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Name of Journal: *World Journal of Gastroenterology***Manuscript NO:** 54275**Manuscript Type:** ORIGINAL ARTICLE**Basic Study**

Combining protein arginine methyltransferase inhibitor and anti-programmed death-ligand-1 inhibits pancreatic cancer progression

Zheng NN *et al.* PRMT inhibitor plus anti-PD-L1 in PDAC

Nan-Nan Zheng, Min Zhou, Fang Sun, Man-Xiu Huai, Yi Zhang, Chun-Ying Qu, Feng Shen, Lei-Ming Xu

Abstract**BACKGROUND**

Immunotherapy targeting programmed death-1 (PD-1) or programmed death-ligand-1 (PD-L1) has been shown to be effective in a variety of malignancies but has poor efficacy in pancreatic ductal adenocarcinoma (PDAC). Studies have shown that PD-L1 expression in tumors is an important indicator of the efficacy of immunotherapy. Tumor cells usually evade chemotherapy and host immune surveillance by epigenetic changes. Protein arginine methylation is a common posttranslational modification. Protein arginine methyltransferase (PRMT) 1 is deregulated in a wide variety of

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Combination systemic therapies with immune checkpoint ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6174117>

Evidence is emerging to support **combination** systemic therapies on a backbone of immune checkpoint inhibition to overcome resistance to single-agent PD-1/PD-L1/CTLA-4 **blockade** in **pancreatic cancer**. PD-1/PD-L1 inhibitors, in particular, have shown broad single-agent activity across a spectrum of cancers with safety and tolerability profiles that ...

Cited by: 3 Author: Jun Gong, Andrew Hendifar, Richard Tuli, J...
Publish Year: 2018

Resistance to Checkpoint Inhibition in Cancer Immunotherapy

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7047187>

Feb 27, 2020 · Poorly immunogenic tumors show a lack of response to PD-1/PD-L1 **blockade** . In **pancreatic** ... cell conversion and unleashes intratumoural effector T cells thereby enhancing the efficacy of a **cancer** vaccine in a **mouse model**. **Cancer** Immunol Immunother. The efficacy and safety of immune checkpoint **inhibitor combination** therapy in lung **cancer**: a ...

Anti-tumor Activity of the Type I PRMT Inhibitor ...

[https://www.cell.com/cancer-cell/fulltext/S1535-6108\(19\)30256-9](https://www.cell.com/cancer-cell/fulltext/S1535-6108(19)30256-9)

Fedoriw et al. show that the **type I protein arginine** methyltransferases (PRMT) **inhibitor** GSK3368715 has strong anti-**cancer** activity and synergizes with PRMT5 inhibition. MTAP deficiency causes accumulation of an endogenous PRMT5 **inhibitor**, suggesting MTAP status as a predictive biomarker for GSK3368715.

Cited by: 9 Author: Andrew Fedoriw, Satyajit R. Rajapurkar, Sha...
Publish Year: 2019

PD-L1 Expression in Pancreatic Cancer | Request PDF

<https://www.researchgate.net/publication/313033920...>

PD-L1 Expression in **Pancreatic Cancer**. ... excessive desmoplasia and the lack of consensus expression of PD-L1 in this **type of cancer** ... (PD-1/PD-L1) **blockade** in **pancreatic cancer** (PC) remains ...

Author: Lei Zheng

Biochemical Aspects of PD-L1 Regulation in Cancer ...

<https://www.sciencedirect.com/science/article/pii/S0968000418301877>

These results suggest that evaluation of the ZEB1/miR-200 axis-mediated regulation of PD-L1 might be a useful marker of lung **cancer** to guide treatment selection with anti-PD-1/PD-L1 **blockade** therapies. MiR-34, a downstream target of p53, directly binds to the PD-L1 3'-UTR and **inhibits** PD-L1 expression .

Cited by: 15 Author: Jinfang Zhang, Fabin Dang, Junming Ren, ...
Publish Year: 2018

Role and inhibition of GLI1 protein in cancer

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5877502>

Mar 27, 2018 · SHH **protein** binds to the PTCH receptor (1). In the absence of the ligand, PTCH **inhibits** SMO, a downstream **protein** in the pathway (2). The binding of SHH relieves SMO inhibition, leading to activation of the GLI transcription factors: the activators GLI1 and GLI2 and the repressor GLI3 (3).

Cited by: 8 Author: Eloise Mastrangelo, Mario Milani
Publish Year: 2018

Immunoepigenetics Combination Therapies: An Overview of ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6539010>

May 07, 2019 · Mocetinostat, an **inhibitor** of HDAC1 and 3 has been found to exert antitumor effects in both hematological and solid cancers. In an NSCLC murine **model**, mocetinostat was shown to upregulate PD-L1, and when used in **combination** with a murine PD-L1 antibody, significantly decreased tumor burden . Furthermore, mocetinostat upregulated intratumoral ...

Cited by: 7 Author: Debarati Banik, Sara Moufarrij, Alejandro Vi...
Publish Year: 2019

Immune Checkpoint Blockade Therapy for dMMR/MSI-H mCRC

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6612427>

Immune Checkpoint **Blockade** Therapy for dMMR/MSI-H mCRC. The DNA mismatch repair (MMR) system is one of the key DNA repair mechanisms whose primary function is to preserve the fidelity of DNA replication as it recognizes and repairs erroneous bases or insertion-deletion loops of newly replicated DNA strands. 9 Approximately 15% of all CRCs are dMMR/MSI-H and 75%-80% of these patients have ...

Cited by: 9 Author: James J. Lee, Edward Chu
Publish Year: 2018

Frontiers | Combination Therapy With Histone Deacetylase ...

<https://www.frontiersin.org/articles/10.3389/fonc.2018.00092>

Mar 29, 2018 · Genetic and epigenetic changes in DNA are involved in **cancer** development and tumor **progression**. Histone deacetylases (HDACs) are key regulators of gene expression that act as transcriptional repressors by removing acetyl groups from histones. HDACs are dysregulated in many cancers, making them a therapeutic target for the treatment of **cancer**.

Cited by: 117 Author: Amila Suraweera, Kenneth J. O'Byrne, Kenn...
Publish Year: 2018





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[Targeting protein arginine methyltransferase 5 inhibits ...](#)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4673200>

Sep 08, 2015 · Targeting **protein arginine methyltransferase 5** inhibits colorectal **cancer** growth by decreasing **arginine** methylation of eIF4E and FGFR3 Baolai Zhang , 1, 2 Shuhong Dong , 2 Ruiming Zhu , 1 Chunyan Hu , 1 Jing Hou , 1 Yan Li , 1 Qian Zhao , 1 Xue Shao , 1 Qian Bu , 1 Hongyu Li , 1 Yongjie Wu , 2 Xiaobo Cen , 1 and Yinglan Zhao 1

Cited by: 32**Author:** Baolai Zhang, Shuhong Dong, Ruiming...**Publish Year:** 2015

[The Promise for Histone Methyltransferase Inhibitors for ...](#)

<https://link.springer.com/content/pdf/10.1007/s12325-020-01379-x.pdf>

activity in leukemia and **pancreatic cancer** xenografts [120]. LLY-283 is a potent and ... **Protein arginine methyltransferase inhibitors** PRMT5 **inhibitors** GSK3326595, JNJ-64619178, PF-06939999 GlaxoSmithKline, Johnson & Johnson, Pfizer ... death **ligand 1** ...

[Immune Checkpoint Inhibition for Pancreatic Ductal ...](#)

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6104627>

Introduction. **Pancreatic** ductal adenocarcinoma (PDAC), as one of the most fatal malignancies in the world, is the fourth leading cause of **cancer**-related deaths among both men and women in developed countries ().Its mortality almost equals its incidence: for 2018 alone, 55,440 diagnoses of **pancreatic cancer** are projected for the United States with 44,330 associated deaths in the ...

Cited by: 15**Author:** Derya Kabacaoglu, Katrin J. Ciecielski,...**Publish Year:** 2018

[Epigenetic regulators of programmed death-ligand 1 ...](#)

<https://www.sciencedirect.com/science/article/pii/S193152441830094X>

The programmed cell death **protein 1**-programmed death-**ligand 1** (PD-L1) axis has been successfully targeted in clinics and the use of immune check-point **inhibitors** have shown durable antitumor response in untreated or heavily treated advanced stage **cancer**.

Cited by: 5**Author:** Sachin Kumar, Surender Kumar Shara...



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Targeting protein arginine methyltransferase 5 inhibits ...

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Sep 08, 2015 · Targeting **protein arginine methyltransferase 5** inhibits colorectal **cancer** growth by decreasing **arginine** methylation of eIF4E and FGFR3 Baolai Zhang , 1, 2 Shuhong Dong , 2 Ruiming Zhu , 1 Chunyan Hu , 1 Jing Hou , 1 Yan Li , 1 Qian Zhao , 1 Xue Shao , 1 Qian Bu , 1 Hongyu Li , 1 Yongjie Wu , 2 Xiaobo Cen , 1 and Yinglan Zhao 1

Cited by: 32

Author: Baolai Zhang, Shuhong Dong, Ruiming Z...

Publish Year: 2015

The Promise for Histone Methyltransferase Inhibitors for ...

<https://link.springer.com/content/pdf/10.1007/s12325-020-01379-x.pdf>

activity in leukemia and **pancreatic cancer** xenografts [120]. LLY-283 is a potent and ... **Protein arginine methyltransferase inhibitors** PRMT5 inhibitors GSK3326595, JNJ-64619178, PF-06939999 GlaxoSmithKline, Johnson & Johnson, Pfizer ... death **ligand 1** (PD-L1) blockade. The study also

Immune Checkpoint Inhibition for Pancreatic Ductal ...

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Cited by: 15

Author: Derya Kabacaoglu, Katrin J. Ciecielski, Di...

Publish Year: 2018

Anti-Cancer Activity of PAK4/NAMPT Inhibitor and ...

<https://kidney360.asnjournals.org/content/1/5/376>

Background Kidney **cancer** (or renal cell carcinoma, RCC) is the sixth most common malignancy in the United States and is increasing in incidence. Despite new therapies, including targeted therapies and immunotherapies, most RCCs are resistant to treatment. Thus, several laboratories have been evaluating new approaches to therapy, both with single agents as well as combinations.