virus that specifically replicates in cancer cells, but leave normal cells unharmed. However, there have been challenges in designing viruses that selectively replicate in cancer cells. Thus, there is a need for additional viruses that selectively replicate in cancer cells.

SUMMARY

[0005] Provided herein is an adenovirus comprising an E1A polypeptide comprising one or more modifications, an E4orf6/7 polypeptide comprising one or more modifications, or an E4orf1 polypeptide comprising one or more modifications or a combination thereof. Compositions and kits comprising the modified adenoviruses are also provided. Further, provided is a method of treating a proliferative disorder in a subject comprising administering to the subject an adenovirus comprising an E1A polypeptide comprising one or more modifications, an E4orf6/7 polypeptide comprising one or more modifications, or an E4orf1 polypeptide comprising one or more modifications or a combination thereof.

[0005a] In one embodiment, there is provided the use of the adenovirus described herein or the pharmaceutical composition described herein, in the manufacture of a medicament for treating a proliferative disorder in a subject.

[0006] The details of one or more embodiments are set forth in the accompanying drawings and the description below. Other features, objects, and advantages will be apparent from the description and drawings, and from the claims.

DESCRIPTION OF DRAWINGS

[0007] Figure 1 is a schematic showing the general rationale of oncolytic viral cancer therapy.

[0008] Figure 2 is a schematic showing the structural features of adenovirus (Ad) and a map of the adenovirus genome with transcriptional units in boxes and labeled genes.

[0009] Figure 3 are images of immunoblots of cell lysates from infected primary small airway epithelial cells and tumor cells infected with wild type Ad5 and the "RB/p16/E2F pathway" selective viruses. Tumor and primary human cells were infected with either

50. The adenovirus of any one of claims 30-33, wherein the E1A polypeptide comprises a deletion of amino acid residues 122-126 of E1A and a substitution at residue Y47.

51. The adenovirus of any one of claims 30-50, wherein the E1A polypeptide comprises SEQ ID NO:1.

52. The adenovirus of any one of claims 30-50, wherein the E1A polypeptide comprises SEQ ID NO:2.

53. The adenovirus of any one of claims 1-52, wherein the adenovirus selectively replicates in Rb-deficient cells.

54. A pharmaceutical composition comprising the adenovirus of any one of claims 1-53 and a pharmaceutically acceptable carrier.

55. A kit comprising the pharmaceutical composition of claim 54 and instructions for use.

56. The kit of claim 55, further comprising one or more additional therapeutic agents.

57. The kit of claim 56, wherein the therapeutic agent is a chemotherapeutic agent.

58. ~~A method of treating a proliferative disorder in a subject comprising administering~~ Use of the adenovirus of any one of claims 1-53 or the pharmaceutical composition of claim 54 in the manufacture of a medicament for treating a proliferative disorder in a ~~to the~~ subject.

59. The ~~method~~ use of claim 58, wherein the adenovirus or pharmaceutical composition is to be administered intravenously, intravascularly, intrathecally, intramuscularly, subcutaneously, intraperitoneally, or orally.

60. The ~~method~~ use of claim 58 or 59, wherein the medicament further comprise~~sing administering to the subject~~ one or more additional therapeutic agents.

61. The ~~method~~ use of claim 60, wherein the therapeutic agent is a chemotherapeutic agent.

62. The ~~method~~ use of any one of claims 58-61, wherein the proliferative disorder is selected from the group consisting of lung cancer, prostate cancer, colorectal cancer, breast cancer, thyroid cancer, renal cancer, liver cancer and leukemia.

63. The ~~method~~ use of any one of claims 58-62, wherein approximately 10^3 to 10^{12} plaque forming units of the adenovirus is to be administered to the subject.

64. The ~~method~~ use of any one of claims 58-63, wherein the proliferative disorder is metastatic.