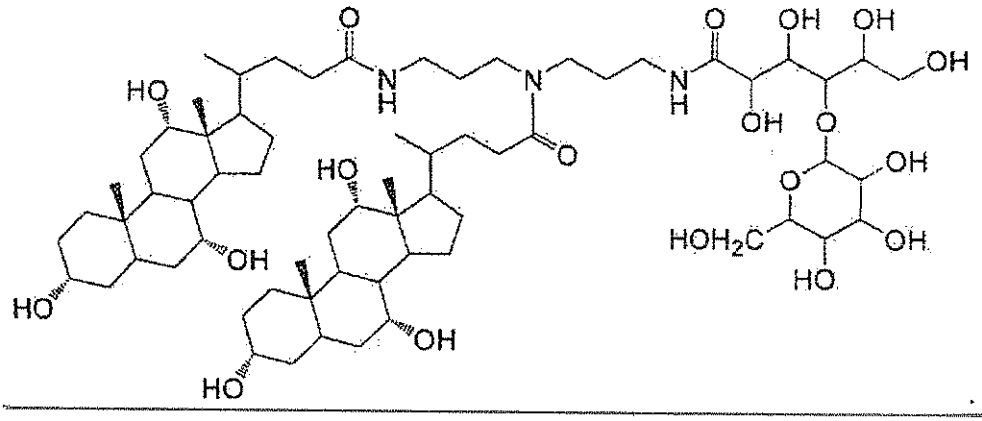
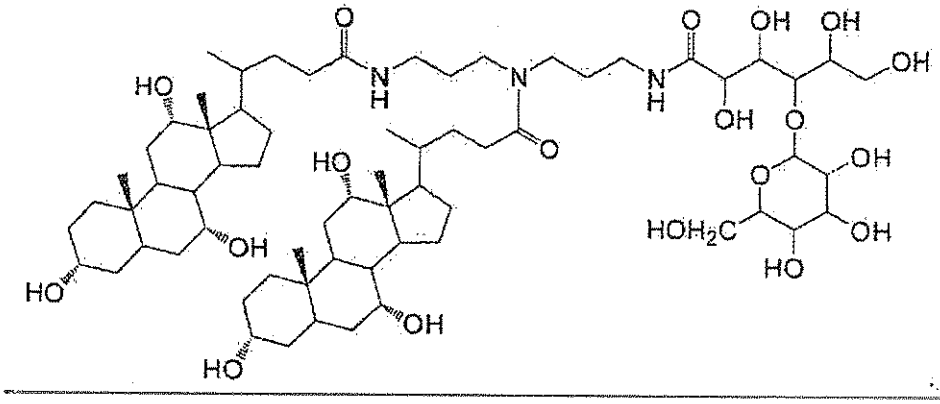
SUMMARY OF THE ~~INVENTION~~DISCLOSURE

[0007] The present ~~invention~~disclosure provides methods for the treatment of interferon resistant tumors through the use of recombinant vectors encoding interferon species. In particular, it is noted that interferon species provided by recombinant vectors possess properties not associated with the available recombinantly produced interferon proteins. The present ~~invention~~disclosure further provides compositions useful in the treatment of interferon resistant tumors using recombinant vectors encoding interferons.

[0007a] In a first aspect, there is provided a replication deficient recombinant adenovirus encoding an interferon α2b for use in treating an interferon resistant tumor of the bladder, wherein the adenovirus is to be used in conjunction with an enhancing agent having the formula:

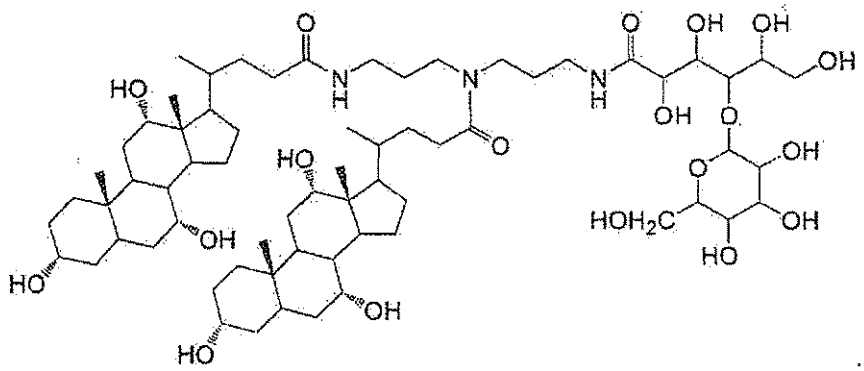


[0007b] In a second aspect, there is provided an enhancing agent having the formula:

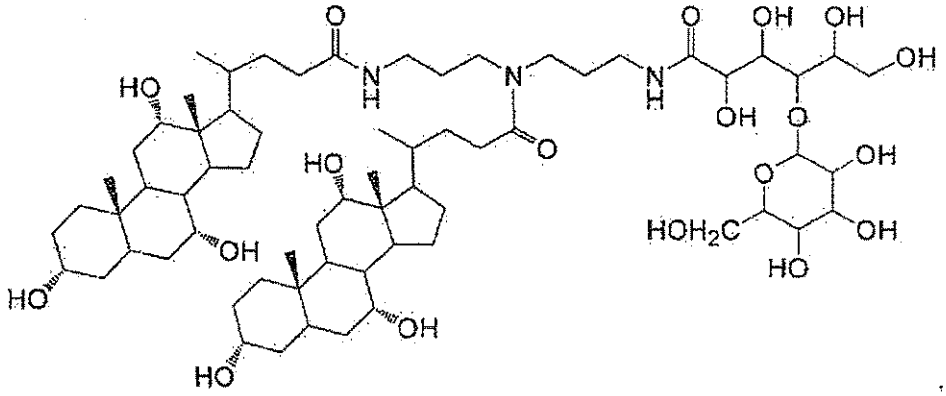


for use in treating an interferon resistant tumor of the bladder, wherein the enhancing agent is to be used in conjunction with a replication deficient recombinant adenovirus encoding interferon α2b.

[0007c] In a third aspect, there is provided the use of a replication deficient recombinant adenovirus encoding an interferon α2b for the manufacture of a medicament for use in treating an interferon resistant tumor of the bladder, wherein the medicament is to be used in conjunction with art enhancing agent having the formula:

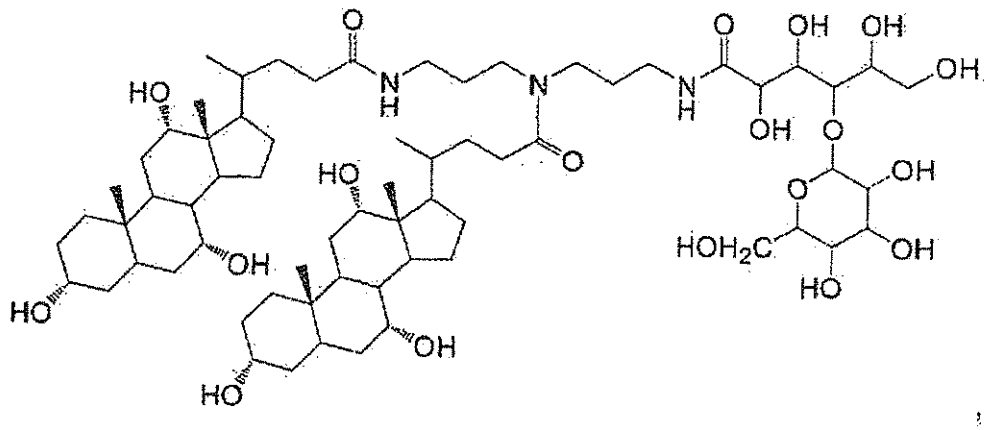


[0007d] In a fourth aspect, there is provided the use of an enhancing agent having the formula:



for the manufacture of a medicament for use in treating an interferon resistant tumor of the bladder, wherein the medicament is to be used in conjunction with a replication deficient recombinant adenovirus encoding an interferon α2b.

[0007e] In a fifth aspect, there is provided a formulation for intravesical instillation to the bladder comprising an enhancing agent, or a pharmaceutically acceptable salt thereof having the formula:



and a replication deficient recombinant adenoviral vector encoding interferon α2b for use in treating an interferon resistant tumor of the bladder.

BRIEF DESCRIPTION OF THE DRAWINGS

[0008] Figure 1 provides a data of the effect of intravestical Ad-IFN-α2α1/Syn 3 or Ad-IFN-α2b/Syn3 on tumor regression. The graph at the left of the panel shows marked decrease in the pre-treatment tumor size 21 days after Ad-IFNα2α1/Syn 3 or Ad-IFNα2b/Syn3 treatment*, P =0.0024. All other treatment groups showed progressive tumor growth including Ad-IFNα2α1 without Syn3 or the IFN-α2α1 protein alone. To the right are a series of fluorescence micrographs providing a representative example of pre-treatment tumor images and those taken 21 days later from individual mice in each treatment group.

[0009] Figure 2 provides a demonstration of prolonged IFN expression following Ad-IFN/Syn3 intravesical treatment. Panel A demonstrates that sustained levels of IFN are seen in the bladder homogenates of athymic mice treated once with Ad-IFNα2b/Syn3 which was increased after two exposures. In contrast, similar treatment with 200,000 IU of Intron A protein itself did not show any such high or prolonged IFN levels. Arrows indicate when treatment 1 and 2 were given. Panel B provides data indicating that the same high levels of IFN in the urothelium and adjacent bladder tumor is seen by immunohistochemical analysis 2 days after two treatments with Ad-IFNα2α1/Syn 3 in athymic mice. Arrows show strong perinuclear IFN staining present in many cells. Panel C demonstrates that similar high levels of IFN are seen in the urothelium of outbred Balb-C mice 7 days after treatment with either Ad-IFNα2α1/Syn 3 or Ad-IFNα2b/Syn3. No morphological changes in the urothelium were seen by histological examination or H&E stained sections.

[0010] Figure 3 provides a comparison of Ad-IFN cytotoxicity to bladder cancer cell lines resistant to over 100,000 IU of Intron A. Panel A shows the negative IFN staining in control cells (10X Magnification) and marked perinuclear IFN staining in 253J-BV cells treated with Ad-IFNα2α1 (40X Magnification). Panel B is data from a flow cytometric analysis showing increase in the number of subdiploid cells at 48 hrs after

CLAIMS

1. The use of an adenoviral vector capable of expressing an interferon alpha for the manufacture of a medicament for treating interferon-resistant tumors.

2. The use of an adenoviral vector capable of expressing an interferon alpha for the manufacture of a medicament for treating interferon-resistant tumors, wherein said interferon-resistant tumors were previously treated with Syn3.

3. The use of an adenoviral vector capable of expressing an interferon alpha for the manufacture of a medicament for treating interferon-resistant tumors comprised of neoplastic bladder cells.

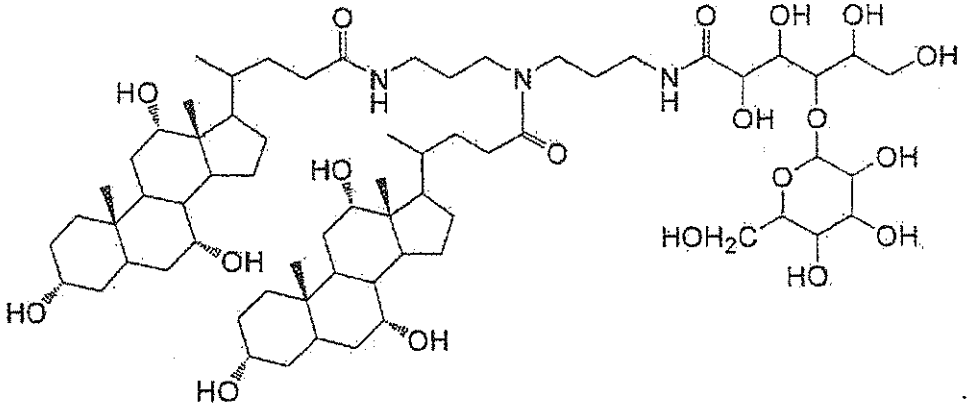
4. The use claim 1, 2 or 3, wherein said interferon alpha is interferon alpha2b.

5. The use of an adenoviral vector capable of expressing an interferon alpha for the manufacture of a medicament for treating interferon-resistant tumors comprised of neoplastic bladder cells, wherein said neoplastic bladder cells were previously treated with Syn3.

6. The use of an adenoviral vector capable of expressing an interferon alpha2b for the manufacture of a medicament for treating interferon-resistant tumors comprised of neoplastic bladder cells, wherein said neoplastic bladder cells were previously treated with Syn3.

CLAIMS

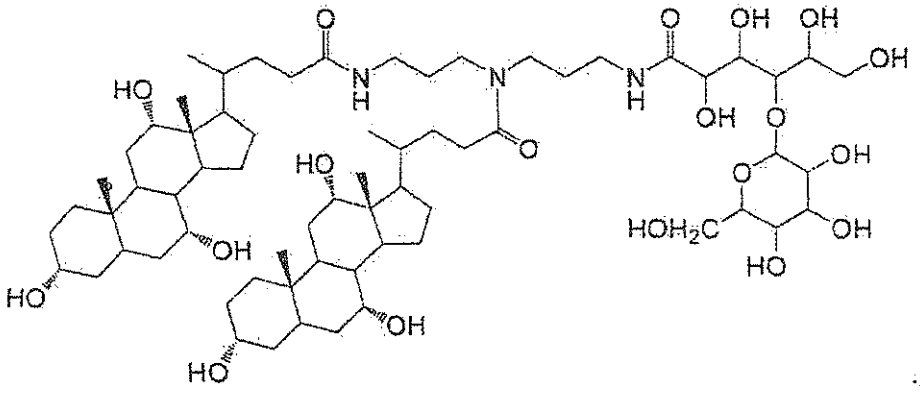
1. A replication deficient recombinant adenovirus encoding an interferon α2b for use in treating an interferon resistant tumor of the bladder, wherein the adenovirus is to be used in conjunction with an enhancing agent having the formula:



2. The adenovirus of claim 1 for use in treating an interferon resistant tumour of the bladder, wherein the adenovirus is used contemporaneously of exposing the bladder to the enhancing agent, preferably within an hour of exposing the bladder to the enhancing agent.

3. The adenovirus of claim 1 or 2 for use in treating an interferon resistant tumour of the bladder, wherein the adenovirus and enhancing agent are to be administered contemporaneously.

4. An enhancing agent having the formula:



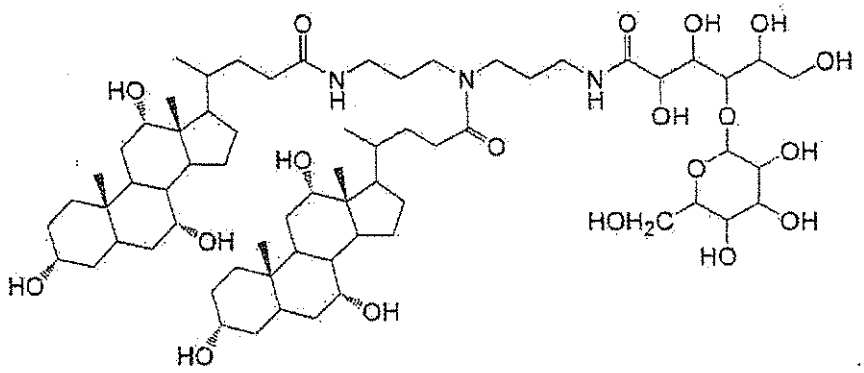
for use in treating an interferon resistant tumor of the bladder, wherein the enhancing agent is to be used in conjunction with a replication deficient recombinant adenovirus encoding interferon α2b.

5. The enhancing agent of claim 4 for use in treating an interferon resistant tumour of the bladder, wherein the adenovirus is used contemporaneously of exposing the bladder to the enhancing agent, preferably within an hour of exposing the bladder to the enhancing agent.

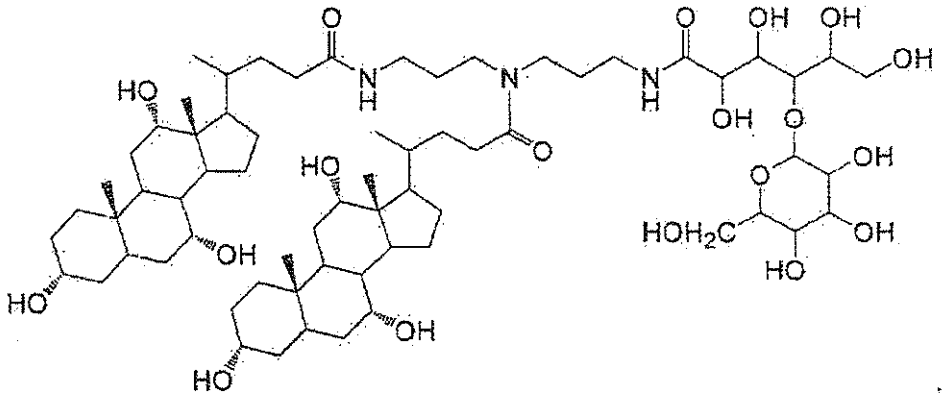
6. The enhancing agent of claim 4 for use in treating an interferon resistant tumour of the bladder, wherein the adenovirus and enhancing agent are to be administered contemporaneously.

7. The enhancing agent of any one of claims 4 to 6 for use in treating an interferon resistant tumour of the bladder, wherein the tumor is a superficial tumor.

8. The use of a replication deficient recombinant adenovirus encoding an interferon α2b for the manufacture of a medicament for use in treating an interferon resistant tumor of the bladder, wherein the medicament is to be used in conjunction with art enhancing agent having the formula:



9. The use of an enhancing agent having the formula:



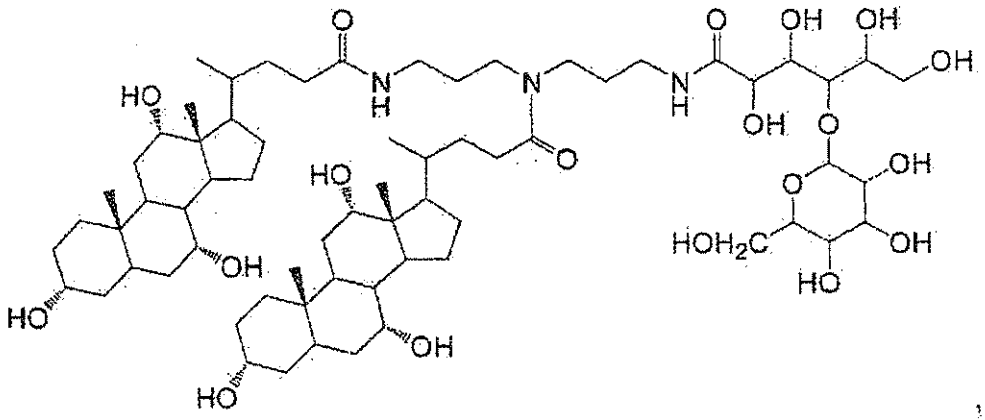
for the manufacture of a medicament for use in treating an interferon resistant tumor of the bladder, wherein the medicament is to be used in conjunction with a replication deficient recombinant adenovirus encoding an interferon α2b.

10. The use of any one of claims 8 or 9, wherein the adenovirus is used contemporaneously of exposing the bladder to the enhancing agent, preferably within an hour of exposing the bladder to the enhancing agent.

11. The use of any one of claims 8 or 9, wherein the adenovirus and enhancing agent are to be administered contemporaneously.

12. The use of any one of claims 8 to 11, wherein the tumor is a superficial tumor.

13. A formulation for intravesical instillation to the bladder comprising an enhancing agent, or a pharmaceutically acceptable salt thereof having the formula:



and a replication deficient recombinant adenoviral vector encoding interferon α2b for use in treating an interferon resistant tumor of the bladder.

14. The adenovirus of any one of claims 1 to 3 for use in treating an interferon resistant tumour of the bladder, or the formulation of claims 13 for use in treating an interferon resistant tumour of the bladder, wherein the tumor is a superficial tumor.

15. The adenovirus or enhancing agent of any one of the preceding claims for use in treating an interferon resistant tumour of the bladder, which is to be administered intravesically.

16. The use of any one of the preceding claims, wherein the medicament is to be administered intravesically.