaggaggag
 2341 ttgcgatagt taaaagagga gatggcgcgg tatttgaggg agtattagga gttttttaac
 2401 gttaagatgg ttttggatat cgagatcggt atttatcgta agttgttga gggcaggag
 2461 agtcggtgag ggtggagttg ttggggcggg gtagggcggg gtcgggattg ggtcgggtag
 2521 ggcgggggtt gggtaggggc gttgataatt tgttcgttt ttaggatttt cgtgttcgtt
 2581 tatttttttg tttttttaaa tataaagaog attggtgagt ttggtttata gtttgtattt

SEQ ID NO: 71

Sequenza non metilata del gene PRPH (top strand), derivata da SEQ ID NO.14

1 aggtataggt tgtaagttag atttattagt tgtttttata ttttaaggagg taaaagaatg
 61 gatgggtatg gagatttttag aggtgaagta agttgttagt gtttttgttt aggttttgtt
 121 ttgttttggt tagttttgat ttgttttgt ttgttttag tagttttatt tttatttggt
 181 ttttttgttt ttttagtagt tgtggtaggt ggtgattttg atgtttaggg ttattttgat
 241 gttgaggagt ttttggatatt ttttaggtg ttgtgttatt tttttttta gttgtttag
 301 ttttttttg agttgttag tggttgtttg gtagtttttt gtttttaggg tgaattgttt
 361 ttttagtttt ttttaattgt tgagtagtgt ttgttttgg gtaggagag tggagggggt
 421 tagttgtaga atattttatt gttgttttt tgggtttgag tgtgtagttt tgtatttatt
 481 gtgttggtta gttgtttat ttgtatgtt agattttgga ttggtgttg ggatttgttt
 541 attttttgtt tgggttggtg tagggttttg tgggtttggt tggtagtgtt ggatagggtt
 601 gtgtattgag aagtgggggt aatttaggtt ttagttggtt gggatgtgtg atattatttt
 661 agtgttttgt ttgtaggtt ttttgggtt ttgtattttg gatttattt attttttgt
 721 ttttttagg ttttttggg tgatgttttt gtattgtgtg tggatgtttt ttagtgtgt

781 tgttagtttg gggtttattg tgggttttat tttatttgt tgtattgtt gggttttat
 841 atttatttgt aggttttgta gtttttatgg ttgggagtag gtagaggatg gatagtggg
 901 taaattttat gtgggttatg tagtttgtgt atagaaaaga gaagaaatgt ttgaatgaat
 961 agaagtgggt gttaggagg gtaggggtga tagtttgtg ttttgtggg tgtgagatta
 1021 gaggttaggt tttggaggta tagtttgtt gttgtgtt aggtgggtga agggggggag
 1081 ttttaattatt tgtagattag ggtggagggg ttgtgttat ttagtattgt ttgattttt
 1141 aggggtgatgt ttttgttta tttgttagt ttagtgagat tattttataa ttttagaat
 1201 tgtttttgat attgggttta tttattttt tgtgtagtt tttgaggaat ttaattttat
 1261 ttattagaga ttaattttg tgttttagt ttaggtggga tagagtggta ttgtttatgt
 1321 ttttgaggg gtggtagtgg aggtttaaga taagttaggg gttgtgtaga ttaaggaagg
 1381 attaggtttt ttttgtttgt tttaggagg atttgggtta ttttttttt tttgtgtta
 1441 ttgatgttat ttttgatat tgagattggg ggtagtggg gggaggtga atttgagag
 1501 gggtttggat ttattttgtg gaagagtatg aggttgtgtt ttgtgtttt ttgtttgtg
 1561 gtttttttt ttaatttgat ggaagagtg tgtagaggtt gaattgtggg gttgtgttt
 1621 agtttgtatt ttagattgta tgttttttag gatttggta gaggttgtt tgttgttag
 1681 gattttaaat ggagggtga ggttgttta tggaaattgt ttgtattgtt ttaattgat
 1741 tgggagtga aaaggggtt tttttattat ttagggagg tatagatatt tattttttt
 1801 attttttta atatttagag taaaggggtg gtgggggtg tttggagtt gtggtaggg
 1861 atgttgttg tatatattg ggttggttaagg gggagttata ttttgggtt gttgatggg
 1921 aggggaagtg aggggaggta agagtattg tttgatgtt tgttttgatt ttgtttgat
 1981 ggtagtgtt tagtttgtt tttgatttt tgtttgagt ttgttaggt tttgttagt
 2041 ttgttgtgtt ttatttgat ttggttatgt ttgtggtta atagtttag ttttgttgt
 2101 agtttgtgta gttttgttg gtatagtgg ttggtgtgtg ttggttttg gtttgggtt
 2161 tggtttagt ttttgttag ggttgtgtt tgttgttta gaaagtgtat tttttgatg
 2221 aagttggtga agtgggtgtt gagttttgt agttttgtt tttgttgtt gtgtgtggt

2281 aggaattttt ggttgagggt tttggttatg gagaagtga ggtgttttga gggtaggtgt
 2341 aggaggggtgt ttgtttttgt ttgggggta tggaagtgt ttaggtgtat tgaggagttt
 2401 ggggatgtgg agtttagtag gtggttgttg gagaagtggg agttggatga gtaggagaag
 2461 gttttggggg atagtggggg tgggtgattg aaggatatgt ggtatgaggt ggagttgaag
 2521 ttggtttgga ggtttgatgg gtggtggttt attgtggtta aggatgggta gttattgttt
 2581 gtagagttag gttgggggtt ggaaggagt ttagattgt tgtgaggtgg tttatagtt

SEQ ID NO: 72

Sequenza non metilata del gene PRPH (bottom strand), derivata da SEQ ID NO.14

1 ggttataaag ttgttttga gtggtttgtg gttttttttt agtttttgg ttagttttgt
 61 gaatggtgat tgtttatttt tggttgtaat gatttattat ttgttgggtt ttgggttgg
 121 ttttagtttt attttatatt gttgtatttt tggtttattg tttttattat tttttggggt
 181 ttttttttat ttgttagtt tttgtttttt tagtagttgt ttgttgggtt ttgtgttttt
 241 gaggtttttg gtgtgttttg gtagtttttg tagtttttga gtgggagtgg gtgttttttt
 301 gtgtttgttt ttggagtgtt ttgatttttt tatggttgag gtttttaatt aggagttttt
 361 ggttatgtgt agtaatgaga agtaggagtt gtaggagttt aatgattgtt ttgttaattt
 421 tattgagaag gtatgttttt tggagtagta gaatgtggtt ttgtgtgggg agttgagtta
 481 agtttggggg taggagttgg tgtgtgttga ttagttgtgt tagtaggagt tgtgtgagtt
 541 gtggtgagag ttggagttgt tgggttgtga gtgtgattgg gtgtaggtgg agtgtgatgg
 601 gttggtggag gatttgggtg tgtttaagta gaggttaggg ggtagggttg ggttgttgtt
 661 gttgaggtga ggttgaagtg gttgttgagg tgggtgtttt tgtttttttt tgtttttttt
 721 ttttattagt agtttaaggg tgtggttttt ttatttaatt taggtgtgtg tgggtagtat
 781 ttttgtttat ggtttttaag tgtttttgtt ttttttttg ttttgagtgt ttggggaggt
 841 gggagaagtg ggtatttgtg ttttttttga gtaatgagga aatttttttt ttagttttta

901 gtttgtaga gataatgtgg ggtaatttta ttagatagtt ttagtttttt atttagagtt
 961 ttgggttagta gaatagtttt taattggatt ttgggggggtg tgtggtttgg ggtgtgagtt
 1021 ggggtggtgat tttgtagttt agtttttgta tgtttttttt gttaggttgg aggaggagat
 1081 gtgtaagtgg gaggatgtgg agtataattt tgtgtttttt tgtaagggtga gtttgagttt
 1141 ttttttgagt ttagtttttt tattgttatt tttgatttta gtatttagag gtggtattgg
 1201 tgggtgtggg gagaaggggg taatttagat gttttttgag gtagataggg aagggttggg
 1261 ttttttttgg tttgtgtagt ttttaattta ttttgaattt ttattgttat tttttgaagg
 1321 atgtggatga tgttattttg tttgttttgg aattagagtg taagattgag tttttgatgg
 1381 atgagattga gttttttaag aagttgtatg aggaggttaag tgggttttggg attaggggtg
 1441 gtttttgagg ttgtgggggtg gttttgttgg agttgggtggg tggagtggag gtattgtttt
 1501 ggggattagg atgatgttgg gtagatgtag tttttttatt ttagtttata ggtgggttaga
 1561 tttttatttt tgtgttattt ggtgggtggg agtgggggtg ttttttgaa atttggtttt
 1621 tgggtttgtg ttgtgggggtg ttaggggttg tatgttttgt ttttttggg gtttattttt
 1681 gtttgtttaa gtgttttttt ttttttttgt gtatgaattg tgtggtttgt gtggaatttg
 1741 tgttgttgtt ttttttttgt ttgtttttgg ttgtaggagt tgtgagattt gtaggtgagt
 1801 gtggagagtt agtaggtgta gtaggtggag gtggaagtta tgggtgaagtt tgagttgatg
 1861 gtagtggtga gggatatttg tgtgtagtat gagagtattg ttgtgaagaa tttgtaggag
 1921 gtggaggagt ggtataagtt taagggttaa gagttgggag ggtttgtgag gtgggatgtt
 1981 ggggtggtgt tgtgtgtttt agttgattaa agtttgggtt atttttattt ttagtatgt
 2041 ggatttgttt gatgttgtta attggaatta tgaggttttg tgttaggtta agtaggagat
 2101 gaatgagttt tgatgttaga tttagagttt aatgtgtgag gtggatgggt tgtgtggtat
 2161 ggtgagtatg aagttgtgtg tttgggtttg gggagtggat gatgaaatgt tttgtaattg
 2221 gtttttttta tttttttatt ttagaatgag gtgttgttta ggtagttgag agagttggag
 2281 gagtagtttg ttttgaggtt ggggggttat taggtgggtg ttgtgtggtt tgaggaggag
 2341 ttgtgatagt taaaagagga gatggtgtgg tatttgaggg agtattagga gttttttaat

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2401 gttaagatgg ttttgatat tgagattgtt atttattgta agttgttggg gggtagggag
2461 agttggtgag ggtggagttg ttgggggtggg gtaggggtggg gttgggattg ggttgggtag
2521 ggtgggggttt gggtaggggt gttgataatt tgttttgttt ttaggatttt tgtgtttgtt
2581 tatttttttg tttttttaa tataaagatg attggtgagt ttggtttata gtttgtattt

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SEQ ID NO: 73

Sequenza metilata del gene PTGER3(top strand), derivata da SEQ ID NO.15

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1 aattttggaa ttatttatta ggagcggaga ttagtagatc gatagtacgt atatgatttt
61 tataagttga atggtcgttt cggtcgtgat gcggttttat tgggtattgg attgagatgt
121 cgtggttttg gttcggtagc gggatattag ggttttaatg gtggttaggt tgtaggaaaa
181 ggtgattgtt agcgttaaga gttttaggaa ggtaaaggta gaggcgaaga aaaggttgtt
241 ttagttatgc gaagagttag ttcgttgtt ttttcgttcg gtgttgatga agtattacgt
301 ttcgggttat tggacggtgt attggtttac gtttagtacc ggtagtaggg cgaaggcgag
361 tacggttagt tatacgtcga gtagtatagc gcgggtggta cgcgttttta tgtggttcgt
421 atattagtgc gcggttttga tggtagcgt tcgttcgacg gttatggcgt tggcgatgaa
481 taacgaggag agtcgaaaa tagttatggt tagttcgaaa aaggtgtaga gtcgtttcga
541 cgggtcgatg tgtttttaac gttgtttgga taggtatacg acgatgacga tcgggggtgt
601 gagaagttgt tcgattaggt cggtagcgt tagttagtcg atgtatagta ggaaggattt
661 tttgcgtttg ttttttcggc gtcggtagtt gcgcgatacg agtagtatgg ttagtgcggt
721 gtttacgaaa ttagtgagta gtatggtgat cgggaagggt acggatatcg attcgtaatt
781 ttcgtagat tttggagggc gcgtgaggtt gtttcgcgtt tcggcggaac gttcgggcgt
841 ttatatgttt gtgtaggagt ggttgaggcg ggtgtagaag ggggtatttt tttcgtagtt
901 tcgggttttt tttatgttg tttcgaggtg aggaggggat gccgtttaga ggtcgttagc
961 gggagggggg agacgcggcg cgggcggcgg cggaggtcgg cgtttatcgc ggttgggggt

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1021 gggttgtttt ttatggtgog gggcgtagtc gtcgttttat ttcgttggtg ggatcgcggt
 1081 cgcggcggcg ttagggttta ttggttcggg agggagttac gttttttttt ttgggaaatt
 1141 tttggtggcg aggcgcgcgg aggtgtcgag ttttttttat aaggtogagg ggcggggcg
 1201 ttcgtgggtg tggatagaat cgaggtggga ggaggggtga aagtaattga gcgttttttt
 1261 tggttgttgt ttattttgat cgtttgggtt gggaagtttt agacggtttt ttttgaaacg
 1321 ttttgttttt ggtcggatcg ggagtttatt ggggtttttt ttagtttttc gttaaagtgt
 1381 cgggtggacgg taagtagtta ataagtagta ttggatttgc ggattttagg taaattgtcg
 1441 aggcgtattt gagcgttcgt tttttgttt ttttaattat aaacgtttt atagggacgg
 1501 gatttttttt ttgaagtttt ttagtaattt tggtaaagtg aaaatcgttt gtttttaagt

SEQ ID NO: 74

Sequenza metilata del gene PTGER3 (bottom strand), derivata da SEQ ID NO.15

1 gttaaaggat aggcgatttt tattttatta gagttattaa aggattttag gagaaggatt
 61 tcgtttttgt aggagcgttt gtggttgaag aagtaggagg acgagcgttt aggtgcgttt
 121 cggtagtttg tttggggttc gtaagtttag tgttatttat tagttgtttg tcgtttatcg
 181 atatttttagc ggagaattgg aggcgatttt agtgggtttt cgttcgggtt aggcgtaggg
 241 cgttttagag gagatcgttt ggggtttttt aatttaggcg attaggatag gtaatagtta
 301 agagaggcgt ttagttgttt tgtatttttt ttttatttcg gttttgttta tatttaacgg
 361 cgtttcgttt ttcgggtttt ataaagggga ttcggtattt tcgcgcgttt cgttattaga
 421 ggttttttag agaggaaggc gtgggttttt ttcgggttag tgagtttttg cgtcgtcgcg
 481 gtcgcggttt tagtagcgga gtagggcggc ggttcggttt cgtattatgg ggggtagttt
 541 agtttttagtc gcggtaaacg tcgattttcg tcgtcgttcg cgtcgcgttt gtttttttc
 601 gttgcggttt tttggacgtt attttttttt tatttcgaag ttaatatgaa ggagattcgg
 661 ggttacggag gggatgtttt tttttgtatt cgttttaatt atttttatat aggtatgtgg

721 gcgttcgagc gtttcgtoga ggcgcggggg aattttacgc gttttttagg gtttggcgag
 781 gattgoggat cgggtgtcgt ggttttttcg attattatgt tgtttattgg ttctgtgggt
 841 aacgtattgg ttatgttggt cgtgtcgcgt agttatcggc gcggggagag taagcgtaag
 901 aagttttttt tgttgtgtat cggttgggtg gcgtttatcg atttggtcgg gtagtttttt
 961 attatttcgg tcgttatcgt cgtgtatttg ttttaagtagc gttgggagta tatcgattcg
 1021 tcggggcggt tttgtatttt ttctgggttg attatgattg ttttcgggtt ttttctgtg
 1081 tttatcgtta gcgttatggt cgtcgcgcgg gcgttggtta ttagggcgtc gtattggtat
 1141 gcgagttata tgaagacggc tgttattcgc gttgtgttgt tcggcgtgtg gttggtcgtg
 1201 ttctgttttcg ttttgtgtgc ggtgttgggc gtgggttagt atatcgttta gtggttcggg
 1261 acgtggtggt ttattagtat cgggcgaggg ggtaacggga ttagtttttc gtataattgg
 1321 ggtaattttt tttctgtttt tgtttttgtt tttttgggtt ttttggcgtt gatagttatt
 1381 tttttttgta atttggttat tattaagggt ttggtgtttc gttgtcgggt taaggttacg
 1441 gtatttttagt ttagtggtta gtggggtcgt attacgatcg agacggttat ttagtttatg
 1501 gggattatgt gcgtgttgtc ggtttgttgg tttctgtttt tggtaggtag ttttaggggt

SEQ ID NO: 75

Sequenza non metilata del gene PTGER3(top strand), derivata da SEQ ID NO.15

1 aattttggaa ttatttatta ggagtggaga ttagtagatt gatagtatgt atatgatttt
 61 tataagttga atggttggtt tgggtgtgat gtggttttat tgggtattgg attgagatgt
 121 tgtggttttg gtttggtagt gggatattag ggttttaatg gtggttaggt ttaggaaaa
 181 ggtgattggt agtgtaaga gttttaggaa ggtaaaggta gaggtgaaga aaagggtgtt
 241 ttagttatgt gaagagttag ttttgtgtt tttttgttg gtgttgatga agtattatgt
 301 tttgggttat tggatggtgt attggtttat gtttagtatt ggtagtaggg tgaaggtag
 361 tatggttagt tatatgtga gtagtatagt gtgggtggta tgtgttttta tgtggttgt

421 atattagtggt ggtgttttga tggtagtggt ttgtttgatg gttatgggtg tggtagtgaa
 481 taatgaggag agtttgaaaa tagttatggg tagtttgaaa aagggtgtaga gttgttttga
 541 tgggttgatg tgtttttaat gttgtttgga taggtatatg atgatgatga ttgggggtgt
 601 gagaagttgt ttgattaggt tggtagtggt tagttagttg atgtatagta ggaaggattt
 661 tttgtgtttg tttttttggt gttggtagtt gtgtgatatg agtagtatgg ttagtggttt
 721 gtttatgaaa ttagtgagta gtatggtgat tgggaagggt atggatattg atttgaatt
 781 tttgttagat tttggagggt gtgtgaggtt gttttgtgtt ttggtggaat gtttgggtgt
 841 ttatatgttt gtgtaggagt ggttgaggtg ggtgtagaag ggggtatttt tttttagtt
 901 ttgggttttt tttatgttgg ttttgaggtg aggaggggat ggtgtttaga gagtgtagt
 961 gggagggggg agatgtggtg tgggtggtgg tggaggttgg tgtttattgt ggttgggtt
 1021 gggttgtttt ttatggtgtg ggggttagtt gttgttttat tttgttgtg ggattgtggt
 1081 tgtggtggtg ttaggggtta ttggtttggg agggagtatt gttttttttt ttgggaaatt
 1141 tttggtggtg aggtgtgtgg aggtgttgag ttttttttat aaggttgagg ggggtgggtg
 1201 tttgtgggtg tggatagaat tgaggtggga ggaggggtga aagtaattga gtgtttttt
 1261 tgggtgttgt ttattttgat tgtttgggtt gggaagtttt agatggtttt tttgaaatg
 1321 ttttgttttt ggttggttgg ggagtttatt ggggtttttt ttagtttttt gttaaagtgt
 1381 tgggtgatgg taagtagtta ataagtagta ttggatttgt ggattttagg taaattgttg
 1441 aggtgtattt gagtgtttgt tttttgttt ttttaattat aaatgttttt atagggatgg
 1501 gatttttttt ttgaagtttt ttagtaattt tggtaaagtg aaaattgttt gtttttaagt

SEQ ID NO: 76

Sequenza non metilata del gene PTGER3(bottom strand), derivata da SEQ ID NO.15

1 gtttaaggat aggtgatttt tattttatta gagttattaa aggatttttag gagaaggatt
 61 ttgtttttgt aggagtgttt gtggttgaag aagtaggagg atgagtgttt aggtgtgttt

121 tggtagtttg tttggggttt gtaagtttag tgttatttat tagttgtttg ttgtttattg
 181 atatttttagt ggagaattgg aggagatttt agtgggtttt tggtttggtt aggagtaggg
 241 tgttttagag gagattgttt ggggtttttt aatttaggtg attaggatag gtaatagtta
 301 agagaggtgt ttagttgttt tgtatttttt tttatttttg gttttgttta tatttatggg
 361 tgttttggtt ttttggtttt ataaagggga tttggtattt ttgtgtgttt tgttattaga
 421 ggttttttag agaggaaggt gtggtttttt tttgggttag tgagtttttg tgtgtttgtg
 481 gttgtggttt tagtagtga gtaggggtgt ggtgtgtttt tgtattatgg ggggtagttt
 541 agtttttagt gtggtaaatg ttgatttttg ttgtgtttg tgtgtgtttt gttttttttt
 601 gttgtggttt tttggatggt atttttttt tattttgaag ttaatatgaa ggagatttgg
 661 ggttatggag gggatgtttt tttttgtatt tgttttaatt atttttatat aggtatgtgg
 721 gtgtttgagt gttttgttga ggtgtgggtt aattttatgt gttttttagg gtttggtag
 781 gattgtggat tgggttttgt ggtttttttg attattatgt tgtttattgg ttttgggtt
 841 aatgtatttg ttatgttgtt tgtgttgtgt agttattggt gttgggagag taagtgaag
 901 aagttttttt tgttgtgtat tggttggttg gtgtttattg atttgggttg gtagtttttt
 961 attatttttg ttgttattgt tgtgtatttg ttttaagtagt gttgggagta tattgatttg
 1021 ttgggggtgt tttgtatttt ttttgggttg attatgattg tttttgggtt tttttgttg
 1081 tttattgtta gtgttatggt tgttgagtgg gtgttggtta ttagggtgtt gtattggtat
 1141 gtgagttata tgaagatgtg tgttatttgt gttgtgttgt ttggtgtgtg gttggttgtg
 1201 tttgtttttg ttttgttgtt ggtgttgggt gtgggttagt atattgttta gtggtttggg
 1261 atgtggtgtt ttattagtat tgggtgaggg ggtaatggga ttagtttttt gtataattgg
 1321 ggtaattttt tttttgtttt tgtttttgtt tttttgggtt ttttgggtgt gatagttatt
 1381 tttttttgta atttggttat tattaagggt ttggtgtttt gttgttgggt taaggttatg
 1441 gtatttttagt ttagtgttta gtgggttgtt attatgattg agatggttat ttagtttatg
 1501 gggattatgt gtgtgttgtt ggtttgttgg tttttgtttt tggtaggtag ttttaggggt

SEQ ID NO: 77

Sequenza metilata del gene PTPRM (top strand), derivata da SEQ ID NO.16

1 agtattttgt attagatata gaaattacgg gttatgttta aattttgggt ttggtgtgat
61 tatcgttttt cgtgtattgt ttgcggttcg ttccgggttt atacgggata tcgaggtatg
121 atgaggacgt agaatagtag aagcgcgttt tggttttcgg gcgttagtgt tcggggtagt
181 cggcgtgtat tcggcgggtt cggtcgggag cgggttggcg atcgcggggt tcggcgtttt
241 cggtttttcg gttatttttc ggcgttcgtt aatttcgttt cgttcgcggc gtagagaagt
301 tcgtagtttt tcggagtttt agcgtatttt tggttcgttt ttttcgtagt cgtcagtag
361 cgtaggttcg gcgatttcgg gtgtagtggg ttttgcgg tgatctgc gttcggcgtt
421 aggttcgaag tcgtttgcgc gcgttcgcgg ggtcgtaggt cgttggttc gttcggcgc
481 gtttataaat tattcgcgtt tcgtgattcg gataaattt ttggcggcgg cgtagttttt
541 tttatagtta ttttttttag agttagtatt taaaatagaa gacgcggtcg gggcggagg
601 gtgggcgggg ggagttcggg ggtcgttttt ttccgcgcgg ttgacgttcg ttccggcggc
661 ggtagtgggt gtggtcgcgg ggtcgttttt agtcaggttt tcggaggcgt tcgggcgcgg
721 gtccgcgggg tacgggcgtt tacgtttttt agcgggtcgc ggcggcgtcg ggcggtcgtg
781 acgtgagcgt tttttttagt cggtttcggg ggtatcgtta gttagtcggg gtagaagagt
841 ttccgcgcga gtccgcgcgg gttcggttat cggcgcgtcg tcgttcgggg ttgggtttgg
901 ggttgtttgt ggagaggcgg cgggcggaac gcgcgcggtt acggttacgg ttatcgttac
961 ggttacggtc ggtagttcgg gtttcgggtt tcgggtaggg gaaggggaga ggcggcaggt
1021 ttagtaatcg gaatcgaggg aagattttgg ttccgcgggt tcgtttttcg tttttttgt
1081 tagcggcgtt agacgtcgag tggggtagg gataggggag gaggatttag gattttgtgt
1141 tcgcgttttt ggagtcgttg gatttcggat ttttgaatt gttggtattt tgggggtttg
1201 gtttagcgtt ttgttggtta ttctttttt ttcttggtt cgaattaaa gtttcgggtt
1261 ttttcgttt tcgcgcgttt atttatcgc gtccgggagc ggttcggttc gtatttagta
1321 ttatgagggg atttgggatt tggttggcga ttttggtcgg atttttgtta attgcggcgg

1381 gcgagacggt tttaggttaag cgggacggtt ttgtcggtt tcgaggcgcg cgggtcggcg
 1441 cgggacgttc gggacgtcga tagttttttg gtggtagagt ttaagggtg gcgtcggggt
 1501 cgggcggggg gcgcggcggg tcggatatcg tttttgtttg tgagtcgggc gttgggcgag
 1561 gggtcgtggg gttggtaggt atttagtttt cgggcgggcg gagcggacgg atttcgaggg
 1621 cgagtttttt agtcgggatt gttagttcgg tcgtcggttt ttgcgggttt gggttagtgt
 1681 ttaagggttg gcggtttgta tttttgagtt ttggtcgggt tgtaaaagga atagtagaaa
 1741 attttgtttg aagtttttag ttgtagtcgt cgggtcggtt ggctagggcg ttgcggggtt
 1801 ttctcgatt tcgagtagcg gtccgggtta ggtcgttggg gttcgggttc gttcgtagcg
 1861 atcgtcggga attggcggtc gtttcggcgg cggcgatttt tcgggtgttt gttttttttg
 1921 tcgttttttg ttgcgcggg ttggcgattt cgggaggttt tcgcggtcgt gtagcgtttg
 1981 cggagagggt ggggggagtt ttctcggtt ttagcggta gggtttggcg gtcgcggagg
 2041 gaagcgggta ggttttttagg ttttggttac ggttttgcgt ttcttggggt tttttttttt
 2101 tattttcgtt tttttagcgg agcgtcggg ttagttgtaa ttgtttatt tagttcgggt
 2161 gttcgggggt tttaggtggg aaggagaggt attggcggcg tcgcagtaag cgtgtgagtg
 2221 tgtgcgcgtg tgtgtttgta cgcgcgcgcg ggggcgtttt aagtttagag gaatttttta
 2281 cggagaggat ttgtggatcg ggtcggggg ttgcgcgtgg ggcgaattc ggtacgttgt

SEQ ID NO: 78

Sequenza metilata del gene *PTFRM* (bottom strand), derivata da SEQ ID NO.16

1 atagcgtgc gggttcgtt ttaoctcga ttttcgattt cgatttatag atttttttcg
 61 tgaggggttt tttgggttt agaactttt cgcgcgcgcg ttaggtata tacogtata
 121 tatttatacg ttgttcgta tctcgttagt gttttttttt ttatttggg atttcgggt
 181 agtcgggttg gatgaataag ttgtagttgg tcgcgcgtt tcgttagggg gacgagggcg
 241 gggaggggga gtttagcggg gcgtagggtc gtggttaggg ttgggggatt tgttcgtttt

301 ttttcgcggt cgtaaagttt tatcggtggg atcggcgagg aatttttttt agttttttcg
 361 tagacgttgt acgatcgcg ggatttttcg gggtcgtag tcgcgcggg tagggggcga
 421 tagggagggg agggatcgcg gagatcgctc tcgctggagc ggtcgtagt tttcggcgat
 481 cgttcgggc gtagtgaat attagcggtt tgggttcggt cgttgctcg ggtcggcggg
 541 gatcgctag cgtttacgtt aggcggttcg gcggttgtaa ttgggaattt taagtaaagt
 601 tttttgttgt tttttttgta gtcggttagg gatttaagag tgtaagtcgt ttaattttga
 661 gtattagttt aggtcgcgga aggacggcgg tcgagttggt agtttcggtt ggggagttcg
 721 ttttcggggg tcgttcgttt cgttcgttcg aggattgggt gtttgtagt tttacggttt
 781 ttcgttttag gttcggttta taggtagaag cggcttcggt ttcgctcggt ttttcgttcg
 841 gtttcgacgt tagttttagg gttttattat tagggagttg tcggcgtttc gggcgtttcg
 901 cgtcggttcg cgcgttcggt gggcggtaga ggcggttcg tttatttgag aacgtttcgt
 961 tcgctgtagt tagtaaaagt tcggttaaag tcgttaggta agttttaagt ttttttatgg
 1021 tgttgagtgc gggtcgggtc gtttttcggc ggcggtgggt gggcgcgga gggcgaggg
 1081 ggtcgggagt tttggttcg aggtagcgag gagagacggg taaatagtag agcgtaagt
 1141 taagttttta aagtgttaat agttgtagaa gttogaattt tagcggtttt agggcgcgcg
 1201 gtatagggtt ttgggttttt tttttttgtt ttggtttta ttggcgttt ggcgtcgttg
 1261 gtagagggag cggagggcga gttcgggag ttaaaatttt ttttcggtt cgggtgttga
 1321 gttcgtcgtt tttttttttt ttttgttcg gattcgggat tcgagttgtc ggtcgtggtc
 1381 gtggcggtgg tcgtggtcgt ggtcgcgcgc gtttcgttcg tcgttttttt ataggtagtt
 1441 ttaagtttag tttcgggcgg cggcgcgctc atgatcgagt tcgcgtcgtt tcgcgcggg
 1501 gtttttggtt ttcgattgat tggcggtgtt tcgtaggtcg gttgaaggga gcgtttaagt
 1561 tacggtcgtt cggcgctcgc gcggttcgtt agaggcggtg agcgttcgtg tttcgtcgtt
 1621 tcgcgttcga gcgttttcgg gagttcgggt gggggcggtt tcgcggttat agttattatc
 1681 gtcgtogaag cggcggttag tcgcgcgggg aggagcggtt atcgggtttt tttcgtttat
 1741 ttttcgttt cggtcgcgtt ttttattttg gtagttgggt ttggggaggg tgattgtgga

1801 agaggttgcg tcgtcgtag aagtttgttt cgggttacga gtcgcgagta gtttgtgagc
 1861 gcggtcgggc gggattagcg gtttgcgatt tcgcgggcgc ggtagggcg tttcagttt
 1921 ggcgtcggac ggcgatgtta tcgtataggg ttagttgtat tcggagtcgt cgggtttgcg
 1981 ttgttcggcg gttgcgggaa aagcagatta ggagatcggt gaggtttcgg agggttgcga
 2041 gtttttttac gtcgcgggcg gacgaagtt ggcgggcgc gggagatggc gcgggagtcg
 2101 ggagcgtcga gtttcgcgat cgttagttcg ttttcggtcg ggttcgtcgg gtatacgtcg
 2161 ttggtttcga gtattggcgt tcgggaagta ggcgcggttt ttgttgttt gcgtttttat
 2221 tatgtttcgg tgtttcgtgt gggttcgaag cgagtcgtag gtagtatacg gaaggcggcg
 2281 gttatattaa aattagggtt tggatataat tcgtggtttt tgtatttggg gtaaagtgtt

SEQ ID NO: 79

Sequenza non metilata del gene PTPRM (top strand), derivata da SEQ ID NO.16

1 agtatattgt attagatata gaaattatgg gttatgttta aattttggtt ttggtgtgat
 61 tattgttttt tgtgtattgt ttgtggtttg ttttgggttt atatgggata ttgaggtatg
 121 atgaggatgt agaatagtag aagtgtgttt tgttttttgg gtgttagtgt ttggggttag
 181 tgggtgtgat ttggtgggtt tggttgggag tgggttggtg attgtggggt ttggtgtttt
 241 tgggttttgt gttatttttt ggtgtttgtt aattttgttt tgtttgtggt gtagagaagt
 301 ttgtagtttt ttggagtttt agtgattttt tggtttgttt tttttgtagt tgttgagtag
 361 tgtaggtttg gtgatttttg gtgtagtttg ttttgtgtgg tgatattgtt gtttgggtgt
 421 aggtttgaag ttgtttggtt gtgtttgtgg ggttgtaggt tgttggtttt gtttgggtgt
 481 gttataaat tatttgtggt ttgtgatttg ggataaattt ttggtggtgg tgtagttttt
 541 tttatagtta ttttttttag agttagttat taaaatagaa gatgtggttg gggtgaggag
 601 gtgggtgggg ggagtttggg ggttggtttt ttttgtgtgg ttgatgtttg ttttgggtgt
 661 ggtagtgggt gtggttgtgg ggttggtttt agttgagttt ttggaggtgt ttgggtgtgg

721 gttgggtggg tatgggtggt tatgtttttt agtgggttgt ggtggtgttg ggtgggtgtg
 781 atgtgagtgt tttttttagt tggtttgtgg ggtattgtta gttagtggg gagtaagagt
 841 tttgtgtgta gttgggtggt gtttgggtat tgggtgtgtg ttgtttggg ttgggtttgg
 901 ggttgtttgt ggagaggtgg tgggtggaat gtgtgtggtt atggttatgg ttattgttat
 961 ggttatgggt ggtagtttgg gtttgggtt ttgggtaggg gaaggggaga ggtgggtgagt
 1021 ttagtaattg gaattgaggg aagattttgg ttttgggg ttgtttttt tttttttgt
 1081 tagtgggtgt agatgttgag tgggggttagg gataggggag gaggatttag gattttgtgt
 1141 ttgtgttttt ggagttgtg gagtttggat ttttgaatt gttggtattt tgggggtttg
 1201 gtttagtgtt ttgttgtta tttgttttt tttgttgtt tggaaataaa gtttttggtt
 1261 ttttttgtt ttgtgtgtt atttattgtt gttggggagt ggtttgggtt gtatttagta
 1321 ttatgagggg atttgggatt tgtttggtga ttttgggtg atttttgta attgtggtg
 1381 gtgagatgtt ttaggtaag tgggattgtt tttgttgtt ttgaggtgtg tgggttggg
 1441 tgggatgtt ggatgttga tagttttttg gtggtagagt ttaagggtg gtgttgggt
 1501 tgggtggggg gtgtgggtg ttgatattg ttttgtttg tgagttgggt gttgggtgag
 1561 gggttgtggg gttggtagg atttagttt tgggtgggtg gagtggtg attttgagg
 1621 tgagttttt agttgggatt gttagtgtg ttgttgttt tttgtgggtt gggttagtgt
 1681 ttaagggtg gtggtttga ttttgagtt tttggttgt tgtaaaagga atagtagaaa
 1741 attttgtttg aagtttttag tttagttgt tgggttgtt ggtgtagggt ttgtgtggt
 1801 tttgttgatt ttgagtgtg gttgggttta ggttgttgt gttgttgtt gttgtagtg
 1861 attgttggga attggtggtt gtttgggtg tgggtattt ttggtgttt gtttttttg
 1921 ttgtttttt ttggtgtgg ttgtgattt tgggaggtt ttgtggtgt gtagtgtttg
 1981 tggagaggtt ggggggagtt tttgttgtt tttagtgtg gggtttggt gttgtggag
 2041 gaagtggga ggttttttag ttttgggtat ggttttgtgt tttgttggt ttttttttt
 2101 tatttttgtt ttttagtgg agtgttgtg ttagttgtaa tttgtttatt tagtttggt
 2161 gtttgggggt tttaggtggg aaggagaggt attggtggtg tgtgagtaag tgtgtgagt

2221 tgtgtgtgtg tgtgtttgta tgtgtgtgtg ggggtgtttt aagtttagag gaatttttta

2281 tggagaggat ttgtggattg gagtggggg tttgggtgtg ggggaattt ggtatgtgt

SEQ ID NO: 80

Sequenza non metilata del gene PTPRM (bottom strand), derivata da SEQ ID NO.16

1 atagtgtgtt gggtttgttt ttatgttga tttttgattt tgatttatag attttttttg
61 tgaggggttt ttttgggttt agaattgttt tgtgtgtgtg ttaggtata tatgtgtata
121 tatttatatg tttgtttgta tattgttagt gttttttttt tttatttggg atttttgggt
181 agttgggttg gatgaataag ttgtagtgtg ttgtgtgtt ttgttagggg gatgagggtg
241 gggaggggga gtttagtggg gtgtagggtt gtggttaggg tttggggatt tgtttgtttt
301 tttttgtggt tgttaagttt tattgttggg attggtgagg aatttttttt agtttttttg
361 tagatgttgt atgattgttg ggattttttt gggttgttag ttgtgttggg taggggggtga
421 tagggagggg agggatttgg gagattgttg ttgttgaggt ggttgttagt ttttggat
481 tgttgtgggt gtagttgaat attagtgtt tgggtttggt tgttgttttg ggttgggttg
541 gattgtgtag tgtttatgtt aggtggtttg gtggttgtaa ttgggaattt taagtaaagt
601 tttttgttgt tttttttgta gttggttagg gatttaagag tgaagttgt ttaattttga
661 gtattagttt aggttgtgga aggatggttg ttgagttggt agttttggtt ggggagtttg
721 tttttggggt ttgtttgttt tgtttgtttg aggattgggt gtttgttagt tttatgggtt
781 tttgtttagt gtttggttta taggtagaag tgggttttgg tttgttgtgt tttttgtttg
841 gttttgatgt tagttttagg gttttattat tagggagttg ttggtgtttt ggggtgtttg
901 tgttgggttg tgtgttttgg ggggtgtaga ggtggttttg tttatttgag aatgttttgt
961 ttgtttagt tagtaaaagt ttggttaaag ttgttaggta agttttaagt ttttttatgg
1021 tgttgagtgt gggttgggtt gttttttggt ggtggtgggt ggggtgtgtg ggggtggagg
1081 ggttgggagt tttggttttg aggtagttag gagagatggg taaatagtag agtgtaagt

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1141 taagttttta aagtgttaat agttgtagaa gtttgaattt tagtggtttt aggggtgtgg
1201 gtataggggtt ttgggttttt tttttttgtt ttgggtttta ttgggtgttt ggtgtgttg
1261 gtagagggag tggaggggtga gtttgtggag ttaaaatttt tttttggttt tgggtgttga
1321 gtttgttgtt tttttttttt ttttgttttg gatttgggat ttgagttgtt ggttgtggtt
1381 gtggtggtgg ttgtggttgt ggttgtgtgt gtttgttttg ttgttttttt ataggtagtt
1441 ttaagtttag ttttgggtgg tgggtgtgtg atgattgagt ttgtgttgtt tgtgtgtggg
1501 gttttttgtt ttgattgat tgggtgtgtt ttgtaggttg gttgaaggga gtgtttatgt
1561 tatggttgtt tgggttgttt gtggtttgtt agaggggtgt agtgtttgtg ttttgttgtt
1621 ttgtgtttga gtgttttttg gagtttggtt ggggggtggt ttgtggttat agttattatt
1681 gttgttgaag tgggtgttag ttgtgtgggg aggagtgggt attgggtttt ttttgtttat
1741 ttttttgttt tgggtgtgtt ttttattttg gtagttgggt ttggggaggg tgattgtgga
1801 agaggttgtg ttgtgttag aagtttgtt tgggttatga gttgtgagta gtttgtgagt
1861 gtggttgggt gggattagtg gtttgtgatt ttgtgggtgt ggttaggtgg ttttgagttt
1921 ggtgttggtt ggtgatgtta ttgtataggg ttagttgtat ttggagttgt tgggttgtg
1981 ttgtttgtg gttgtgggaa aagtgagtta ggagattgtt gaggttttgg aggggttga
2041 gtttttttat gttgtgggtg gagtgaagtt ggtgggtgtt gggagatggt gtgggagttg
2101 ggagtgttga gttttgtgat tgttagttt ttttgggtt ggtttgttgg gtatatgtt
2161 ttggttttga gtattggtgt ttgggaagta ggtgtgttt ttgttgtttt gtgtttttat
2221 tatgttttgg tgttttgtgt gggtttgaag tgagttgtag gtagtatatg gaagggtgtg
2281 gttatattaa aattaggggt tggatataat ttgtggtttt tgtatttgggt gtaaagtgtt

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SEQ ID NO: 81

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID

NO: 18

AGTTTTTATTGTCCGGCGCGC

SEQ ID NO: 82

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:18

ACGAAAAACGACGACGCTACC

SEQ ID NO: 83

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO: 21

CGCGGACGGGGTCGGTTTTTC

SEQ ID NO: 84

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:21

TACTCCTCGACCCGCGAC

SEQ ID NO: 85

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:25

TAAGCGGCGGGGTAACCGAC

SEQ ID NO: 86

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:25

CGCCTAACCGACTAACCCGC

SEQ ID NO: 87

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:29

TCGTTGAGTTTCGGTTGCGCGC

SEQ ID NO: 88

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:29

TACGCGCTCGTTGTCGGCC

SEQ ID NO: 89

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:33

TTGGGGTCTGTTATTTGCG

SEQ ID NO: 90

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:33

CAAAAGGAATACGGGCCCC

SEQ ID NO: 91

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:37

GCGTACGTTTCGGGGGC

SEQ ID NO: 92

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:37

AAAAACGACCGGAACCGAAC

SEQ ID NO: 93

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:42

CGGTGTTGTTTCGGGTC

SEQ ID NO: 94

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:42

CTAACCGAACGAAAAACGAAAC

SEQ ID NO: 95

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:46

CGGTTTTGGTTAGACGACGAGTC

SEQ ID NO: 96

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:46

CCTACGCGGTCTCGCATAC

SEQ ID NO: 97

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:49

ATAAAAGCGGCGTCGTTTTTTC

SEQ ID NO: 98

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su complementare invertita di SEQ ID NO:49

CTATACCTCGACGAAATATCTC

SEQ ID NO: 99

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID NO:54

TTAGGGCGTCGTGTTTTCGCGC

SEQ ID NO: 100

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-

plementare invertita di SEQ ID NO:54

ACCGCCGCGAAAACCGTCC

SEQ ID NO: 101

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID

NO:57

GAGGGTTTCGTTTCGTTTAGC

SEQ ID NO: 102

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-

plementare invertita di SEQ ID NO:57

AACGCCGTTTCGCTAAAAATCG

SEQ ID NO: 103

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID

NO:61

TAGTATTGGTAACGACGATAGTATC

SEQ ID NO: 104

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-

plementare invertita di SEQ ID NO:61

AAATTCGAAACTAACGCGACACG

SEQ ID NO: 105

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID

NO:66

TTTGCGTATTTCGGGGTTCG

SEQ ID NO: 106

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-

plementare invertita di SEQ ID NO:66

GACCCGCGACGAACTACGC

SEQ ID NO: 107

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID
NO:70

TTCGTCGGGTTTTCGGGTC

SEQ ID NO: 108

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-
plementare invertita di SEQ ID NO:70

AAAACGCCCGCTCCCGCTC

SEQ ID NO: 109

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID
NO:74

GGATTCGGTATTTTCGGGC

SEQ ID NO: 110

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-
plementare invertita di SEQ ID NO:74

GAAACGACGACGAAAATCGAC

SEQ ID NO: 111

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su SEQ ID
NO:77

TACGTTTTTTAGCGGGTCGC

SEQ ID NO: 112

Sequenza oligonucleotidica per Methylation-Specific PCR (MSP) disegnata su com-
plementare invertita di SEQ ID NO:77

CGAAACCCGAACTACCGACC

RIVENDICAZIONI

1. Acido nucleico comprendente una sequenza nucleotidica scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, 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: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80.

2. Oligonucleotide di almeno 10 nucleotidi di lunghezza complementare o identico a un segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID

NO: 25, SEQ ID NO: 26, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 43, SEQ ID NO: 44, 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: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 63, SEQ ID NO: 64, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 67, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 71, SEQ ID NO: 72, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 76, SEQ ID NO: 77, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 80.

3. Oligonucleotide secondo la rivendicazione 2, di almeno 18 nucleotidi di lunghezza.

4. Oligonucleotide secondo la rivendicazione 2 o 3, in cui detta sequenza bersaglio è scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 57, SEQ ID NO: 58,

SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77, SEQ ID NO: 78 ed in cui detto segmento della sequenza bersaglio comprende almeno un dinucleotide CpG.

5. Oligonucleotide secondo la rivendicazione 2 o 3, in cui detta sequenza bersaglio è scelta nel gruppo che consiste di SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO: 43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, 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: 79, SEQ ID NO: 80 ed in cui detto segmento della sequenza bersaglio comprende almeno un dinucleotide TpG.

6. Oligonucleotide secondo la rivendicazione 1, scelto dal gruppo che consiste di SEQ ID NO: 81, SEQ ID NO: 82, SEQ ID NO: 83, SEQ ID NO: 84, 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, SEQ ID NO: 93, SEQ ID NO: 94, SEQ ID NO: 95, SEQ ID NO: 96, SEQ ID NO: 97, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 100, SEQ ID NO:

101, SEQ ID NO: 102, SEQ ID NO: 103, SEQ ID NO: 104, SEQ ID NO: 105, SEQ ID NO: 106, SEQ ID NO: 107, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 110, SEQ ID NO: 111, SEQ ID NO: 112.

7. Procedimento per la diagnosi di malattia neoplastica, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica dell'isola CpG di un gene umano scelto dal gruppo che consiste dei geni elencati in tabella 1, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

8. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene ARHGAP20 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 42661 e 45840 della sequenza Genbank AP003460 versione 3, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

9. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene CDH11 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 52081 e 55500 della sequenza Genbank AC137643 versione 3, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

10. Procedimento secondo la rivendicazione 7, comprendente

la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene FLI1 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 40001 e 47460 della sequenza Genbank AP001122 versione 5, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

11. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene FOSL2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 52801 e 57000 della sequenza Genbank AC104695 versione 2, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

12. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene HES2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 31741 e 34020 della sequenza Genbank AL031848 versione 11, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

13. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene HTR6 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 92521 e 95340 della sequenza Genbank

AL031727 versione 43, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

14. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene LHX3 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 111001 e 116040 della sequenza Genbank AL138781 versione 13, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

15. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene LOC51149 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 117001 e 119700 della sequenza Genbank AC008393 versione 7, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

16. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene MAP1B compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 39361 e 41460 della sequenza Genbank AC093218 versione 2, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

17. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo

stato di metilazione della sequenza nucleotidica del gene MDM2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 140401 e 144660 della sequenza Genbank AC025423 versione 32, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

18. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene NID1 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 36661 e 38520 della sequenza Genbank AL122018 versione 37, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

19. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene NID2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 75001 e 77340 della sequenza Genbank AL118557 versione 5, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

20. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene PNU TL2 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 108541 e 111200 della sequenza Genbank AC005666 versione 1, la metilazione di detta sequenza es-

sendo indicativa di malattia neoplastica.

21. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene PRPH compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 149821 e 152460 della sequenza Genbank AC125611 versione 4, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

22. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene PTGER3 compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 123001 e 124560 della sequenza Genbank AL031429 versione 11, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

23. Procedimento secondo la rivendicazione 7, comprendente la fase di analizzare, in un campione di DNA genomico, lo stato di metilazione della sequenza nucleotidica del gene PTPRM compresa tra le posizioni nucleotidiche corrispondenti ai nucleotidi 64321 e 66660 della sequenza Genbank AP001091 versione 5, la metilazione di detta sequenza essendo indicativa di malattia neoplastica.

24. Procedimento secondo la rivendicazione 7, comprendente le fasi di:

(i) pretrattare chimicamente un campione di DNA genomico

con un reagente atto a convertire le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina;

(ii) sottoporre un filamento del DNA genomico pretrattato ad amplificazione utilizzando come primers di amplificazione almeno una coppia di oligonucleotidi, ciascuno della lunghezza di almeno 10 nucleotidi, uno di detti oligonucleotidi essendo complementare ad un primo segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77, SEQ ID NO: 78 e l'altro di detti oligonucleotidi essendo identico ad un secondo segmento di detta sequenza bersaglio, il secondo segmento essendo localizzato a valle del primo segmento, almeno uno di detti primo e secondo segmento della sequenza bersaglio comprendendo almeno un dinucleotide CpG; e

(iii) rivelare la presenza di frammenti amplificati del DNA genomico pretrattato, la presenza di frammenti ampli-

ficati essendo indicativa di malattia neoplastica.

25. Procedimento secondo la rivendicazione 7, comprendente le fasi di:

(i) pretrattare chimicamente un campione di DNA genomico con un reagente atto a convertire le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina;

(ii) sottoporre un filamento del DNA genomico pretrattato ad amplificazione utilizzando come primer di amplificazione almeno una coppia di oligonucleotidi, ciascuno di almeno 10 nucleotidi di lunghezza, uno di detti oligonucleotidi essendo complementare ad un primo segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 21, SEQ ID NO: 22, SEQ ID NO: 25, SEQ ID NO: 26, SEQ ID NO: 29, SEQ ID NO: 30, SEQ ID NO: 33, SEQ ID NO: 34, SEQ ID NO: 37, SEQ ID NO: 38, SEQ ID NO: 41, SEQ ID NO: 42, SEQ ID NO: 45, SEQ ID NO: 46, SEQ ID NO: 49, SEQ ID NO: 50, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 61, SEQ ID NO: 62, SEQ ID NO: 65, SEQ ID NO: 66, SEQ ID NO: 69, SEQ ID NO: 70, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 77, SEQ ID NO: 78 e l'altro di detti oligonucleotidi essendo identico ad un secondo segmento di detta sequenza bersaglio, il secondo segmento essendo localizzato a valle del primo segmento;

(iii) rivelare la presenza di frammenti amplificati del DNA genomico pretrattato mediante ibridazione con una sonda oligonucleotidica di almeno 18 nucleotidi di lunghezza complementare ad un terzo segmento di detta sequenza bersaglio, detto terzo segmento essendo situato fra detto primo e detto secondo segmento e comprendendo almeno un dinucleotide CpG, la presenza di frammenti amplificati essendo indicativa di malattia neoplastica.

26. Procedimento secondo la rivendicazione 21, in cui detta sonda è marcata con un marcatore rivelabile.

27. Procedimento secondo una qualsiasi delle rivendicazioni 20 a 22, in cui detta amplificazione è una reazione a catena della polimerasi (PCR).

28. Procedimento secondo la rivendicazione 23, in cui detta amplificazione è una PCR primaria seguita da una PCR secondaria semi-nested o nested.

29. Procedimento secondo una qualsiasi delle rivendicazioni 20 a 24, in cui detto reagente è bisolfito, preferibilmente sodio bisolfito, in combinazione con idrochinone.

30. Procedimento secondo una qualsiasi delle rivendicazioni 7 a 25, in cui detta malattia neoplastica è un tumore solido o un neoplasia ematologica.

31. Procedimento secondo la rivendicazione 26, in cui detta malattia neoplastica è scelta nel gruppo che consiste di tumori primari del sistema nervoso centrale, metastasi

cerebrali, tumori dell'occhio, tumori dell'ipofisi, tumori della tiroide, tumori della corteccia surrenalica, tumori del sistema endocrino diffuso, tumori della testa-collo, tumore del polmone, mesotelioma maligno, timomi e tumori timici, tumori del cuore e dei grandi vasi, tumori primari delle cellule germinative del torace, tumori metastatici nel torace, tumori dell'esofago, tumori del fegato, tumori gastrici, tumore della colecisti e dei dotti biliari, tumori del pancreas esocrino, tumori dell'ampolla di Vater, tumori del piccolo intestino, tumori dell'appendice e del peritoneo, tumori del colon e del retto, tumori dell'ano, tumori renali, tumori delle pelvi e dell'uretere, tumore della vescica, tumori della prostata, tumori del pene e dell'uretra, tumore del testicolo, tumori della vulva e della vagina, tumori della cervice, cancro dell'endometrio, tumori delle tube di Fallopio, tumore ovarico, sarcomi ginecologici, tumori della mammella, melanoma maligno, tumori della pelle, tumori dell'osso, sarcomi dei tessuti molli, tumore di Wilms, neuroblastoma, rabdomiosarcoma, sarcoma di Kaposi, sindrome mielodisplastica, leucemia mieloide acuta dell'adulto e del bambino, leucemia mieloide cronica, leucemia linfocitica acuta dell'adulto, leucemia linfoblastica acuta del bambino, leucemia linfocitica cronica, hairy cell leukemia, leucemia delle mast cell, malattia di Hodgkin's, linfomi non-

Hodgkin's, micosi fungoide e Sézary Sindrome, tumori delle plasma cellule, disordini mieloproliferativi cronici.

32. Procedimento secondo la rivendicazione 26, in cui detta malattia neoplastica è scelta nel gruppo che consiste di carcinoma gastrico, carcinoma colon-rettale e carcinoma mammario.

33. Kit per la diagnosi di malattia neoplastica, comprendente una coppia di primer di amplificazione come definiti nella rivendicazione 20 o 21.

34. Kit secondo la rivendicazione 29, comprendente inoltre una sonda di ibridazione come definita nella rivendicazione 21.

35. Kit secondo la rivendicazione 29 o 30, comprendente inoltre un reagente atto a convertire le basi citosina non metilate in uracile od altra base atta ad appaiarsi con una base diversa da guanina.

36. Kit secondo una qualsiasi delle rivendicazioni 29 a 31, comprendente inoltre una seconda coppia di primers oligonucleotidici di amplificazione di almeno 10 nucleotidi di lunghezza, uno di detti oligonucleotidi essendo complementare ad un primo segmento di una sequenza bersaglio scelta dal gruppo che consiste di SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 27, SEQ ID NO: 28, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 35, SEQ ID NO: 36, SEQ ID NO: 39, SEQ ID NO: 40, SEQ ID NO:

43, SEQ ID NO: 44, SEQ ID NO: 47, SEQ ID NO: 48, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 59, SEQ ID NO: 60, 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: 79, SEQ ID NO: 80 e l'altro di detti oligonucleotidi essendo identico ad un secondo segmento di detta sequenza bersaglio, il secondo segmento essendo localizzato a valle del primo segmento.

37. Kit secondo la rivendicazione 32, in cui almeno uno di detti primo e secondo segmento della sequenza bersaglio comprende almeno un dinucleotide TpG.

38. Kit secondo una qualsiasi delle rivendicazioni 29 a 33, comprendente inoltre mezzi di amplificazione del DNA e/o reagenti di rivelazione del DNA.