[0006] Despite importance of PRMT5 on cell viability and its prevalence in cancers, effective therapies that inhibit PRMT5 have been elusive. Thus, there remains a need to develop new PRMT5 inhibitor therapies to treat wide range of cancers.

SUMMARY OF THE DISCLOSURE

[0007] One aspect of the disclosure provides methods for treating cancer in a subject. Such methods include administering to the subject a therapeutically effective amount of a CDK4/6 inhibitor and a therapeutically effective amount of a PRMT5 inhibitor.

[0007a] In another aspect, there is provided a use of a protein arginine N-methyl transferase 5 (PRMT5) inhibitor for the manufacture of a medicament for treating cancer in a subject, wherein a therapeutically effective amount of a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor and a therapeutically effective amount of the PRMT5 inhibitor are to be administered to the subject.

[0008] Also provided herein is a method for treating cancer in a subject in need thereof. Such methods include determining that the cancer is associated with MTAP homozygous deletion (e.g., an MTAP-associated cancer). These methods optionally further include determining that the cancer is associated with a CDKN2A homozygous deletion. Such methods further include administering to the subject a therapeutically effective amount of a CDK4/6 inhibitor and a therapeutically effective amount of a PRMT5 inhibitor.

[0008a] In yet another aspect, there is provided a use of a cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitor for the manufacture of a medicament for treating cancer in a subject, wherein a therapeutically effective amount of the CDK4/6 inhibitor and a therapeutically effective amount of a protein arginine N-methyl transferase 5 (PRMT5) inhibitor are to be administered to the subject.

[0009] These and other features and advantages of the present invention will be more fully understood from the following detailed description taken together with the accompanying claims. It is noted that the scope of the claims is defined by the recitations therein and not by the specific discussion of features and advantages set forth in the present description.

BRIEF DESCRIPTION OF THE DRAWINGS

[0010] The accompanying drawings are included to provide a further understanding of the methods of the disclosure, and are incorporated in and constitute a part of this specification. The drawings illustrate one or more embodiment(s) of the disclosure and, together with the description, serve to explain the principles and operation of the disclosure.

[0011] Figure 1 illustrates the results of the methods of Example 1 in the $KRAS^{G12C}$ and $CDKN2A/MTAP^{DEL}$ lung tumor xenograft LU99 model grown in immunodeficient mice. The PRMT5 inhibitor used in this method was MRTX9768 administered at 100 mg/kg twice a day (BID), and the CDK4/6 inhibitor was palbociclib administered at 130 mg/kg once a day (QD). Average tumor volume ± standard error is plotted of the mean at study day as indicated.

[0012] Figure 2 illustrates the results of the methods of Example 2 in the $KRAS^{G12C}$ and $CDKN2A/MTAP^{DEL}$ lung tumor xenograft LU99 model grown in immunodeficient mice. The PRMT5 inhibitor used in this method was MRTX7477 administered at 200 mg/kg BID, and the CDK4/6 inhibitor was palbociclib administered at 130 mg/kg QD. Average tumor volume ± standard error is plotted of the mean at study day as indicated