

INFORME DE BÚSQUEDA DE PATENTES				
N° de solicitud: NC20170008403				
CRITERIOS PARA LA BÚSQUEDA (anexar pantallazo o reporte en PDF, junto con los boléanos utilizados**)				
Palabras clave utilizadas		PRMT5; CANCER; ADENOSYL AND METHIONINE; S-ADENOSYL METHIONINE; PROTEIN AND ARGININE AND METHYLTRANSFERASE; CELL S PROLIFERATION; ARGININE AND RESIDUES AND METHYLATION.		
CLASIFICACIONES UTILIZADAS PARA LA BÚSQUEDA		CIP: C07H 19/14, C07H 19/167, C07H 19/24, A61K 31/52, A61P 35/00.		
		CPC (Opcional):		
DOCUMENTOS CONSIDERADOS RELEVANTES (documentos patentes, literatura no patente, etc...)				
Informes/Base de datos	N° de solicitud/ Autor*	Fecha de Publicación/Presentación (DD/MM/AAAA)	Reiv. afectadas (con indicación, si procede, de las partes relevantes)	Categoría especiales de los documentos citados**
ORBIT, ESPACENET, USPTO, EPOQUENET Y PATBASE	WO2012082436	21/Junio/2012	1 a 17 Nivel Inventivo	X,Y
	US6492348	10/Diciembre/2002	No aplica	A
	CHRISTA E MÜLLER ET AL	23/Diciembre/2010	No aplica	A
	US2004043960	04/Marzo/2004	No aplica	A
	KANCHAN DEVKOTA ET AL	2014	No aplica	A
	RITESH KUMAR ET AL	2007	No aplica	A
	PEI-PEI KUNG ET AL	02/Junio/2005	No aplica	A
** Categorías especiales de documentos citados:				
“A” documento que define el estado general de la técnica no considerado como particularmente relevante. “E” solicitud de patente o patente anterior pero publicada en la fecha de presentación internacional o en fecha posterior. “P” documento publicado antes de la fecha de presentación internacional pero con posterioridad a la fecha de prioridad reivindicada.		“X” documento particularmente relevante; la invención reivindicada no puede considerarse nueva o que implique una actividad inventiva por referencia al documento aisladamente considerado. “Y” documento particularmente relevante; la invención reivindicada no puede considerarse que implique una actividad inventiva cuando el documento se asocia a otro u otros documentos de la misma naturaleza, cuya combinación resulta evidente para un experto en la materia.		

Literatura no patente	
*Se incluye entre otros, toda la referencia de la literatura no patente.	
Fecha del reporte de búsqueda:	12/12/2018

ESPACENET

Cited in	International search	[XPAI] * WO2015200680 (EPIZYME INC [US]) [XP] 1-3 * pages 171-178; claims 1-15,56,57,79,86-89; tables 1A,10 * [A] 5-25 [I] 4;
		[X] * US6492348 (BAYS DAVID EDMUND [GB], et al) [X] 1-4 * examples 2,3,6,7,11,13-18,...; claims 1,2,16 *;
		[X] * US2004043960 (ZABLOCKI JEFF [US], et al) [X] 1-4 * example 9; claim 1 *;
		[A] - MATTHIJS VAN HAREN ET AL, "Synthesis and evaluation of protein arginine N-methyltransferase inhibitors designed to simultaneously occupy both substrate binding sites", ORGANIC & BIOMOLECULAR CHEMISTRY, (20141023), vol. 13, no. 2, doi:10.1039/C4OB01734J, ISSN 1477-0520, pages 549 - 560, XP055271873 [A] 1-25 * the whole document * * schemes 1-5;; figure 3; table 1 * DOI: * http://dx.doi.org/10.1039/C4OB01734J
		[A] - DONGHANG CHENG ET AL, "Small Molecule Regulators of Protein Arginine Methyltransferases", JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 279, no. 23, doi:10.1074/JBC.M401853200, ISSN 0021-9258, (2004), pages 23892 - 23899, (20040331), XP002647699 [A] 1-25 * the whole document * * figure 1; table 1 * DOI: * http://dx.doi.org/10.1074/JBC.M401853200
		[XPA] - DAVID SMIL ET AL, "Discovery of a Dual PRMT5-PRMT7 Inhibitor", ACS MEDICINAL CHEMISTRY LETTERS, (20150302), vol. 6, no. 4, doi:10.1021/ml500467h, ISSN 1948-5875, pages 408 - 412, XP055271830 [XP] 1-3 * the whole document * * supporting information;; figure 1 * [A] 4-25 DOI: * http://dx.doi.org/10.1021/ml500467h
		[X] - CHRISTA E MÜLLER ET AL, "Recent developments in adenosine receptor ligands and their potential as novel drugs", BIOCHIMICA ET BIOPHYSICA ACTA (BBA) - BIOMEMBRANES, vol. 1808, no. 5, doi:10.1016/J.BBAMEM.2010.12.017, ISSN 0005-2736, (2010), pages 1290 - 1308, (20101223), XP028157805 [X] 1-4 * figure 1; compound 7 * DOI: * http://dx.doi.org/10.1016/j.bbamem.2010.12.017
		[X] - KANCHAN DEVKOTA ET AL, "Analogues of the Natural Product Sinefungin as Inhibitors of EHMT1 and EHMT2", ACS MEDICINAL CHEMISTRY LETTERS, (2014), vol. 5, no. 4, doi:10.1021/ml4002503, ISSN 1948-5875, pages 293 - 297, XP055271475 [X] 1-4 * figure 1; compounds 3,4 * DOI: * http://dx.doi.org/10.1021/ml4002503
		[X] - RITESH KUMAR ET AL, "Activation and inhibition of DNA methyltransferases by S-adenosyl-L-homocysteine analogues", BIOORGANIC & MEDICINAL CHEMISTRY, (2007), vol. 16, no. 5, doi:10.1016/J.BMC.2007.11.075, ISSN 0968-0896, pages 2276 - 2285, XP022526127 [X] 1-3 * table 1; compounds 5,9 * DOI: * http://dx.doi.org/10.1016/j.bmc.2007.11.075
		[X] - PEI-PEI KUNG ET AL, "Design, synthesis, and biological evaluation of novel human 5'-deoxy-5'-methylthioadenosine phosphorylase (MTAP) substrates", BIOORGANIC & MEDICINAL CHEMISTRY LETTERS, vol. 15, no. 11, ISSN 0960-894X, (2005), pages 2829 - 2833, (20050602), XP027801098 [X] 1-3 * tables 1-4; compounds 1,2,9-34 *
		[X] - ERICA W VAN TILBURG ET AL, "5'-O-ALKYL ETHERS OF N,2-SUBSTITUTED ADENOSINE DERIVATIVES: PARTIAL AGONISTS FOR THE ADENOSINE A1 AND A3 RECEPTORS", JOURNAL OF MEDICINAL CHEMISTRY, (2001), vol. 44, no. 18, doi:10.1021/JM001114O, ISSN 0022-2623, pages 2966 - 2975, XP002197488 [X] 1-3 * table 1; compounds 18-29 *

USPTO

Claims **1-25** are rejected under 35 U.S.C. §102(a)(1) as being anticipated by **van Haren et al.** (PTO-1449 ref. **AT2**).

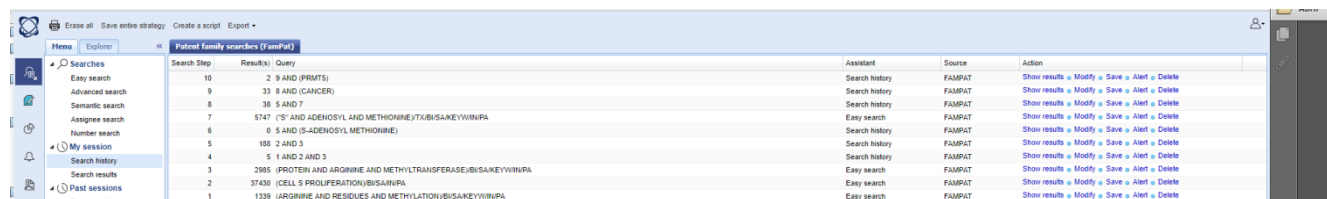
Applicant is referred to the abstract at page 549 wherein he reference teaches the importance of PRMT activity in the treatment of “cancer”, and to page 550 wherein Figures 3A and 3B disclose two pyrrolo[2,3-**d**]pyrimidine nucleoside-like compounds and four adenosine nucleoside analogues that have the noted activity, thereby anticipating the instant claimed subject matter.

Claims **1-25** are rejected under 35 U.S.C. §102(a)(2) as being anticipated by **Cortez et al. ‘532** (PTO-892 ref. **I**; US **9,840,532**).

Applicant is referred to chemical structures, associated substituent definitions, and medicinal testing results beginning at the bottom of column 1 and ending at columns 67-70 wherein pyrrolo[2,3-**d**]pyrimidines have been disclosed and claimed to be active in the treatment of cancer, thereby anticipating the instant claimed subject matter.

No claim is allowed.

ORBIT



Search Step	Results	Query	Assistant	Source	Action
10	2	9 AND (PRMTS)	Search history	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
9	33	8 AND (CANCER)	Search history	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
8	38	5 AND 7	Search history	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
7	5747	(‘S’ AND ADENOSYL AND METHIONINE)/TX/BISAKKEYWIRPA	Easy search	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
6	9	5 AND (S-ADENOSYL METHIONINE)	Search history	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
5	188	2 AND 3	Search history	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
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3	2985	(PROTEIN AND ARGININE AND METHYLTRANSFERASE)/BISAKKEYWIRPA	Easy search	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
2	37430	(CELL S PROLIFERATION)/BISAKKEYWIRPA	Easy search	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete
1	1339	(ARGININE AND RESIDUES AND METHYLATION)/BISAKKEYWIRPA	Easy search	FAMPAT	Show results ▾ Modify ▾ Save ▾ Alert ▾ Delete

Easy search

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33 results for 8 AND (CANCER) - Collection: FAHPAT

#	Title	Publ. date	Publication number	1st app. date	Relevance
1	Earliest application date : 2017-11-30				
1	Methods of treating cancer	2016-06-07	WO2016109536	2017-11-30	N/A
2	Earliest application date : 2016-12-02				
2	Mat2a inhibitors for treating mta1 null cancer	2017-06-08	CA3008743	2016-12-02	N/A
3	Earliest application date : 2016-03-10				
3	Pim1 inhibitors for the treatment of cancer with reduced mta1 activity	2016-09-15	WO2016145150	2016-03-10	N/A
4	Earliest application date : 2016-02-01				
4	Combination therapy for treating cancer	2016-08-04	WO2016123626	2016-02-01	N/A
5	Earliest application date : 2015-11-06				
5	Ezh2 inhibitors and uses thereof	2016-05-12	CA2964629	2015-11-06	N/A
6	Earliest application date : 2013-02-11				
6	Modulators of methyl modifying enzymes, compositions and uses thereof	2013-08-15	CA2862289	2013-02-11	N/A
7	Earliest application date : 2012-05-31				
7	Suv39h2 as a target gene for cancer therapy	2012-12-06	WO2012164936	2012-05-31	N/A
8	Earliest application date : 2011-08-17				
8	Ehmt2 as a target gene for cancer therapy and diagnosis	2012-02-23	WO2012023285	2011-08-17	N/A
9	Earliest application date : 2011-06-22				
9	Ctcf for target genes of cancer therapy and diagnosis	2011-12-29	WO2011161960	2011-06-22	N/A
10	Earliest application date : 2011-02-02				
10	Pim1 and pim1 for target genes of cancer therapy and diagnosis	2011-08-11	WO2011096210	2011-02-02	N/A
11	Earliest application date : 2009-08-25				
11	Vhs1 and vhs1 for target genes of cancer therapy and diagnosis	2011-08-11	WO2011096211	2011-02-02	N/A
12	Earliest application date : 2005-04-15				
12	Pim1 for target genes of cancer therapy and diagnosis	2010-03-04	WO2010023877	2009-08-25	N/A
13	Earliest application date : 2005-01-18				
13	Series of recipe of alive liver cell element, and application	2006-04-19	CN1758045	2005-01-18	N/A
14	Earliest application date : 2003-06-20				
14	Methods of detecting methyltransferase activity and methods of screening for methyltransferase activity modulators	2005-08-04	WO2005071102	2003-06-20	N/A
15	Earliest application date : 2002-11-25				
15	Oligonucleotide inhibitors of mtd2/dna demethylase and uses thereof	2003-12-31	WO200401027	2003-06-20	N/A

Preview Image

Translate Edit Preview

Blood concentration of ADMA	Cancer patients	Healthy individuals	Positive predictive value a/(a+b)
High	a: True positive	b: False positive	Positive predictive value a/(a+b)
Low	c: False negative	d: True negative	Negative predictive value d/(c+d)
	Sensitivity a/(a+c)	Specificity d/(b+d)	

List of publications

Publ. number	Publ. date	Document type
PCT WO2011096210	2011-08-11	A1 - Published application with search report
Priority Numbers & Dates	2010US-61301020	2010-02-03
Application Numbers & Dates	2011WO-JP00562	2011-02-02

Abstract

Objective methods for diagnosing a predisposition to developing cancer, particularly bladder cancer, gastric cancer, colorectal cancer, breast cancer, esophageal cancer, lung cancer, lymphoma, pancreatic cancer and testicular cancer, are described herein. In one embodiment, the diagnostic method involves determining an expression level of PRMT1 or PRMT6 gene. The present invention further provides methods of screening for therapeutic agents useful in the treatment of PRMT1 or PRMT6 associated diseases, such as a cancer, e.g., bladder cancer, diffuse-type gastric cancer, breast cancer, esophageal cancer, NSCLC, SCLC, lymphoma, pancreatic cancer, testicular cancer, cervical cancer, osteosarcoma, prostate cancer and CML. The present invention further provides methods of inhibiting the cell growth and treating or alleviating symptoms of PRMT1 or PRMT6 associated diseases. The present invention also features products, including double-stranded molecules and vectors encoding thereof as well as to compositions containing them.

Inventor(s)

HAMAMOTO RYUJI
NAKAMURA YUSUKE
TSUNODA TAKUYA

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Search 3: "2 AND (PRMT5)" 1-10 of 16 next>>

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1) Family number: 31118016 (US2009298155A)

Title: [EN] EPIGENETIC REGULATORY COMPLEX FOR CONTROL OF GENE EXPRESSION

Abstract: Source: US2009298155A [EN] An epigenetic regulatory polypeptide complex comprises at least a first domain having site-specific DNA binding activity and at least a second domain having an arginine methyltransferase activity, wherein the second domain is capable of methylating an arginine residue located in the tail region of a histone H2A. The complex is able to regulate gene expression in cells, particularly in mammalian stem cells by controlling the methylation of R3 in the tail regions of histones H2A and H4. The complex is exemplified by a polypeptide complex comprising the DNA binding activity of Blimp1 and the arginine methyltransferase activity of Pim1.

Classifications: Classification Explorer

International (IPC): A61K38/45 A61P35/00 A61P43/00 C07K14/47 C07K19/00 C12N15/09 C12N15/11 C12N15/54 C12N15/63 C12N5/02 C12N5/08 C12N5/10 C12N9/10 (Advanced/Invention); A61K38/43 A61P35/00 A61P43/00 C07K14/43 C07K19/00 C12N15/09 C12N15/11 C12N15/54 C12N15/63 C12N5/02 C12N5/08 C12N5/10 C12N9/10 (Core/Invention)

International (IPC): C12N9/10

CPC: C07K14/4702 C07K14/4748 C07K2319/80 C12N9/1007 C07K2319/00

European: C07K14/47A1 C07K14/47A34 C12N9/10A1 M07K319/00E M07K319/80

US: 435/193 435/193P 435/320 1 435/320 100S 435/366 435/366S 435/375 435/375S 435/377 435/377S

Display results

Similar Translate Full-text Status Citations

PatBase - US2009298155_A1

Figure 1: Schematic diagram of the epigenetic regulatory polypeptide complex. The complex consists of a DNA binding domain (Blimp1) and an arginine methyltransferase domain (Pim1). The DNA binding domain is shown binding to a DNA sequence, and the arginine methyltransferase domain is shown methylating an arginine residue on a histone H2A protein.

EPOQUENET



New connection on: : 11-12-2018 : 15:28:22 - Last disconnection on: : 10-12-2018 : 17:43:20

V 4.0.0.44803(LP,U,linux) (Rev:43856 2017-04-27 09:03:29 +0200#(D201820)) (RPM D201820)

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Database: EPODOC

Records: 111.791.323

Terms: 1.480.396.693

Occurrences: 22.647.330.578

Last Update: 20181210

[EPODOC: SS 1] PRMT5

Results in EPODOC **132**

[SS 2] cancer

Results in EPODOC **221.752**

[SS 3] ADENOSYL AND METHIONINE

Results in EPODOC **624**

[SS 4] 1 and 2 and 3

Results in EPODOC **0**

[SS 5] 1 and 3

Results in EPODOC **0**

[SS 6] 1 and 2

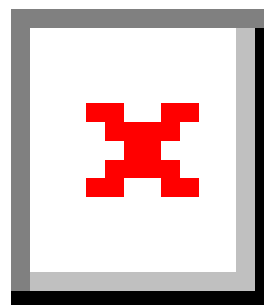
[SS 7] ..li ti ab pn



1/21 © EPODOC / EPO

TI - SELECTIVE TREATMENT OF **PRMT5**
DEPENDENT **CANCER**

AB - The present invention generally relates to therapeutic inhibition of protein arginine methyltransferase 5 (**PRMT5**). In particular, cell lines having MTAP loss and increased intracellular MTA concentrations show selective dependence on **PRMT5**. Thus, the invention also relates to methods of identifying and treating **PRMT5**-related diseases in subjects or tissues which have an MTAP deficiency, alone or in combination, with a second agent that reduces MTAP activity and/or increases intracellular MTA levels, and/or provides an MTA analogs to the cell or tissue. The invention also relates to the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas System and components thereof. More specifically, the present invention relates to the delivery, use and therapeutic applications of the CRISPR-Cas systems and compositions in tumor cells ex vivo and/or in vivo. For example using methods disclosed herein, cells can be sensitized to **PRMT5** inhibition.

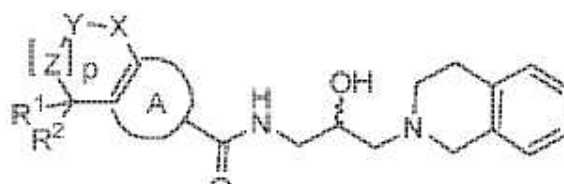


PN - [US2018271891](#) A1 20180927

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TI - COMPOUND HAVING **PRMT5** INHIBITORY
ACTIVITY, PREPARATION FOR COMPOUND,
AND APPLICATIONS THEREOF

AB - The present invention relates to a



compound having **PRMT5** inhibitory activity, a preparation for the compound, and applications thereof. Specifically, the compound of the present invention has a structure as represented by formula I, where the definitions of the groups and substituents are as presented in the description. Also disclosed are a preparation method for the compound and uses thereof in preventing and/or treating **cancer**-related diseases. The compound of the present invention has great protein arginine N-methyltransferase 5 inhibitory activity and thus is applicable in preparing a series of medicaments for treating diseases related to protein arginine N-methyltransferase 5 activity.

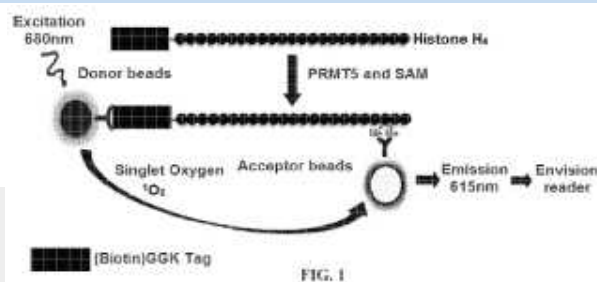
PN - [WO2018161922](#) A1 20180913

3/21 © EPODOC / EPO

TI - SMALL MOLECULE PROTEIN ARGININE METHYLTRANSFERASE 5 (**PRMT5**) INHIBITORS AND METHODS OF TREATMENT

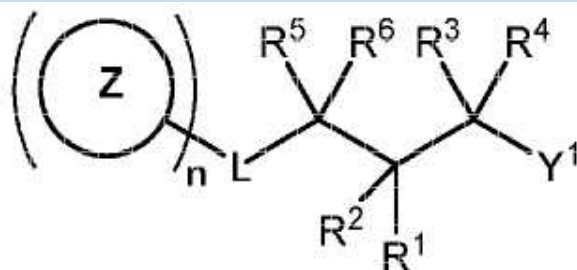
AB - Provided are compounds of formulas (I), (II), (III), and (IV), which effectively inhibit protein arginine methyltransferase 5 (**PRMT5**). Also provided are methods of using the compounds, including a method of treating **cancer**, a method of inhibiting the activity of **PRMT5** in a cell, and a method of treating a disease associated with increased activity of **PRMT5**.

PN - [WO2018081451](#) A1 20180503



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TI - TRICYCLIC COMPOUNDS FOR USE IN TREATMENT OF PROLIFERATIVE DISORDERS



AB - The present invention relates to compounds of Formula (I) as defined herein, and salts, hydrates and solvates thereof. The present invention also relates to pharmaceutical compositions comprising compounds of Formula (I), and to the use of compounds of Formula (I) in the treatment or prevention of **PRMT5**-mediated disorders, such as **cancer**.

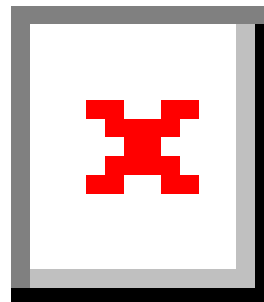
PN - [WO2018167276](#) A1 20180920

5/21 © EPODOC / EPO

TI - COMPOUNDS USEFUL IN THE TREATMENT OR PREVENTION OF A **PRMT5**-MEDIATED DISORDER

AB - The present disclosure relates to compounds suitable for the inhibition of protein arginine methyl-transferase (PRMT), in particular **PRMT5**. These compounds may be for use as therapeutic agents, in particular, agents for use in the treatment and/or prevention of proliferative diseases, such as **cancer**.

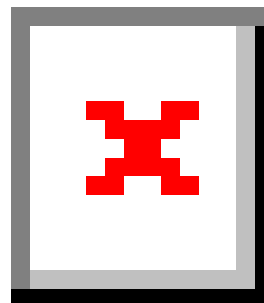
PN - [WO2018167269](#) A1 20180920



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TI - USE OF BIOMARKERS IN IDENTIFYING **CANCER** PATIENTS THAT WILL BE RESPONSIVE TO TREATMENT WITH A **PRMT5** INHIBITOR

AB - The present invention concerns a method of identifying a patient that is likely to be responsive to treatment with a protein arginine N-methyltransferase 5 (**PRMT5**) inhibitor comprising: evaluating a biological sample from the patient for the presence of a spliceosome alteration, wherein the presence of any said alteration indicates a



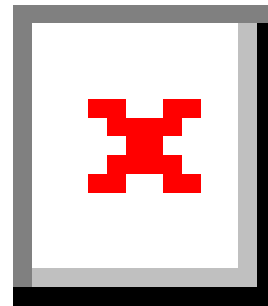
higher likelihood for said patient to be responsive to treatment with said **PRMT5** inhibitor than in the absence of any said mutation or alteration.

PN - [WO2018154104](#) A1 20180830

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TI - INHIBITION OF **PRMT5** TO TREAT MTAP-DEFICIENCY-RELATED DISEASES

AB - The invention provides novel personalized therapies, kits, transmittable forms of information and methods for use in treating patients having **cancer**, wherein the **cancer** is MTAP-deficient and/or MTA-accumulating and thus amenable to therapeutic treatment with a **PRMT5** inhibitor. Kits, methods of screening for candidate **PRMT5** inhibitors, and associated methods of treatment are also provided.

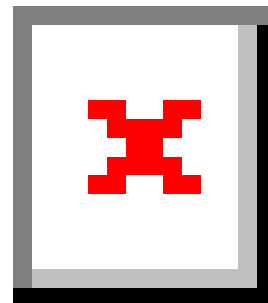


PN - [US2018010132](#) A1 20180111

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TI - METHOD FOR EXAMINING THE EFFECT OF ANTICANCER DRUG FOR TREATMENT OF LUNG **CANCER**

AB - PROBLEM TO BE SOLVED: To provide a method for examining the effect of an anticancer agent using the expression rate of a specific gene as an index.SOLUTION: According to the present invention, there is provided a method for determining a susceptibility of a **cancer** to a tyrosine kinase inhibitor and obtaining supplementary data for determining whether a tyrosine kinase inhibitor has a therapeutic effect on **cancer**, the method comprising the step of, to determine a Gli1 expression rate, **PRMT5** expression rate,



and MEP50 expression rate in a biological sample derived from a human subject, (1) detecting the Gli1 expression rate; (2) detecting the **PRMT5** expression rate; and (3) detecting the MEP50 expression rate, followed by, based on the Gli1 expression rate, **PRMT5** expression rate, and MEP50 expression rate, determining the susceptibility of the **cancer** to the tyrosine kinase inhibitor to obtain supplementary data to determine whether the tyrosine kinase inhibitor has a therapeutic effect on the **cancer**.SELECTED DRAWING: None

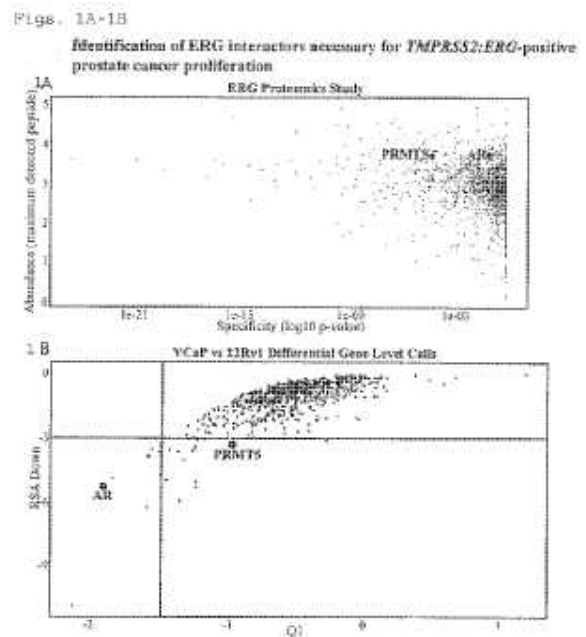
PN - [JP2017201920](#) A 20171116

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TI - COMPOSITIONS AND METHODS FOR DIAGNOSIS AND TREATMENT OF PROSTATE **CANCER**

AB - The invention provides novel personalized therapies, kits, transmittable forms of information and methods for use in treating subjects having TMPRSS2:ERG positive prostate **cancer**, which we show is amenable to therapeutic treatment with a **PRMT5** inhibitor. Kits, methods of screening for candidate **PRMT5** inhibitors, and associated methods of treatment are also provided.

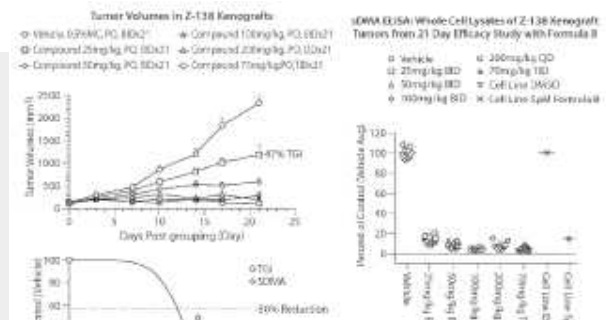
PN - [US2017283807](#) A1 20171005



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TI - **PRMT5** INHIBITORS AND USES THEREOF

AB - Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions



thereof. Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof.

PN - [US2017224685](#) A1 20170810

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TI - **PRMT5** INHIBITORS AND USES THEREOF

AB - Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof. Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof.

PN - [CA2953572](#) A1 20160211

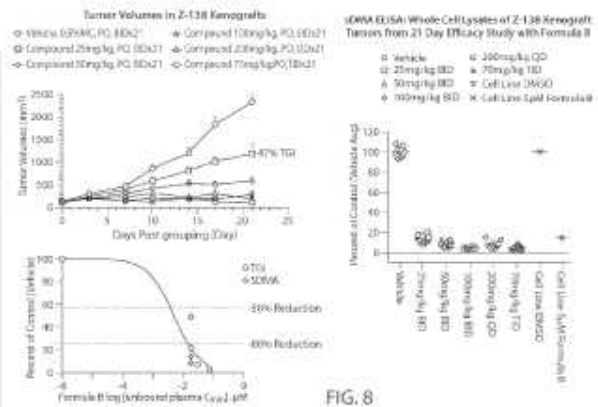


FIG. 8

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TI - **PRMT5** inhibitors and uses thereof

AB - Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof. Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof,

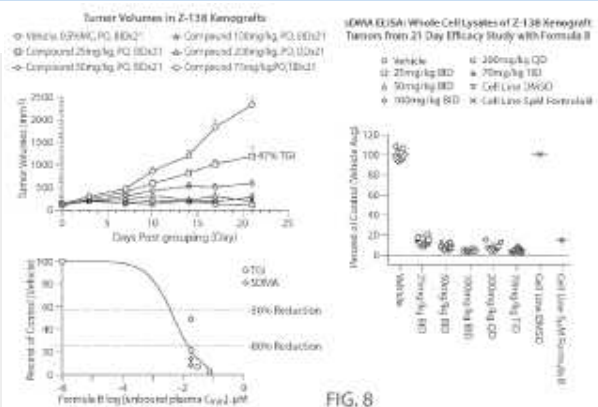


FIG. 8

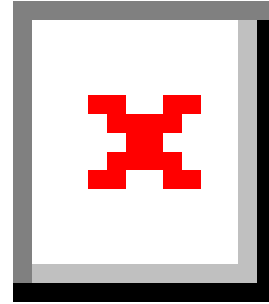
and/or pharmaceutical compositions thereof.

PN - [AU2015301196](#) A1 20170112

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TI - **PRMT5** INHIBITORS FOR THE TREATMENT OF **CANCER** WITH REDUCED MTAP ACTIVITY

PN - [EP3268044](#) A2 20180117

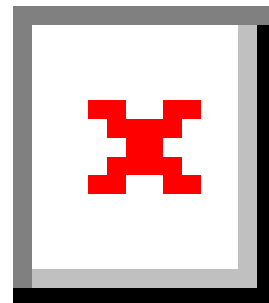


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TI - (A2)
SELECTIVE TREATMENT OF **PRMT5**
DEPENDENT **CANCER**

-(A3)
PRMT5 INHIBITORS FOR THE TREATMENT
OF **CANCER** WITH REDUCED MTAP ACTIVITY

AB - (A2 A3)
The present invention generally relates to therapeutic inhibition of protein arginine methyltransferase 5 (**PRMT5**). In particular, cell lines having MTAP loss and increased intracellular MTA concentrations show selective dependence on **PRMT5**. Thus, the invention also relates to methods of identifying and treating **PRMT5**-related diseases in subjects or tissues which have an MTAP deficiency, alone or in combination, with a second agent that reduces MTAP activity and/or increases



intracellular MTA levels, and/or provides an MTA analogs to the cell or tissue. The invention also relates to the Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-Cas System and components thereof. More specifically, the present invention relates to the delivery, use and therapeutic applications of the CRISPR-Cas systems and compositions in tumor cells ex vivo and/or in vivo. For example using methods disclosed herein, cells can be sensitized to **PRMT5** inhibition.

PN - [WO2016145150](#) A2 20160915

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TI - (A1)
COMPOSITIONS AND METHODS
FOR **CANCER** DETECTION AND TREATMENT
- (B2)
Compositions and methods for **cancer**
detection and treatment

AB - (A1 B2)
Disclosed herein are compositions and methods for **cancer** detection and treatment. Compounds that inhibit **PRMT5** are contemplated, as are pharmaceutical compositions comprising a therapeutically effective amount of at least one **PRMT5** inhibitor. In some embodiments pharmaceutical compositions further comprising at least one HDAC inhibitor are contemplated. Methods of treating disorders in a mammal by inhibiting **PRMT5** by administering to a mammal, a therapeutically effective amount of a **PRMT5** inhibitor are also disclosed.

PN - [US2016052910](#) A1 20160225

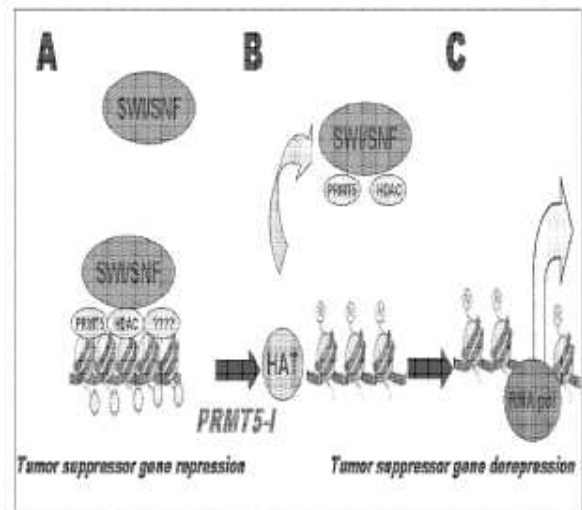


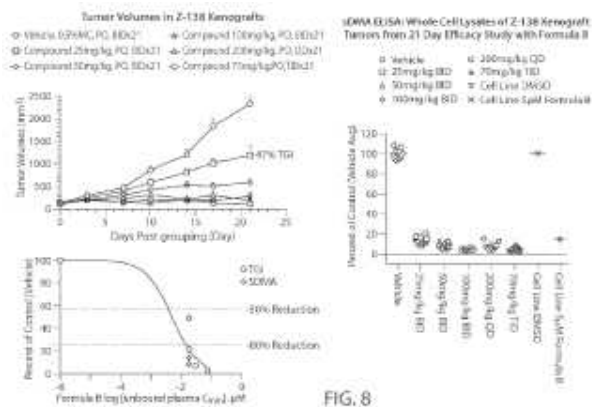
Figure 1

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TI - **PRMT5** INHIBITORS AND USES THEREOF

AB - Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof. Described herein are methods of treating **cancer** using one or more **PRMT5** inhibitors, for example using one or more compounds of Formulae (1-5) or (A-F), pharmaceutically acceptable salts thereof, and/or pharmaceutical compositions thereof.

PN - [WO2016022605](#) A1 20160211

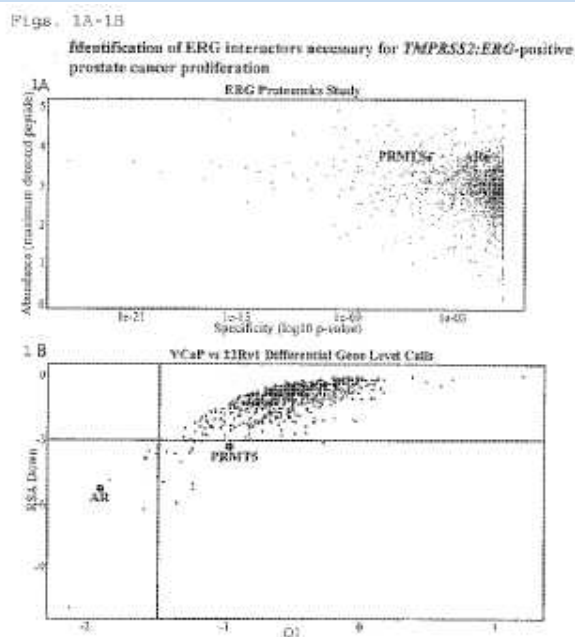


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TI - COMPOSITIONS AND METHODS FOR DIAGNOSIS AND TREATMENT OF PROSTATE **CANCER**

AB - The invention provides novel personalized therapies, kits, transmittable forms of information and methods for use in treating subjects having TMPRSS2:ERG positive prostate **cancer**, which we show is amenable to therapeutic treatment with a **PRMT5** inhibitor. Kits, methods of screening for candidate **PRMT5** inhibitors, and associated methods of treatment are also provided.

PN - [WO2016089883](#) A1 20160609



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TI - INHIBITION OF **PRMT5** TO TREAT MTAP-DEFICIENCY-RELATED DISEASES

AB - The invention provides novel personalized therapies, kits, transmittable forms of information and methods for use in treating patients having **cancer**, wherein



the **cancer** is MTAP -deficient and/or MTA-accumulating and thus amenable to therapeutic treatment with a **PRMT5** inhibitor. Kits, methods of screening for candidate **PRMT5** inhibitors, and associated methods of treatment are also provided.

PN - [WO2016038550](#) A1 20160317

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TI - (A1 B2)
Compositions and Methods for **Cancer** Detection and Treatment

AB - (A1 B2)
Disclosed herein are compositions and methods for **cancer** detection and treatment. Compounds that inhibit **PRMT5** are contemplated, as are pharmaceutical compositions comprising a therapeutically effective amount of at least one **PRMT5** inhibitor. In some embodiments pharmaceutical compositions further comprising at least one HDAC inhibitor are contemplated. Methods of treating disorders in a mammal by inhibiting **PRMT5** by administering to a mammal, a therapeutically effective amount of a **PRMT5** inhibitor are also disclosed.

PN - [US2013059892](#) A1 20130307

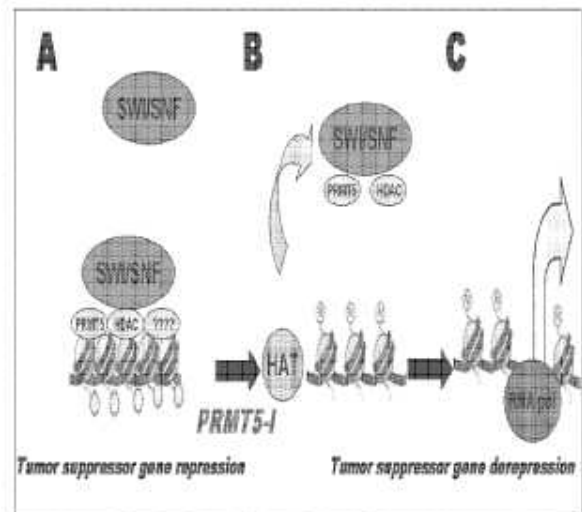


Figure 1

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TI - (A1)
METHOD OF TREATMENT AND SCREENING METHOD
- (B2)
Protein arginine N-methyltransferase-5 method of **cancer** treatment

AB - (A1 B2)

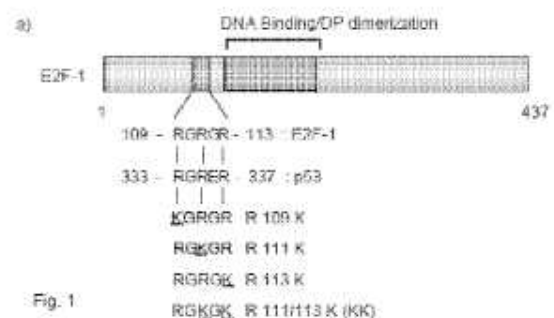


Fig. 1

A method for the treatment of a proliferative disease comprising providing a E2F-1 protein which is arginine-methylation defective or administering a substance which reduces the expression and/or activity of **PRMT5**. The invention also provides antibodies, screening methods and kits.

PN - [US2013011497](#) A1 20130110

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TI - COMPOSITIONS AND METHODS
FOR **CANCER** DETECTION AND TREATMENT

AB - Disclosed herein are compositions and methods for **cancer** detection and treatment. Compounds that inhibit **PRMT5** are contemplated, as are pharmaceutical compositions comprising a therapeutically effective amount of at least one **PRMT5** inhibitor. In some embodiments pharmaceutical compositions further comprising at least one HDAC inhibitor are contemplated. Methods of treating disorders in a mammal by inhibiting **PRMT5** by administering to a mammal, a therapeutically effective amount of a **PRMT5** inhibitor are also disclosed.

PN - [WO2011079236](#) A1 20110630

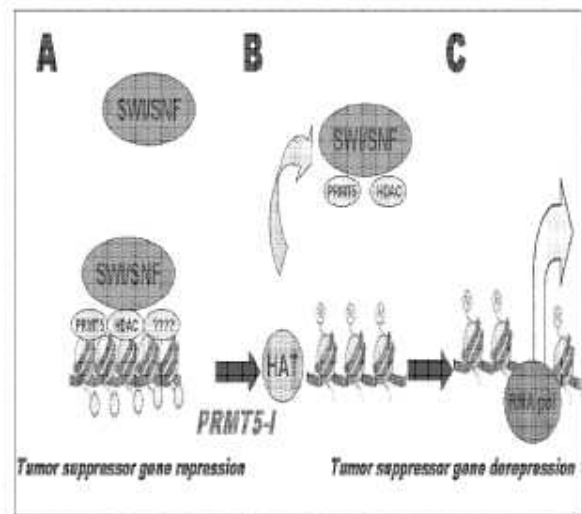


Figure 1