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13. Abstract ***(Maximum 200 Words)*** *(abstract should contain no proprietary or confidential information)*

An adenovirus encoding the genes for human somatostatin receptor subtype 2 and bacterial cytosine deaminase (AdSSTR2CD) was constructed. The SSTR2 allows for non-invasive imaging of gene transfer and therapy with radiolabeled somatostatin analogues. The CD converts the prodrug 5-fluorocytosine (5-FC) to the toxic and radiosensitzing 5-fluorouracil (5-FU). Thus, it is hypothesized that AdSSTR2CD can be used for the simultaneous expression of SSTR2 and CD for the detection and treatment of prostate cancer. In vitro experiments were performed with DU-145 and PC-3 human prostate cancer cells. Expression levels of SSTR2 were determined using ^{125}I-somatostatin in competitive inhibition assays on cell membrane preparations. Activity of CD was determined using an MTS assay to demonstrate sensitivity of the infected cells to 5-FC. In vivo experiments were conducted in athymic nude mice bearing subcutaneous DU-145 or PC-3 cells (n = 3-4). AdSSTR2CD was injected intratumorally followed 48 h later by an i.v. injection of ^{99m}Tc-P2045 (a radiolabeled somatostatin analogue kindly provided by Diatide Research Laboratories). The mice were imaged 5 h later with an Anger gamma camera equipped with a pinhole collimator and terminated for biodistribution analyses. The expression of SSTR2 on PC-3 cells was 209 fmol/mg of protein after AdSSTR2CD infection at 10 pfu/cell. DU-145 cells showed that SSTR2 expression was 4215 fmol/mg after infection at 10 pfu/cell. The IC50 values of 5-FC were 682 μM in PC-3 cells and 29 μM in DU-145 after infection with AdSSTR2CD at 10 pfu/cell. The PC-3 and DU-145 tumors injected with AdSSTR2CD could be visualized by imaging ^{99m}Tc-P2045 uptake. The PC-3 tumors averaged 1.1 +/- 0.4 % dose/g, while the DU-145 tumors averaged 0.7 +/- 0.3 % dose/g. Uninfected tumors demonstrated < 0.2 % dose/g. These results are significant in that they show expression of both CD and SSTR2 in human prostate cancer cells after infection with AdSSTR2CD and SSTR2 expression in xenograft models.

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Introduction

It is estimated that approximately 37,000 U.S. men died in 1999 from prostate cancer. It is clear that novel treatments for prostate cancer are necessary. Radiolabeled monoclonal antibodies have been used to treat hormone-refractory prostate cancer with limited success. Reasons for these limitations include, bone marrow toxicity from the long serum half-life of the radiolabeled antibody, heterogeneous tumor distribution of the large molecular weight antibody, and low tumor antigen/receptor expression. A strategy to overcome these limitations is to combine peptide radiotherapy with gene therapy. Radiolabeled peptides can overcome problems associated with bone marrow toxicity and tumor penetration due to their small molecular weight, while gene therapy can be used to increase the tumor antigen/receptor expression. Previous studies have shown that an adenovirus encoding for the somatostatin receptor subtype 2 (AdSSTR2) can be used to increase tumor localization of radiolabeled octreotide analogues. **Objective/Hypothesis.** The objective of this proposal is to determine if induction of SSTR2 with AdSSTR2 on human prostate cancer xenografts in mice has a therapeutic effect after targeting with the octreotide analogue, ^{90}Y-SMT 487. Preliminary evidence that suggests this strategy will be successful is provided in the proposal and shows that ^{90}Y-SMT 487 and AdSSTR2 can be used in conjunction to inhibit the tumor growth of non-small cell lung cancer xenografts. **Specific Aims.** SPECIFIC AIM #1. Evaluate the expression of SSTr2 on human prostate cancer cells *in vitro* after infection with AdSSTR2 using radiolabeled SMT 487 binding and internalization assays. SPECIFIC AIM #2. Evaluate the distribution of radiolabeled SMT 487 after i.v. injection by non-invasive gamma camera imaging and by gamma counter analysis in nude mice bearing s.c. human prostate cancer xenografts injected with AdSSTR2. SPECIFIC AIM #3. Perform therapy studies in a mouse model of human prostate cancer utilizing AdSSTR2 and ^{90}Y-SMT 487. **Study Design.** The first aim of the study will evaluate SSTR2 expression on PC-3 and DU-145 human prostate cancer cells *in vitro* after infection with AdSSTR2. These assays will be conducted using ^{111}In-SMT 487 in Scatchard and internalization experiments. The ^{111}In is used instead of ^{90}Y for these assays and the following *in vivo* assays because its physical properties are more appropriate. The Scatchard analysis will determine the level of SSTR2 expression on the cells and the internalization of SSTR2 is important for the subsequent localization and therapy studies. The PC-3 and DU-145 cells will then be implanted s.c. in athymic nude mice and SSTR2 expression will be determined by ^{111}In-SMT 487 tumor

localization following injection of AdSSTR2. These studies will be conducted using gamma camera imaging, tissue counting in a gamma counter and immunohistochemistry. Therapy will be conducted in mice bearing subcutaneous PC-3 and DU-145 tumors following injection of AdSSTR2 and i.v. injections of ^{90}Y-SMT 487. **Relevance.** These studies are directly relevant to improving the treatment of hormone-refractory prostate cancer. Novel therapies are needed for the treatment of this disease and this proposal introduces a new paradigm for its treatment by combining targeted radiolabeled peptide therapy with gene therapy. In addition, this strategy can be used to detect prostate cancer using external gamma camera imaging.

Body

Statement of Work

SPECIFIC AIM #1. Evaluate the expression of SSTr2 on human prostate cancer cells *in vitro* after infection with AdSSTR2 using radiolabeled SMT 487 binding and internalization assays.

Task1: Months 1-9: Radiolabel SMT 487 with ^{111}In and use the ^{111}In-SMT 487 to determine the level of SSTR2 expression in PC-3 and DU-145 human prostate cancer cells after infection with various amounts of AdSSTr2. This will be done by Scatchard analysis. In addition, internalization of SSTR2 and ^{111}In-SMT 487 will be evaluated.

SPECIFIC AIM #2. Evaluate the distribution of radiolabeled SMT 487 after i.v. injection by non-invasive gamma camera imaging and by gamma counter analysis in nude mice bearing s.c. human prostate cancer xenografts injected and with AdSSTr2 AdSSTR2.

Task 1: Months 10-24: Athymic nude mice will be implanted s.c. with PC-3 and DU-145 human prostate cancer cells and injected intratumorally with AdSSTR2 3-5 weeks later. ^{111}In-SMT 487 will then be administered i.v. and the mice imaged using a gamma camera to determine SSTR2 expression and ^{111}In-SMT 487 distribution.

Task 2: Months 10-24: Athymic nude mice will be implanted s.c. with PC-3 and DU-145 human prostate cancer cells and injected intratumorally with AdSSTR2 3-5 weeks later. ^{111}In-SMT 487 will then be administered i.v. and the mice will be sacrificed to determine SSTR2 expression by immunohistochemistry and counting tissues in a gamma counter. These studies will be complementary to those discussed in Task 1.

Task 3: Months 10-24: Athymic nude mice will be implanted s.c. with PC-3 and DU-145 human prostate cancer cells and injected **i.v.** with AdSSTR2 3-5 weeks later. ^{111}In-SMT 487 will then be administered i.v. and the mice will be sacrificed to determine SSTR2 expression by immunohistochemistry and counting tissues in a gamma counter. These studies will be an initial step towards evaluating this system in the context of hormone-refractory disease. Administration of the vectors i.v. will not be used in therapy studies unless the tumor expression of SSTR2 is at least two-fold greater than expression in the liver.

Since the submission of this proposal, a new adenovirus has been produced that encodes for both SSTR2 and cytosine deaminase (CD). CD converts the non-toxic prodrug 5-fluorocytosine (5-FC) to the toxic and radiosensitizing 5-fluorouracil (5-FU). We hypothesize that the combination of SSTR2 and CD will be more efficacious in the treatment of prostate cancer using ^{90}Y-SMT 487 and 5-FC than using SSTR2 alone with ^{90}Y-SMT 487. Therefore, we substituted AdSSTR2CD for AdSSTR2 in the context of the Statement of Work. Also, we are utilizing a peptide (^{99m}Tc-P2045) that is superior to ^{111}In-SMT 487 for the imaging and biodistribution studies of Specific Aim#2.

Specific Aim #1 is completed except for the internalization studies. In addition, expression of CD was determined using an MTS assay. A positive correlation was observed between SSTR2 and CD expression. Task 1 and Task 2 of Specific Aim#2 have been completed, except for the immunohistochemistry in Task 2. Task 3 should be completed in the coming year.

Methods

Determination of SSTR2 expression. The induction of SSTR2 in human prostate cancer cell lines was evaluated using a radiolabeled peptide binding assay to cell membrane

preparations of cells that had been infected with AdSSTR2. The cells were seeded such that they were ~80% confluent at the time they were infected with AdSSTR2 and then harvested for membrane preparations 2 days after adenoviral infection. The AdSSTR2CD (10, 30, 100, 200, or 300 pfu per PC-3 cell (MOI); 1, 3, 10, 30, 100 pfu per DU-145 cell) was added to cells in Optimem® (Gibco-BRL, Grand Island, NY) and incubated at 37°C in 5% CO_2 for 2 h. The cells were then supplemented with complete media and incubated an additional 48 h at 37°C. Cell membranes were then prepared from the infected and uninfected cells using a protocol similar to that previously described. Briefly, the cells were washed with phosphate buffered saline, scraped from the flask, and centrifuged at 90 x g for 5 min at 4°C. The pellet was resuspended in cold lysis buffer (10 mM Tris-HCl, 2 mM EDTA, 2 mM $MgCl_2$, pH 7.2) containing 0.5 mM phenylmethylsulfonyl fluoride and incubated on ice for 15 min. The mixture was vortexed, centrifuged at 600 x g for 15 min at 4°C, and the supernatant removed and stored on ice. An additional lysis step was performed on the pellet and the two supernatants were combined. The supernatant was centrifuged at 28,000 x g for 30 min at 4°C, the resulting supernatant discarded, and the pellet resuspended in 250 mM sucrose, 20 mM glycylglycine, and 1 mM $MgCl_2$. A BioRad (Hercules, CA) protein assay was performed to determine the protein concentration and the samples aliquoted and stored at -80°C.

For the binding assays, the membrane preparations were thawed and diluted in buffer (10 mM HEPES, 5 mM $MgCl_2$, 1 mM EDTA and 0.1% bovine serum albumin, 10 μg/ml leupeptin, 10 μg/ml pepstatin, 0.5 μg/ml aprotinin, and 200 μg/ml bacitracin, pH 7.4) to 25 μg per sample. Individual samples were added to Multiscreen Durapore filtration plates (type FB, 1.0 μm borosilicate glass fiber over 1.2 μm Durapore membrane; Millipore, Bedford, MA) and washed with buffer (10 mM HEPES, 5 mM $MgCl_2$, 1 mM EDTA and 0.1% bovine serum albumin, ph 7.4). One hundred μl [^{125}I]-Tyr^1-somatostatin (~10,000 cpm; specific activity = 1400-2200 Ci/mmol; DuPont/NEN® Research Products, Boston, MA) was added to each well along with various concentrations of Tyr^1-somatostatin (0 to 450 nM) as an inhibitors and incubated for 90 min at room temperature. The samples were washed twice with ice-cold buffer, the filters allowed to dry, and the individual wells punched out and counted in a gamma counter. The receptor density (B_{max}) was calculated using the GraphPad Prism software (San Diego, CA).

Determination of CD expression. PC-3 and DU-145 cells were seeded in T75 flasks and incubated overnight at 37°C. PC-3 cells were then infected with 10, 30, 100, or 300 pfu/cell,

while DU-145 cells were infected at 1, 3, 10, 30, or 100 pfu/cell with AdSSTR2CD in OptiMEM for 1 h at 37°C with rocking. Twenty-four h later, the cells were harvested and plated into 96-well tissue culture plates at 5000 cells/well in 100 µl of complete media. Twenty-four h later, 100 ml of media containing various concentrations of 5-FC were added to the cells in triplicate and the cells allowed to incubate an additional 5 days at 37°C. The fractional cell survival at each drug concentration was determined using an MTS assay calculated as the ratio of absorbance at 490 nm of cells incubated in the presence versus absence of drug, corrected for background absorbance of media alone. Fractional cell survival data were plotted against the logarithm of drug concentration and IC_{50} values were determined using the GraphPad Prism software.

In vivo imaging and biodistribution. Imaging studies were performed in athymic nude mice bearing s.c. PC-3 or DU-145 tumors. The mice were injected s.c. with 1 x 10^7 PC-3 or DU-145 cells (1:1 mixture with matrigel) followed by intratumoral injection with 1 x 10^9 pfu (DU-145) or 1 x10^8 pfu (PC-3) of AdSSTR2CD after the tumors are established. During imaging procedures the animals were anesthetized with halothane gas anesthesia. The mice were imaged with an Anger gamma camera equipped with a pinhole collimator. Mice were positioned in ventral recumbancy with the legs extended from the body. For single image sessions, at least 50,000 total counts per image will be collected. Two days after adenoviral injection, the mice were imaged at 0 and 5 h, after injection of ^{99m}Tc-P2045 (100-200 µCi) using planar imaging techniques. The mice were then sacrificed immediately after the imaging session and tissues harvested and counted in a gamma counter.

Results

The expression of SSTR2 and CD after infection with AdSSTR2CD at various MOI is shown in **Table 1**. SSTR2 expression is represented as fmol/mg and CD expression is represented as an IC_{50} value. The CD expression and IC_{50} value are inversely correlated. This table shows that SSTR2 expression increase in both PC-3 and DU-145 cells upon infection with increasing MOI of AdSSTR2CD. The exception is that at high MOI (300 for PC-3; 100 for DU-145) the expression decreases, probably due to viral toxicity. Similarly, for CD expression, the IC_{50} values decrease with increasing MOI of AdSSTR2CD for both cell lines. There is a significant correlation between MOI and IC_{50} as shown in **Figure 1** for both cell lines ($p = 0.03$).

A significant relationship exists between MOI and SSTR2 expression for PC-3 cells ($p = 0.002$) as shown in **Figure 2**, but not for DU-145 cells ($p = 0.06$). Finally, a significant relationship exists between 5-FC IC_{50} values and SSTR2 expression for DU-145 cells ($p = 0.005$), as shown in **Figure 3**, but not for PC-3 cells ($p = 0.06$).

The in vivo studies demonstrate that SSTR2 is expressed in both PC-3 and DU-145 cells after intratumoral injection of AdSSTR2CD. **Figures 4 and 5** show uptake of ^{99m}Tc-P2045 after intratumoral injection of 1×10^9 pfu of AdSSTR2CD or AdSSTR2, but not a control adenovirus. The biodistribution results (**Figure 6**) show that SSTR2 expression was not significantly different after injection of AdSSTR2CD or AdSSTR2 ($p > 0.05$), but was significantly greater than control tumors ($p < 0.05$). SSTR2 expression could also be non-invasively imaged in PC-3 tumors after intratumoral injection of 1×10^8 pfu of AdSSTR2CD or AdSSTR2, but not a control adenovirus (**Figures 7 and 8**). The biodistribution results (**Figure 9**) show that SSTR2 expression was not significantly different after injection of AdSSTR2CD or AdSSTR2 ($p > 0.05$), but was significantly greater than control tumors ($p < 0.05$).

Key Research Accomplishments

- A novel adenovirus encoding SSTR2 and CD was constructed.
- Expression of SSTR2 and CD were confirmed in both PC-3 and DU-145 human prostate cancer cells after infection with AdSSTR2CD at various MOIs.
- A significant positive correlation ($p = 0.005$) existed between SSTR2 and CD in DU-145 cells and was close to being significant ($p = 0.06$) in PC-3 cells.
- SSTR2 expression in PC-3 and DU-145 tumors injected intratumorally with AdSSTR2CD could be imaged non-invasively.
- SSTR2 expression in PC-3 and DU-145 tumors was not significantly different after injection of AdSSTR2CD or AdSSTR2.

Reportable Outcomes

Poster presentation at the American Association for Cancer Research 93rd Annual Meeting, San Francisco, CA, April 6-10, 2002. **Rogers BE**, Chaudhuri TR, Belousova N, Kirkman RL, Della Manna D, Krasnykh VN, Zinn KR: Evaluation of a dual gene adenovirus encoding somatostatin receptor subtype 2 and cytosine deaminase in the context of human prostate cancer. *Proc Am Assoc Cancer Res*, 43:84, 2002.

Conclusions

These studies demonstrate that AdSSTR2CD can infect both PC-3 and DU-145 human prostate cancer cells and result in expression of both SSTR2 and CD. In addition, infection of PC-3 and DU-145 tumors with AdSSTR2CD results in SSTR2 expression as evidenced by non-invasive imaging of nude mice bearing these tumors and animal biodistribution. It may be possible to determine the level of CD expression in vivo after injection of AdSSTR2CD by non-invasively imaging the expression of SSTR2. Future studies will correlate SSTR2 expression to CD expression in vivo. In addition, it is hypothesized that a greater therapeutic effect will be observed when treating animals with a therapeutic radiolabeled somatostatin peptide analogue and 5-FC, than when treated with either agent alone. Overall, these studies demonstrate significant progress over the first year of funding which will continue over the next two year in accordance with the Statement of Work.

Appendices

Figure and Table Legend

Table and Figures

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Figure and Table Legend

Table 1. Human prostate cancer cells were infected at various MOI (pfu/cell) of AdSSTR2CD for 1 h at 37°C. Two days later, 5-FC was added and IC_{50} values (μM) determined by MTS assay after a 5 day incubation. SSTR2 expression (fmol/mg) was determined 2 days after infection using an ^{125}I-somatostatin homologous competitive binding assay on cell membrane preparations.

Figure 1. Dose response of 5-FC toxicity upon AdSSTR2CD infection of PC-3 (10, 30, 100, 300 MOI) and DU-145 (1, 3, 10, 30 MOI) cells of 3-4 combined experiments.

Figure 2. Dose response of SSTR2 expression upon AdSSTR2CD infection of PC-3 (10, 30, 100, 200 MOI) and DU-145 (1, 3, 10, 30 MOI) cells of 2-3 combined experiments.

Figure 3. Correlation of 5-FC toxicity and SSTR2 expression upon AdSSTR2CD infection for PC-3 (10, 30, 100, and 300 MOI) and DU-145 (1, 3, 10, 30 MOI) cells.

Figure 4. Representative gamma camera image of ^{99m}Tc-P2045 in mice bearing s.c. DU-145 tumors. Imaging position is shown in (A) with an initial image (B) and 5 h (C) after i.v. injection of ^{99m}Tc-P2045. The right tumor (square) was injected i.t. with 1 x 10^9 pfu AdSSTR2CD and the left tumor (circle) was injected with 1 x 10^9 pfu AdSSTR2.

Figure 5. Representative gamma camera image of ^{99m}Tc-P2045 in mice bearing s.c. DU-145 tumors. Imaging position is shown in (A) with an initial image (B) and 5 h (C) after i.v. injection of ^{99m}Tc-P2045. The right tumor (square) was injected i.t. with 1 x 10^9 pfu AdSSTR2CD and the left tumor (circle) was injected with 1 x 10^9 pfu of a control adenovirus.

Figure 6. Biodistribution of ^{99m}Tc-P2045 in mice bearing s.c. DU-145 tumors immediately after the 5 h imaging session. Data represent the mean ± standard deviation (for normal tissues n = 10, for tumors n = 3-5).

Figure 7. Representative gamma camera image of ^{99m}Tc-P2045 in mice bearing s.c. PC-3 tumors. Imaging position is shown in (A) with an initial image (B) and 5 h (C) after i.v. injection of ^{99m}Tc-P2045. The right tumor (square) was injected with 1 x 10^8 pfu AdSSTR2 and the left tumor (circle) was injected with 1 x 10^8 pfu AdSSTR2CD.

Figure 8. Representative gamma camera image of ^{99m}Tc-P2045 in mice bearing s.c. PC-3 tumors. Imaging position is shown in (A) with an initial image (B) and 5 h (C) after i.v. injection of ^{99m}Tc-P2045. The right tumor (square) was injected with 1 x 10^8 pfu of a control adenovirus and the left tumor (circle) was injected with 1 x 10^8 pfu AdSSTR2CD.

Figure 9. Biodistribution of ^{99m}Tc-P2045 in mice bearing s.c. PC-3 tumors immediately after the 5 h imaging session. Data represent the mean ± standard deviation (for normal tissues n = 10, for tumors n = 3-5).

Table 1

MOI	PC-3		DU-145	
	IC_{50} (μM)	SSTR2 (fmol/mg)	IC_{50} (μM)	SSTR2 (fmol/mg)
1	NA	NA	1331.0 ± 635.0	379.3 ± 73.5
3	NA	NA	129.7 ± 41.7	1997.7 ± 134.9
10	682.4 ± 162.4	209.0 ± 3.0	29.4 ± 11.5	4215.0 ± 354.1
30	273.0 ± 52.9	526.5 ± 11.5	16.0 ± 4.6	5661.7 ± 830.4
100	209.7 ± 53.0	1483.0 ± 213.0	8.7 ± 2.2	4451.7 ± 230.1
200	NA	3254.0 ± 339.2	NA	NA
300	129.2 ± 36.6	1482.0 ± 132.3	NA	NA

Figure 1

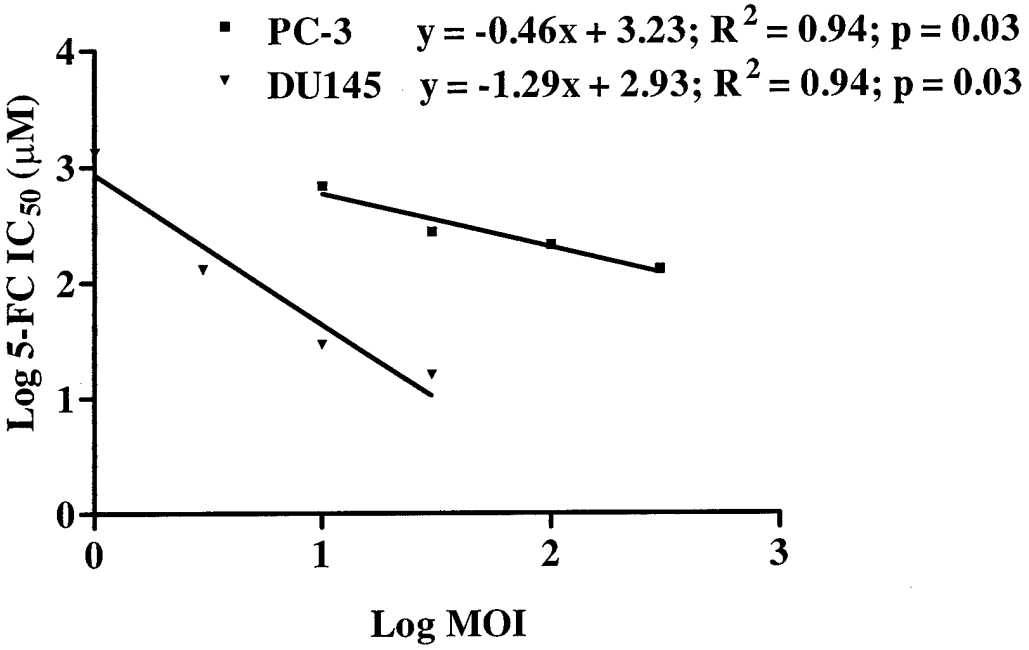

PC-3 y = -0.46x + 3.23; R2 = 0.94; p = 0.03
DU145 y = -1.29x + 2.93; R2 = 0.94; p = 0.03
Log 5-FC IC50 (μM)
4
3
2
1
0
0
1
2
3
Log MOI

Figure 2

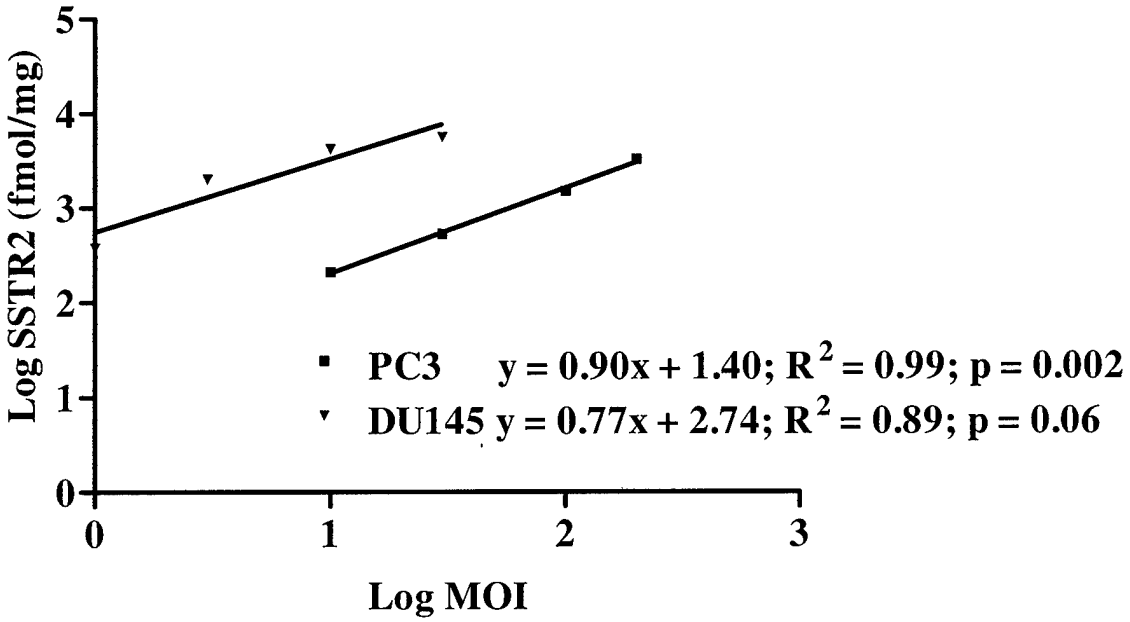

Log SSTR2 (fmol/mg)
5
4
3
2
1
0
0
1
2
3
Log MOI
PC3 y = 0.90x + 1.40; R2 = 0.99; p = 0.002
DU145 y = 0.77x + 2.74; R2 = 0.89; p = 0.06

Figure 3

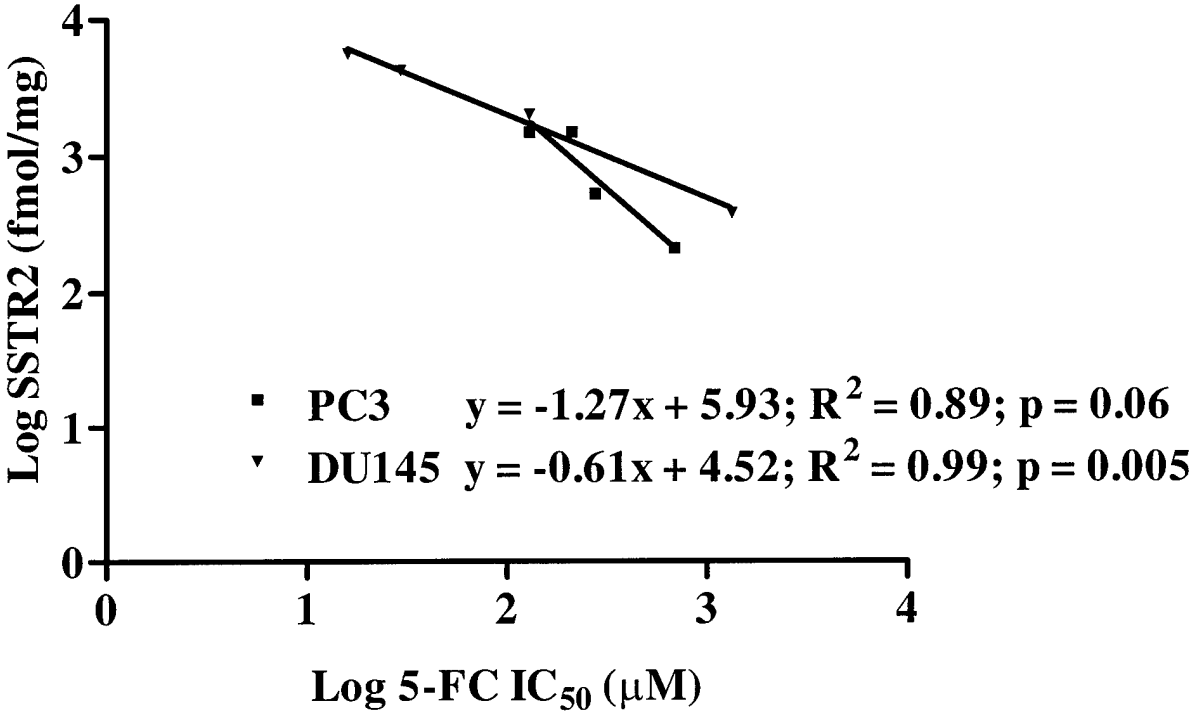
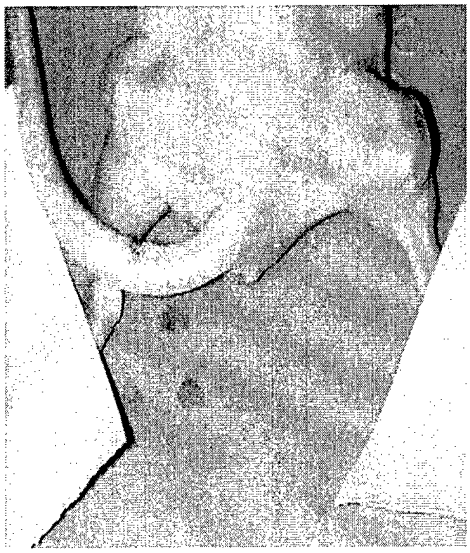

Log SSTR2 (fmol/mg)
4
3
2
1
0
0
1
2
3
4
PC3 y = -1.27x + 5.93; R2 = 0.89; p = 0.06
DU145 y = -0.61x + 4.52; R2 = 0.99; p = 0.005
Log 5-FC IC50 (μM)

Figure 4



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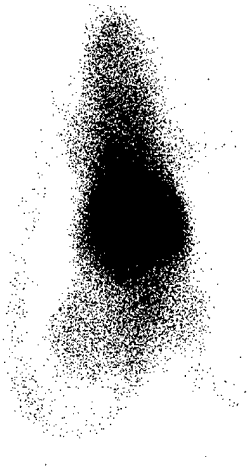

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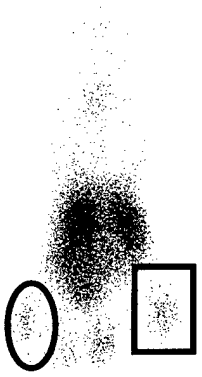
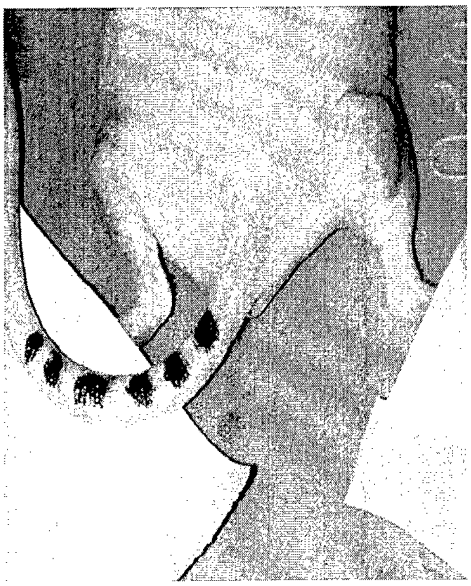


(C)

Figure 5

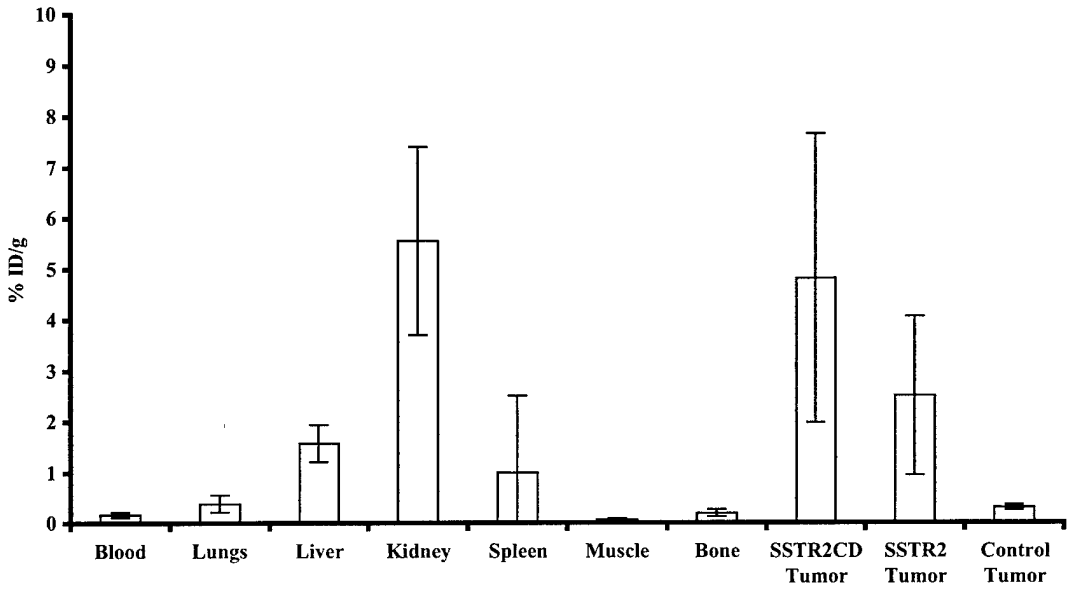


(A)

(B)

(C)

Figure 6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10
9
8
7
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4
3
2
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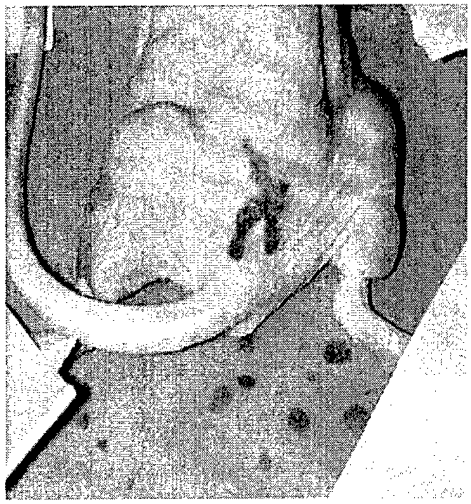
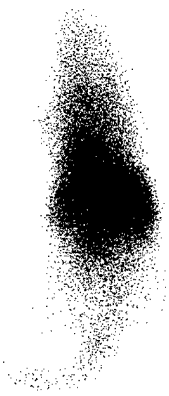
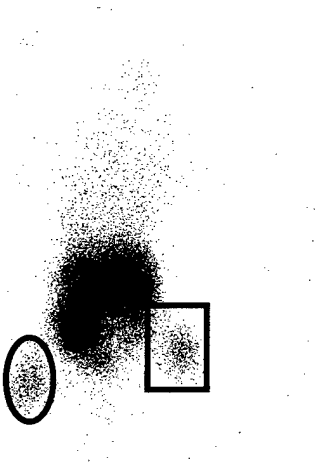
Blood
Lungs
Liver
Kidney
Spleen
Muscle
Bone
SSTR2CD Tumor
SSTR2 Tumor
Control Tumor

Figure 7

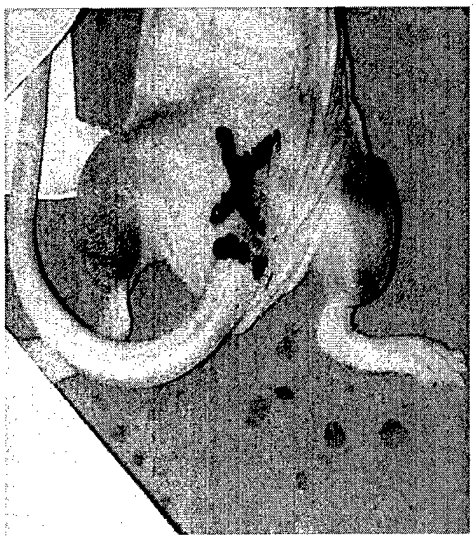






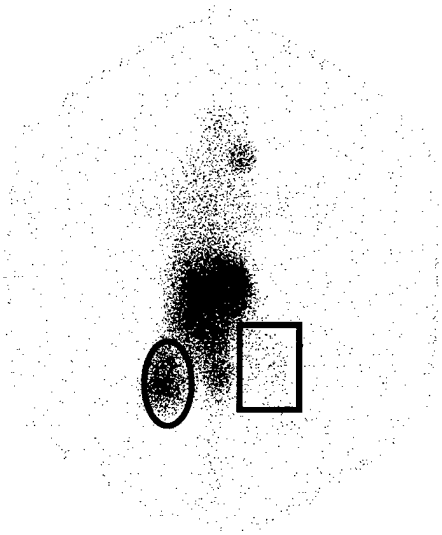
(A) **(B)** **(C)**

Figure 8



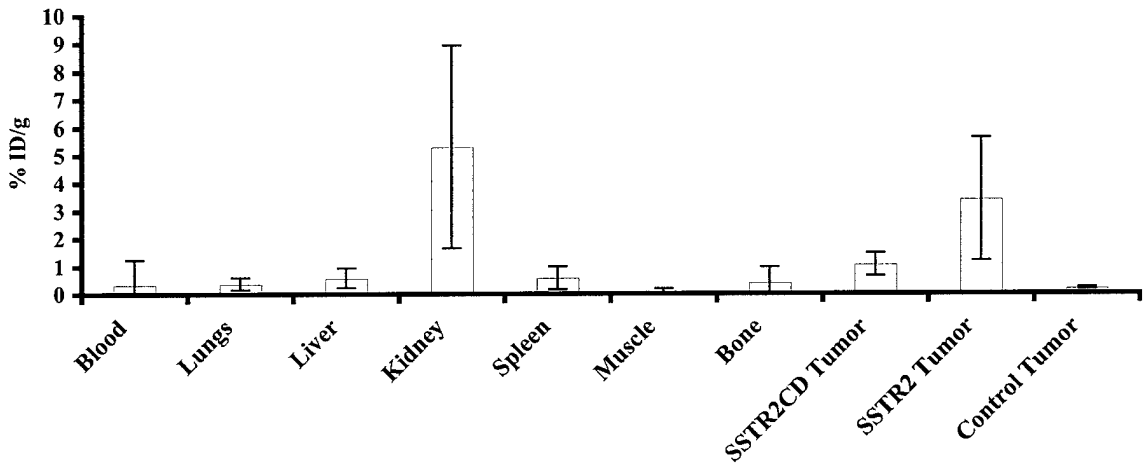
(A)

(B)



(C)

Figure 9


% ID/g
10
9
8
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6
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3
2
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Blood
Lungs
Liver
Kidney
Spleen
Muscle
Bone
SSTR2CD Tumor
SSTR2 Tumor
Control Tumor

#422 **Evaluation of a dual gene adenovirus encoding somatostatin receptor subtype 2 and cytosine deaminase in the context of human prostate cancer.** Buck E. Rogers, Tandra R. Chaudhuri, Natalya Belousova, Richard L. Kirkman, Debbie Della Manna, Victor N. Krasnykh, and Kurt R. Zinn. *University of Alabama at Birmingham, Birmingham, AL.*

Introduction. An adenovirus encoding the genes for human somatostatin receptor subtype 2 and bacterial cytosine deaminase (AdSSTR2CD) was constructed. The SSTR2 allows for non-invasive imaging of gene transfer and therapy with radiolabeled somatostatin analogues. The CD converts the prodrug 5-fluorocytosine (5-FC) to the toxic and radiosensitzing 5-fluorouracil (5-FU). Thus, it is hypothesized that AdSSTR2CD can be used for the simultaneous expression of SSTR2 and CD for the detection and treatment of prostate cancer. **Methods.** *In vitro* experiments were performed with DU-145 and PC-3 human prostate cancer cells. The DU-145 and PC-3 cells were infected with AdSSTR2CD at 10, 30, and 100 pfu/cell. Expression levels of SSTR2 were determined using ^{125}I-somatostatin in competitive inhibition assays on cell membrane preparations. Activity of CD was determined using an MTS assay to demonstrate sensitivity of the infected cells to 5-FC. *In vivo* experiments were conducted in athymic nude mice bearing subcutaneous DU-145 or PC-3 cells (n = 3-4). AdSSTR2CD (1 x 10^8 pfu) was injected intratumorally followed 48 h later by an i.v. injection of ^{99m}Tc-P2045 (a radiolabeled somatostatin analogue kindly provided by Diatide Research Laboratories). The mice were imaged 5 h later with an Anger gamma camera equipped with a pinhole collimator and terminated for biodistribution analyses. **Results.** The expression of SSTR2 on PC-3 cells was 209, 527, and 1483 fmol/mg of protein after AdSSTR2CD infection at 10, 30, and 100 pfu/cell, respectively. DU-145 cells showed that SSTR2 expression increased from 4215 to 5598 fmol/mg after infection at 10 and 30 pfu/cell, but decreased to 4452 fmol/mg after infection at 100pfu/cell. The IC_{50} values of 5-FC were 443, 304, and 264 μM in PC-3 cells after infection with AdSSTR2CD at 10, 30, and 100 pfu/cell, respectively. DU-145 cells had IC_{50} values of 35, 17, and 14 μM, respectively. The PC-3 and DU-145 tumors injected with AdSSTR2CD could be visualized by imaging ^{99m}Tc-P2045 uptake. The PC-3 tumors averaged 1.1 +/- 0.4 % dose/g, while the DU-145 tumors averaged 0.7 +/- 0.3 % dose/g. Uninfected tumors demonstrated < 0.2 % dose/g. **Discussion.** AdSSTR2CD was used to express both SSTR2 and CD in PC-3 and DU-145 cells. Both cell lines showed increasing levels of SSTR2 and CD with increasing infection of AdSSTR2CD. The exception to this is the DU-145 cells at 100 pfu/cell, which shows a decrease in SSTR2 expression, likely due to viral toxicity. *In vivo* studies demonstrated that SSTR2 expression could be imaged non-invasively after i.t. injection of AdSSTR2CD and i.v. injection of ^{99m}Tc-P2045. These studies demonstrate the feasibility of using AdSSTR2CD for the treatment and detection of prostate cancer. This work was supported by the U.S. Army Medical Research and Material Command under PC001216 and the Department of Energy Grant ER63193.