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Efficacy Evaluation of a Twelve Peptide Mixture Against
Established M25 Murine Mammary Carcinoma in BALB/c Mice



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Executive Digest

Treatment with the 12 peptide mixture was well tolerated but inactive regardless of dosage level or schedule of administration. Treatment produced no weight loss and essentially no tumor growth delay.

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Contents

<u>Section</u>	<u>Page</u>
A. Introduction	04
B. Materials and Methods	04
C. Results/Discussion	06
D. Glossary and Endpoint Details	08
E. References	11
F. Tables	
1. Group Toxicity and Response Summary	12
2. Individual Animal Toxicity and Response Summary	14
3. Group Statistics	17
G. Figures	
1. Group Comparisons with Std. Error	19
2. Median Group Comparisons	21
3. Individual Tumor Growth Curves	23
4. Body Weight Change Summary with Std. Error	26
H. Appendices	
1. Protocol Summary	28
2. Raw Data – Tumor Measurements and Body Weights	30
3. Raw Data – Daily Census	34
4. Raw Data – Clinical Signs, Observations, and Comments	36
5. Tumor Burdens	38
6. Consolidated Body Weights	42
7. Consolidated Percent Body Weight Change	46
8. T/C Values	50
9. Fold Growth Values	52
10. Peptide Prep	56

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Introduction

The purpose of this study was to evaluate the efficacy of a twelve peptide mixture against M25 murine mammary carcinoma in female BALB/c mice. The peptide mixture was administered intravenously and evaluated on three separate treatment schedules; daily for twenty one injections, every other day for ten injections, or every three days for seven injections.

Materials and Methods

Chemicals

Twelve peptides (labeled in consecutive order from 4061559-4061570) were obtained from Sanare as white powders. The intent was to administer an amount of each peptide in the mix such that the final aggregate concentration in the mouse blood volume (~2ml) was 0.8mg/ml for the top dose. The peptide mix was prepared by first adding the appropriate amount of phosphate buffered saline (PBS) to each vial of powder to achieve a concentration of 2mg/ml for each peptide. A further dilution was made to account for each of the peptide's molecular weight to provide equimolar concentrations of each peptide at 0.35 μ M. Equal amounts of each of the twelve peptides were then combined to form the top dose solution (Appendix 10). The top dose solution was aliquoted for each dosing day and frozen at -80°C until use. On each day of treatment, one frozen vial of top dose solution was removed from the freezer and thawed at room temperature. The dosing solution was clear and colorless with a pH of 7.1. Lower dosages were prepared by direct dilution of the top dose with the appropriate amount of PBS diluent.

Animals and Husbandry

Female BALB/c mice were obtained from Charles River Laboratories. They were 7-8 weeks old on Day 1 of the experiment. The animals were fed irradiated Rodent Diet 5053 (LabDiet™) and water *ad libitum*. Mice were housed in static cages with Bed-O'Cobs™ bedding inside Biobubble® Clean Rooms that provide H.E.P.A filtered air into the bubble environment at 100 complete air changes per hour. All treatments, body weight determinations, and tumor measurements were carried out in the bubble environment. The environment was controlled to a temperature range of 70°±2°F and a humidity range of 30-70%.

Test animals were implanted subcutaneously on Day 0 with 30 to 70mg tumor fragments using an 11-gauge trocar needle. All animals were observed for clinical signs at least once daily. Animals with tumors in excess of 1g or with ulcerated tumors were euthanized, as were those found in obvious distress or in a moribund condition. All procedures carried out in this experiment were conducted in compliance with all the laws, regulations and guidelines of the National Institutes of Health (NIH) and with the approval of MIR's Animal Care and Use Committee.

Treatment

Treatments began on Day 7, when the mean estimated tumor mass for all groups in the experiment was 100mg (range of group means, 94-106mg). All animals weighed \geq 17.0g at the initiation of therapy. Mean group body weights at first treatment were well-matched (range of group means, 18.0-19.3g). All animals were dosed according to

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individual body weight on the day of treatment (0.2ml/20g) as indicated in the protocol (Appendix 1).

Measurements and Endpoints

Testing in this experiment was generally carried out adhering to the general principles established by the groups of Schabel, Skipper, Griswold, Corbett, Leopold, Ross and the NCI (1-7). Body weights and tumor measurements were recorded twice weekly. Tumor burden (mg) was estimated from caliper measurements by the formula for the volume of a prolate ellipsoid assuming unit density as: Tumor burden (mg) = $(L \times W^2)/2$, where L and W are the respective orthogonal tumor length and width measurements (mm).

The primary endpoints used to evaluate efficacy were: tumor growth delay, %T/C, complete and partial tumor response, and the number of tumor-free survivors at the end of the study. Tumor growth delay for this experiment was expressed as a T-C value, where T and C are the median times in days required for the treatment and control group tumors, respectively, to grow to a selected evaluation size, 750mg. A complete response (CR) is defined as a decrease in tumor mass to an undetectable size (<50mg), and a partial response (PR) is defined as a $\geq 50\%$ decrease in tumor mass from that at first treatment. PRs are exclusive of CRs, as are Tumor-Free Survivors (TFS). %T/C is defined as the median tumor mass of the Treated Group divided by the median tumor mass of the Control Group x 100. In this experiment, %T/C (Day 21) was evaluated when the median Control reached 629mg (the last day of the experiment where medians could be calculated for all groups).

Net Log₁₀ Tumor Cell Kill (Net Kill) is used as a secondary efficacy endpoint. Net Kill is the change in tumor burden (logs) over the treatment period. Traditionally Net Kill is estimated by the method of Schabel et al (1, 3) but this method requires that initial and post treatment regrowth rates be equal, a condition that may not be met by certain differentiation therapies or those that induce significant tumor bed effects. We instead use a modification of the method of Ross et al (7), that can accommodate any regrowth rate and which simply assumes that the tumor regrowth rate between dosage levels are similar to that observed post treatment. This method simply extrapolates (or interpolates) the regrowth curve back to the last day of treatment for the calculation of Net Kill. The two methods converge to the same result if initial and regrowth rates are similar. The Net Kill value allows quantitative comparison of efficacy across multiple experimental protocols and across models by normalizing the efficacy data for treatment regimens of varied duration and differences in tumor growth rates between experiments or models. Positive values indicate that an actual reduction of tumor burden had occurred at the end of therapy relative to the pretreatment burden. Negative values indicate the tumor grew (although possibly more slowly than the control tumors) during treatment. Thus negative Net Kill values do not necessarily imply a complete lack of activity. Tumor-free survivors and tumor-bearing survivors whose tumors had not reached the Evaluation Size by the last day of the experiment were assigned a Time to Evaluation Size of > the last day of the experiment and were included in calculations of Tumor Growth Delay and Net Kill.

The calculation of Net Kill by either method requires the establishment of the tumor volume doubling time (Td), which is the time in days for the tumor burden to double. Doubling time (Td) was estimated from the least squares best-fit straight line from a log-linear plot of tumor burden vs. time over the period of exponential growth (~200 to

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~800mg range). This parameter was calculated and tabulated in Table 2 for every animal in the experiment.

When control and treated group doubling times are not similar, the relative contribution of direct tumor cell killing and hindered tumor re-growth to the overall therapeutic effect are estimated by a modification of the method of Ross et al. (7)

Assessment of Side Effects

All animals were observed for clinical signs at least once daily. Animals were weighed on each day of treatment and at least twice weekly thereafter. Individual body weights were recorded twice weekly.

Treatment-related weight loss in excess of 20% is generally considered unacceptably toxic. In this report, a dosage level is described as tolerated if treatment-related weight loss (during and two weeks after treatment) is <20% and mortality during this period in the absence of potentially lethal tumor burdens is ≤10%.

Upon death or euthanasia, all animals were necropsied to provide a general assessment of potential cause of death and perhaps target organs for toxicity. The presence or absence of metastases was also noted. Remarkable observations of clinical signs and necropsy findings have been tabulated in Appendix 4. Individual and group toxicity findings have been summarized in Tables 1-3 and Figure 3.

Statistics

Day 21 tumor masses for all study groups were analyzed by application of the Kruskal-Wallis rank sum test analysis to determine if any significant differences existed between study groups. No significant differences were identified.

Statistical significance was determined using built-in Microsoft Excel data analysis tools, SigmaPlot 11, and the R-Project (8).

Data Retrieval

MIR Preclinical Services retains permanent “active” copies (on CD) of all experiments unless instructed otherwise, including active graphics applications.

Results/Discussion

Tumor Growth/General Observations/Controls

The mean estimated tumor burden for all groups in the experiment on the first day of treatment was 100mg and all of the groups in the experiment were well-matched (range, 94-106mg). All animals weighed ≥17.0g at the initiation of therapy. Mean group body weights at first treatment were also well-matched (range, 18.0-19.3g). A tumor burden of 750mg was chosen for evaluation of efficacy by tumor growth delay. The Median Control Tumor reached evaluation size on Day 22.4, and the tumor volume doubling time for the Control Group was 4.1 days (Table 2). Vehicle-treated control animals experienced a 0.1g mean weight loss during the treatment regimen. There were no spontaneous regressions in the Control Group. Thioglycolate cultures of donor tumors (2/3) used for implantation of this study were negative for gross bacterial contamination,

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and one culture was inconclusive. Based on historical data for this model, the biology of the Control Group was judged to be within the normal range.

Toxicity

Treatment with the peptide mixture was well tolerated at all tested dosage levels (80, 40, and 20mg/kg) and schedules, producing neither treatment-related mortality nor treatment-related weight loss (Table 1 and 2, Figure 3). One animal receiving the 80mg/kg peptide mixture daily for 21 days was removed from study due to tumor ulceration. All animals had enlarged spleens, including control animals, indicative of tumor progression (Appendix 4).

Efficacy

No treatment regimen with the twelve peptide mixture produced anti-cancer activity against M25 murine carcinoma in BALB/c mice. Tumor growth delays ranged from 1.8 to -2.8days, with T/C values ranging from 83-147%. Efficacy parameters showed no dose or schedule dependence. Neither tumor regressions nor tumor free survivors were observed. The negative net tumor cell kill values indicate tumor progression throughout treatment. The lack of significant body weight loss during treatment suggests that a much higher peptide mix dose could be tolerated by the experimental animals. However, the relatively low solubility of the peptides in aqueous media may preclude the use of higher dose concentrations.

Glossary

Apparent Net Tumor Cell Kill – The net change in tumor burden (measured in logs) between the first and last treatments. An equation is derived for the tumor growth of each mouse in the experiment from a least squares best fit of the exponential portion of the tumor growth curve post treatment. This equation is solved to give the apparent tumor burden surviving the last day of treatment for each animal. Median values are used for comparison of treatment groups to the controls to derive the net reduction in tumor burden during treatment (Net log₁₀ Kill, or NK_{apparent}). This modification of the methods of Schabel et al. (1, 3) and Ross et al (7) allows an estimate of reduction in tumor burden even in the circumstance of tumor regrowth rates that are significantly different from the control growth rates. In general the method of Schabel overestimates net reduction in tumor burden (Net Kill) values. NK_{apparent} values faithfully estimate the tumor burden at last treatment, but they don't really estimate how much of the effect was due to cell killing and how much was due to hindered regrowth during treatment if the regrowth rates are dissimilar to initial or control growth rates. The term Net Kill is actually a misnomer for the combined effects of cell killing and hindered tumor growth between treatments. With the long treatment regimens in common use today, the relative contribution of hindered regrowth to the NK_{apparent} can be large. However the relative contributions of cell killing and hindered regrowth can be estimated. These questions can be important to those designing cytotoxic therapies or those dealing with compounds of mixed mechanisms. For this reason we also report fractional effect values that estimate the relative contributions of cell killing and slowed regrowth to the net change in tumor burden during therapy (NK_{apparent}). As always NK_{apparent} values normalize the data for differences in duration of treatment and also tumor doubling times across tumor models and experiments, allowing quantitative comparison between experiments. Two underlying assumptions are required for our calculations: (1) all treatment fractions produce equivalent cell killing, and (2) the regrowth rate between fractions is identical to the post treatment regrowth rate. These assumptions are also required for the traditional Schabel calculations, but those carry the additional assumption that the regrowth and initial growth rates are equal. (*Group efficacy parameter*)

Complete Regression (CR) – An animal is credited a complete regression if the tumor burden is reduced to an immeasurable volume at any point after the first treatment. Our convention is to record any tumor measurement less than 3 mm as a "0". This is in keeping with the convention of the NCI and reflects the inherent and unacceptably high mechanical error in such measurements in addition to the uncertain biology of what is measured at those small sizes (4). (*Individual efficacy parameter*)

Day 0 – The day tumors are implanted into the animals (Not to be confused with the first day of treatment which is always indicated relative to Day 0).

Day of Max. Body Wt. Loss – The day of body weight nadir (if any) between the first day of treatment and 2 weeks after the last day of treatment. Reported as "NA" if no weight loss occurred. (*Group toxicity parameter*)

Evaluation Size – The tumor burden (mg) selected for calculation of tumor growth delay. The Evaluation Size is selected from the exponential portion of the control tumor growth curve where the error of measurement tends to be minimal (usually between 500 and 1000mg).

Fractional Effect - When initial and post-treatment regrowth rates are different it is possible to estimate the relative contributions of hindered regrowth rate and tumor cell killing to the observed net reduction in tumor burden (NK_{apparent}). This is accomplished by first calculating the Gross Kill for the group (Schabel (1)) based on the median value calculated from best fit equations for the actual regrowth data for each mouse in the experiment. The Gross Kill is then used to calculate a theoretical Net Kill value (NK_{corrected}) that would have been obtained if the tumors had re-grown at their original (pretreatment) growth rates. The ratio of the NK_{corrected} and NK_{apparent} values provides an estimate of the percentage of the therapeutic effect that was due to actual reductions in cell number (Tumor cell kill (%)). The rest of the effect (Hindered Regrowth (%)) is due to hindered post treatment regrowth rates during the treatment regimen. In studies with long durations of treatment, the relative contribution of hindered regrowth to NK_{apparent}

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can be large, even for small differences between growth and regrowth rates. (*Group efficacy parameter*)

Maximum Rx-Related Body Wt. Loss – This is meant to reflect treatment-related weight change. Calculated as the maximum weight loss occurring anytime between the first day of treatment and two weeks from the last day of treatment, expressed as a percentage of the weight on the first day of treatment. (*Group toxicity parameter*)

Partial Regression (PR) – An animal is credited with a partial regression if its tumor burden decreases to less than half of the tumor burden at first treatment. PRs are tabulated exclusive of CRs. (*Individual efficacy parameter*)

Percent Body Wt. Change – Change in body weight between first and last days of treatment expressed as a percentage of the body weight on the first day of treatment. If actual body weight measurements were not recorded on precisely the first and last days of treatment, these values are calculated by interpolation between the closest measurements on either side of the target date. (*Individual toxicity parameter*)

% Rx Related Deaths – The percentage of animals presumed to have succumbed to treatment-related toxicity expressed as a percentage of the number of evaluable animals in the group. An animal is presumed to experience a treatment-related death if it is found dead or is euthanized in moribund condition within 2 weeks of the last treatment with a tumor burden less than half that of the smallest lethal tumor in the control group and shows no evidence of infection, mechanical dosing trauma, or other obvious causes of morbidity at necropsy. Animals dying from non-treatment-related causes prior to reaching an evaluable efficacy endpoint are excluded from this evaluation and the number of animals in the group is reduced accordingly. (*Group toxicity parameter*)

% Tumor Free Survivors (TFS) – Any animal with no measurable evidence of disease on the last day of the experiment. This value is exclusive of CRs. These animals may or may not represent “cures”, depending on when the experiment was terminated. We recommend that no animal be assumed cured unless the animal has been held for a period of time past the last treatment equal to twice the time required to allow a single surviving cell to grow to a tumor burden of 500mg. That time in days can be calculated as $(57.6 \times T_d)$.

Recovery Time – The length of time in days for treatment-related weight loss to be recovered. Measured as the time from the nadir of body weight to return to the pretreatment value. This parameter is an important monitor of lingering or delayed toxicity. (*Group toxicity parameter*)

Rx Related Death – An animal is presumed to experience a treatment-related death if it is found dead or is euthanized in moribund condition within 2 weeks of the last treatment with a tumor burden less than half that of the smallest lethal tumor in the control group and shows no evidence of infection, mechanical dosing trauma, or other obvious causes of morbidity at necropsy. (*Individual toxicity parameter*)

Td (Tumor Doubling Time) – The growth rate of the tumor expressed as the volume doubling time (days). Calculated from a log-linear least squares regression of the exponential portion of the tumor growth curve. These values are used to compute tumor cell kill, fractional effect, and surviving fraction estimates. They are also used to assess the appropriateness of the biology of the tumor in this experiment against historical values.

Therapeutic Index – We define therapeutic index as simply the range of tolerated dosage levels that produce substantial anticancer activity. Substantial activity for this purpose is defined as a tumor growth delay that is \geq the duration of treatment and that is also statistically different from the control at the $P \leq 0.05$ level.

Time to Evaluation Size – The time (days) it takes a tumor to reach the specified Evaluation Size. Calculated from a log-linear least squares best fit of tumor burden versus time for the exponential portion of the final (post-treatment) tumor growth curve. This value is calculated for every animal in the experiment. The group medians are then used to calculate the Tumor Growth Delay. (*Individual efficacy parameter*)

Time to Fold Growth End Point – Occasionally (usually when initial mean tumor burdens across all groups are not well-matched) it is advantageous to display efficacy parameters in terms of fold growth, where the selected endpoint is the time it takes to reach a selected multiple of

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initial tumor burden. This increases the probability of uncovering a statistically significant therapeutic effect by eliminating the confounding effects of disparity in initial tumor sizes. Calculated as described for Time to Evaluation Size from the fold growth data (Appendix 9). (*Individual efficacy parameter*)

Tumor Burden at Last Rx – The tumor burden on the last day of treatment. This value is calculated from a log-linear least squares best fit of tumor burden versus time for the exponential portion of the final (post-treatment) tumor growth curve. (Presented to facilitate T/C comparisons. Additional T/C information is presented in Appendix 8. T/C values presented in Appendix 8 are simple ratios, not the NCI convention)

Tumor Growth Delay – Tumor Growth Delay (T-C) is the difference between the median times it takes the treated group and the control group (always the first group in Table 2) to reach the stated evaluation size. This is calculated from the median times to evaluation size for each animal in the group, not from interpolation of the median growth curve. Net kill values are not presented when the T-C is negative. (*Group efficacy parameter*)

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Table 1 – Group Toxicity and Response Summary

Group Summary

Group #	Treatment	Dose (mg/kg/inj)	Total Dose (mg/kg)	Schedule	Route	Toxicity				Efficacy					
						Maximum Treatment-related Weight Loss (%)	Day of Max. Treatment-related Weight Loss	Recovery Time (days)	% Rx Related Deaths	%T/C (Day 21)	Tumor Growth Delay (days)	Apparent Net Tumor Cell Kill (logs)	% CR	% PR	% TFS
1	Vehicle 0.2ml/20g		NA	QDx21	IV	0.5	10	1.3	0	100	NA	NA	0	0	0
2	Peptide Mix	80.00	1680	QDx21	IV	NA	NA	NA	0	115	-0.9	-1.54	0	0	0
3	Peptide Mix	40.00	840	QDx21	IV	NA	NA	NA	0	147	-2.8	-1.52	0	0	0
4	Peptide Mix	20.00	420	QDx21	IV	NA	NA	NA	0	133	-1.5	-1.60	0	0	0
5	Peptide Mix	80.00	80	QDx1	IV	NA	NA	NA	0	105	-0.6	-0.04	0	0	0
6	Peptide Mix	80.00	560	Q3Dx7	IV	NA	NA	NA	0	83	1.8	-1.08	0	0	0
7	Peptide Mix	80.00	800	Q2Dx10	IV	NA	NA	NA	0	115	-0.8	-1.27	0	0	0

GROUP SUMMARY ENDPOINT DEFINITIONS AND CALCULATION METHODS

Maximum Mean BW Loss (%)	Calculated from the minimum of the mean BW curve (while there are greater than half the animals still surviving) for each group within the Rx period and out to 2 weeks after the end of Rx.
Day of Maximum Mean BW Loss	Calculated from the minimum of the mean BW curve (while there are greater than half the animals still surviving) for each group within the Rx period and out to 2 weeks after the end of Rx.
Recovery Time (days)	The number of days from the time of the minimum mean BW to recover the lost BW. Calculated only for animals which lost BW and later recovered the lost BW.
% Rx Related Deaths	% of mice in each group with treatment-related deaths.
Tumor Growth Delay (days)	The median time to evaluation size is calculated for each group (see Table 1). The tumor growth delay (TGD) is calculated by subtracting the median TGD for the control group from the median TGD for each treatment group.
Apparent Net Tumor Cell Kill (logs)	By interpolation, the log-linear regression line for each animal is used to calculate the tumor weight (TW) at the start of treatment, and the TW at the end of treatment, for control and treatment groups, respectively. For each treatment group, the median TW (end of treatment) is subtracted from the median control TW (start of treatment) to calculate the apparent net cell kill (in log units).
% CR	% of mice in each group that experienced complete regressions.
% PR	% of mice in each group that experienced partial regressions.
% TFS	% of mice in each group that were tumor free survivors.

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Table 2 – Individual Animal Toxicity and Response Summary

Calculated End Points

Evaluation Size 750 mg Last Day of Expt. 35
 Fold Growth End Point 4

Group # 1											
Treatment Vehicle											
Dose 0.2ml/20g											
Growth Endpoints											
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	16.4	0.6	no	4.9	1775	22.2	NA	no	no	no	
2	5.3	0.5	no	3.5	513	31.0	NA	no	no	no	
3	2.1	3.7	no	5.0	1666	23.2	NA	no	no	no	
4	NA	BW GAIN	no	3.4	NA	17.6	NA	no	no	no	
5	NA	0.5	no	3.2	NA	18.5	NA	no	no	no	
6	NA	4.2	no	3.1	NA	20.1	NA	no	no	no	
7	9.1	1.1	no	5.4	1568	22.6	NA	no	no	no	
8	7.0	BW GAIN	no	4.7	1800	24.2	NA	no	no	no	
Mean			Total	4.1	1464	22.4	NA	Total	Total	Total	
SD			Rx Deaths:	0.9	540	4.2	NA	CR:	PR:	TFS:	
Median			0	4.1	1666	22.4	NA	0	0	0	
Group # 2											
Treatment Peptide Mix											
Dose 80.00											
Growth Endpoints											
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	NA	0.5	no	3.7	NA	18.8	NA	no	no	no	
2	NA	BW GAIN	no	3.5	NA	17.6	NA	no	no	no	
3	NA	1.6	no	2.3	NA	22.1	NA	no	no	no	
4	NA	1.0	no	2.9	NA	18.2	NA	no	no	no	
5	NA	BW GAIN	no	4.6	NA	NA	NA	no	no	no	
6	NA	2.8	no	5.4	NA	21.5	NA	no	no	no	
7	11.2	BW GAIN	no	3.4	1089	25.2	NA	no	no	no	
8	5.4	3.0	no	6.1	1183	22.9	NA	no	no	no	
Mean			Total	4.0	NA	20.9	NA	Total	Total	Total	
SD			Rx Deaths:	1.3	NA	2.8	NA	CR:	PR:	TFS:	
Median			0	3.6	NA	21.5	NA	0	0	0	
Group # 3											
Treatment Peptide Mix											
Dose 40.00											
Growth Endpoints											
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	NA	2.1	no	4.3	NA	22.6	NA	no	no	no	
2	NA	BW GAIN	no	3.8	NA	19.0	NA	no	no	no	
3	NA	BW GAIN	no	3.7	NA	19.1	NA	no	no	no	
4	NA	0.6	no	4.7	NA	20.0	NA	no	no	no	
5	3.1	1.5	no	5.6	1000	27.5	NA	no	no	no	
6	NA	BW GAIN	no	3.7	NA	17.3	NA	no	no	no	
7	0.5	1.0	no	7.4	416	32.8	NA	no	no	no	
8	NA	BW GAIN	no	4.4	NA	18.9	NA	no	no	no	
Mean			Total	4.7	NA	22.1	NA	Total	Total	Total	
SD			Rx Deaths:	1.2	NA	5.3	NA	CR:	PR:	TFS:	
Median			0	4.4	NA	19.5	NA	0	0	0	
Group # 4											
Treatment Peptide Mix											
Dose 20.00											
Growth Endpoints											
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	NA	BW GAIN	no	3.3	NA	18.2	NA	no	no	no	
2	NA	BW GAIN	no	4.1	NA	18.9	NA	no	no	no	
3	NA	BW GAIN	no	2.3	NA	21.8	NA	no	no	no	
4	NA	BW GAIN	no	3.7	NA	20.3	NA	no	no	no	
5	NA	BW GAIN	no	3.2	NA	17.9	NA	no	no	no	
6	4.9	2.0	no	6.1	1099	26.2	NA	no	no	no	
7	NA	7.1	no	4.7	NA	21.5	NA	no	no	no	
8	NA	BW GAIN	no	4.6	NA	21.5	NA	no	no	no	
Mean			Total	4.0	NA	20.8	NA	Total	Total	Total	
SD			Rx Deaths:	1.2	NA	2.7	NA	CR:	PR:	TFS:	
Median			0	3.9	NA	20.9	NA	0	0	0	

Group #		5									
Treatment		Peptide Mix									
Dose		80.00									
		Growth Endpoints									
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	0.0	BW GAIN	no	5.3	126	23.4	NA	no	no	no	
2	0.0	BW GAIN	no	3.1	100	16.7	NA	no	no	no	
3	0.0	BW GAIN	no	5.2	100	22.9	NA	no	no	no	
4	0.0	BW GAIN	no	4.5	75	21.9	NA	no	no	no	
5	0.0	BW GAIN	no	3.4	72	20.2	NA	no	no	no	
6	0.0	BW GAIN	no	4.7	88	24.0	NA	no	no	no	
7	0.0	BW GAIN	no	3.3	88	18.5	NA	no	no	no	
8	0.0	1.6	no	5.1	100	21.6	NA	no	no	no	
Mean			Total	4.3	94	21.1	NA	Total	Total	Total	
SD			Rx Deaths:	0.9	17	2.5	NA	CR:	PR:	TFS:	
Median				0	94	21.8	NA	0	0	0	

Group #		6									
Treatment		Peptide Mix									
Dose		80.00									
		Growth Endpoints									
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	NA	1.1	no	3.0	NA	18.2	NA	no	no	no	
2	7.4	BW GAIN	no	3.8	923	25.2	NA	no	no	no	
3	NA	0.6	no	3.4	NA	17.5	NA	no	no	no	
4	7.2	BW GAIN	no	5.2	632	27.6	NA	no	no	no	
5	9.2	BW GAIN	no	4.9	990	25.2	NA	no	no	no	
6	5.0	BW GAIN	no	4.8	500	28.5	NA	no	no	no	
7	NA	BW GAIN	no	4.3	NA	19.2	NA	no	no	no	
8	NA	BW GAIN	no	4.5	NA	23.1	NA	no	no	no	
Mean			Total	4.2	NA	23.0	NA	Total	Total	Total	
SD			Rx Deaths:	0.8	NA	4.3	NA	CR:	PR:	TFS:	
Median				0	NA	24.1	NA	0	0	0	

Group #		7									
Treatment		Peptide Mix									
Dose		80.00									
		Growth Endpoints									
Animal	BW Change During Rx (%)	Max. BW Loss (%)	Rx-related Death	Td (days)	Tumor Burden @ Last Rx	Time to Evaluation Size (days)	Time to Fold Growth EP (days)	Complete Regression	Partial Regression	Tumor Free Survivor	
1	6.9	BW GAIN	no	5.1	922	24.7	NA	no	no	no	
2	NA	BW GAIN	no	4.7	NA	20.6	NA	no	no	no	
3	NA	6.5	no	4.1	NA	21.9	NA	no	no	no	
4	NA	0.5	no	3.5	NA	21.5	NA	no	no	no	
5	5.8	BW GAIN	no	5.3	891	24.6	NA	no	no	no	
6	NA	BW GAIN	no	4.2	NA	21.7	NA	no	no	no	
7	NA	BW GAIN	no	4.4	NA	20.9	NA	no	no	no	
8	NA	0.6	no	3.7	NA	18.7	NA	no	no	no	
Mean			Total	4.4	NA	21.8	NA	Total	Total	Total	
SD			Rx Deaths:	0.6	NA	2.0	NA	CR:	PR:	TFS:	
Median				0	NA	21.6	NA	0	0	0	

ENDPOINT DEFINITIONS AND CALCULATION METHODS

BW Change During Rx (%)	Body weight change during treatment = (End Rx BW - Start Rx BW)
Max. BW Loss (%)	Maximum body weight loss during treatment, and out to 2 weeks following the end of treatment.
Rx-related Death	Treatment-related death, as determined by clinical signs observations (see Comments table), body weight measurements and behavior of other mice within the group.
Td (days)	Tumor doubling time calculated from log-linear regressions over growth data.
Tumor Burden @ Last Rx	Tumor size on day of last treatment as estimated by caliper measurement.
Time to Evaluation Size (days)	Calculated by interpolation of the log-linear regression line on the tumor growth data, to the evaluation size.
Time to Fold Growth EP (days)	Calculated by interpolation of the log-linear regression line on the fold growth data, to the evaluation size.
Complete Regression	Animals for which the tumor size decreased below 50mg.
Partial Regression	Animals for which the tumor size decreased to < 50% of the initial size.
Tumor Free Survivor	Animals for which a complete regression persisted to the end of the study.

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Table 3 – Group Statistics

Kruskal-Wallis One Way Analysis of Variance on Ranks

Data source: Day 21 Tumor Mass in MIR 1058 Stats.JNB

Dependent Variable: Day 21 Tumor Mass

Normality Test (Shapiro-Wilk) Failed (P < 0.050)

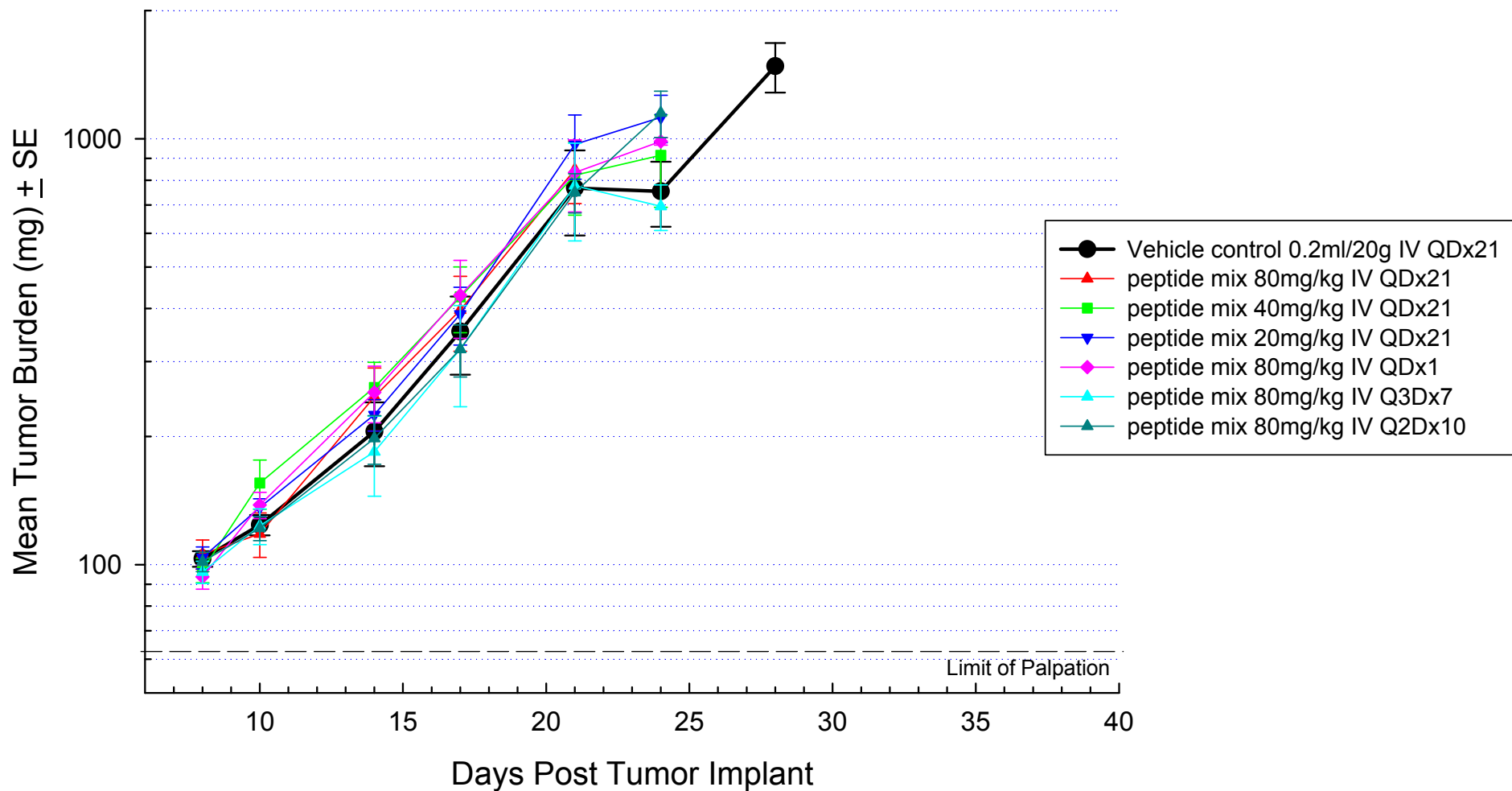
Group	N	Missing	Median	25%	75%
1.000	8	0	629.000	401.500	1242.000
2.000	8	0	725.000	532.750	1259.500
3.000	8	0	922.000	358.000	1137.250
4.000	8	0	837.000	637.500	1492.000
5.000	8	0	658.000	441.250	1207.500
6.000	8	0	523.000	319.250	1368.000
7.000	8	0	726.000	600.000	967.750

H = 1.496 with 6 degrees of freedom. (P = 0.960)

The differences in the median values among the treatment groups are not great enough to exclude the possibility that the difference is due to random sampling variability; there is not a statistically significant difference (P = 0.960)

Figure 1 – Group Comparisons with Std. Error by Mean

SANA200812 (MIR1058)
M25 Tumor Burden
Group Comparison with Std. Error



.....Figure & – ; fci d'7 ca dU]gcb`VmA YX]Ub`

SANA200812 (MIR1058)
M25 Tumor Burden
Group Median Comparison

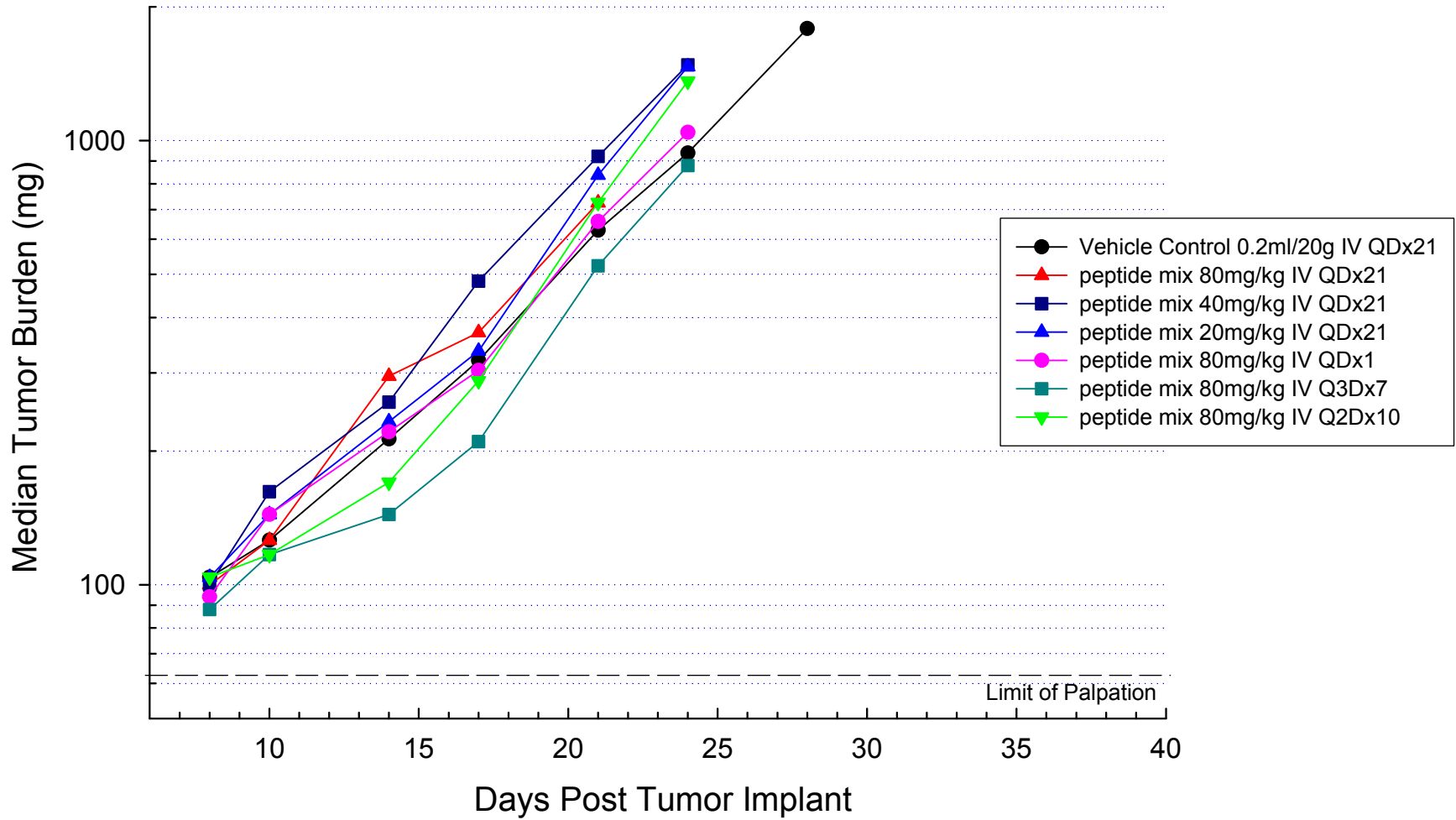
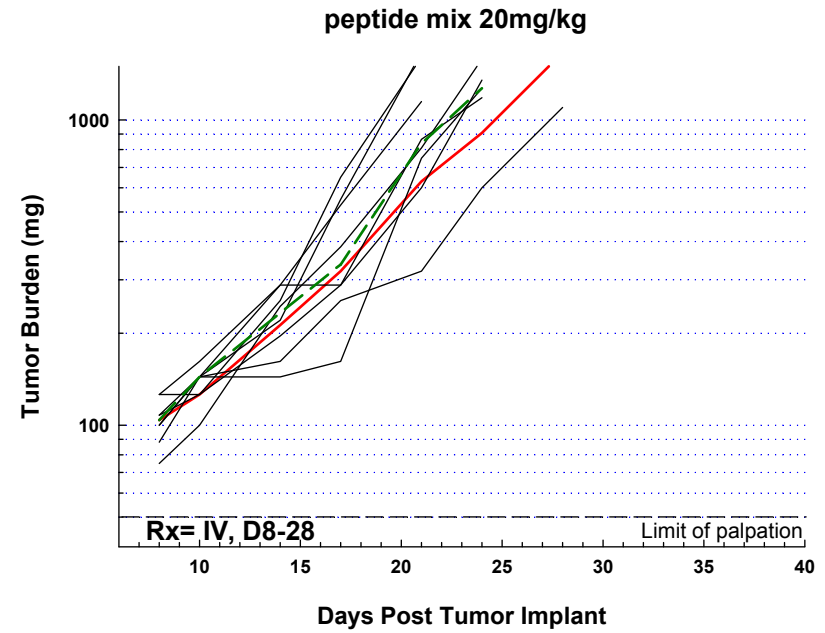
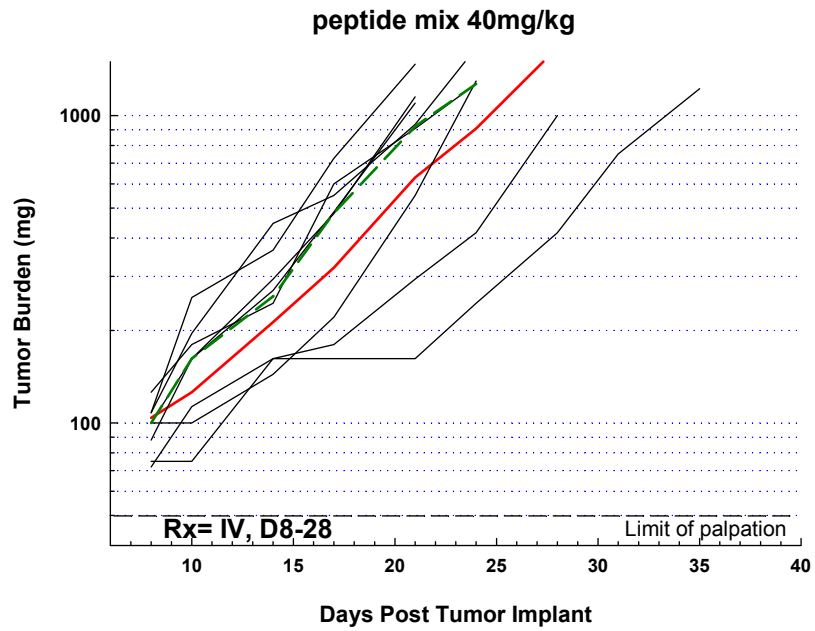
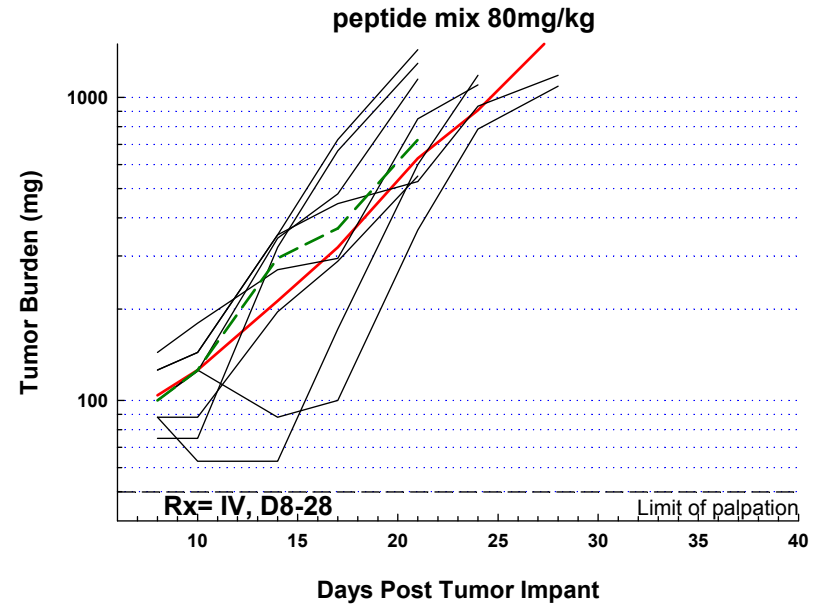
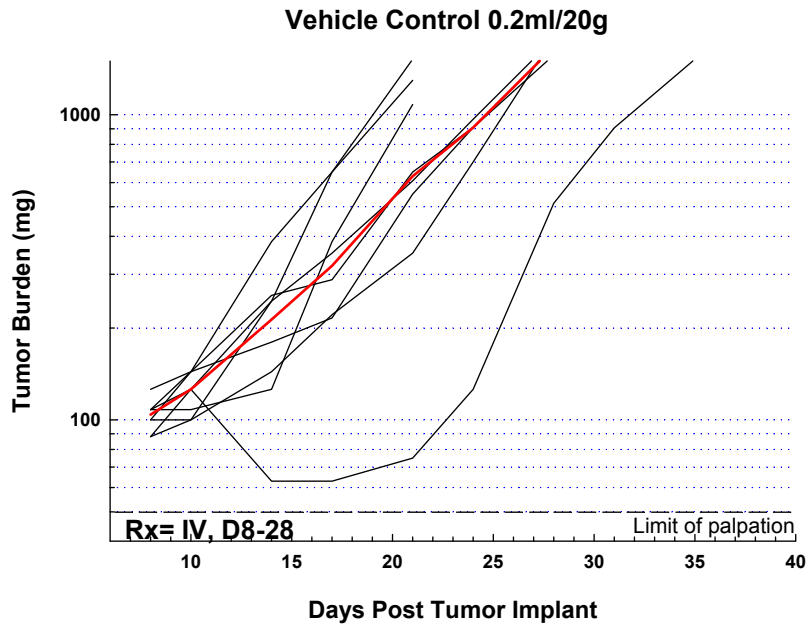
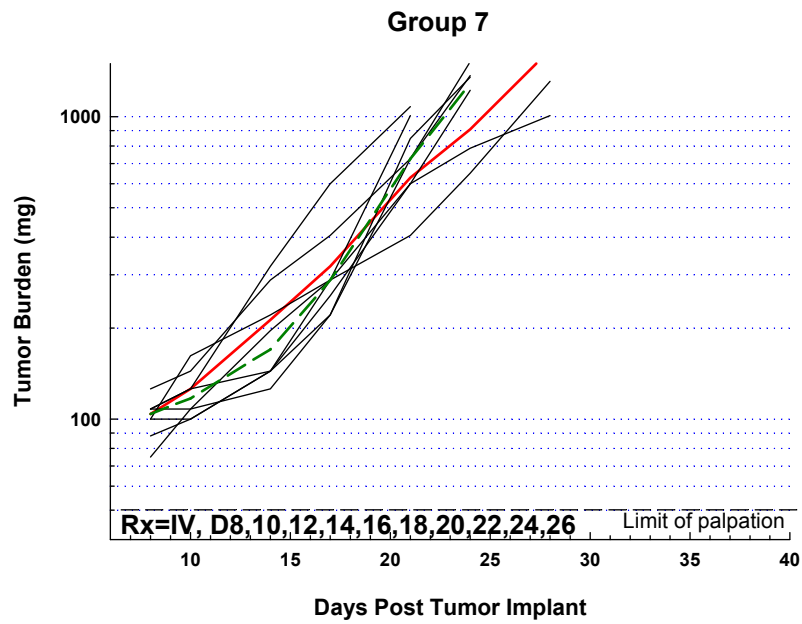
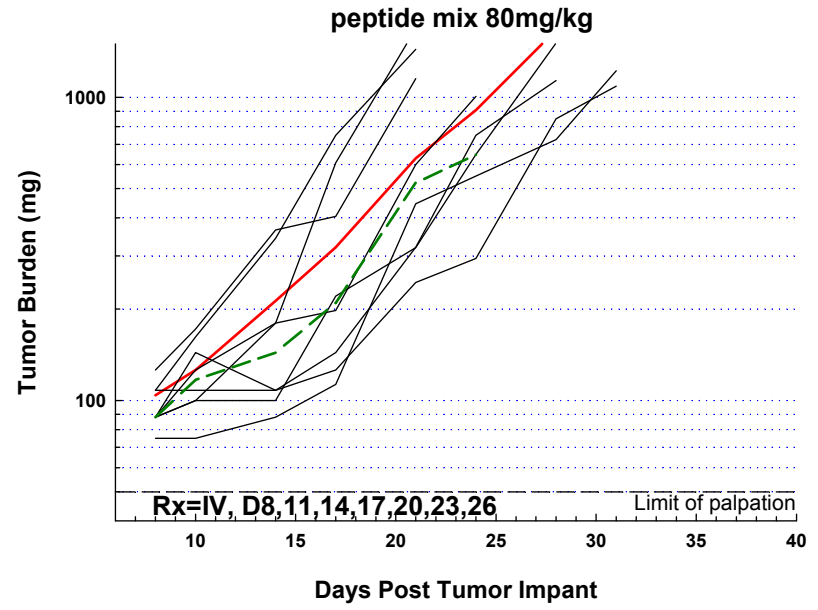
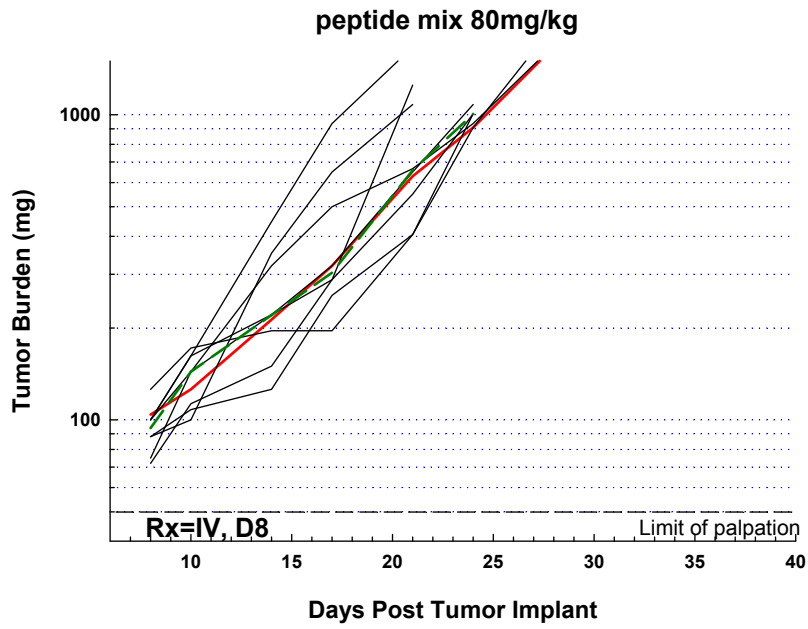


Figure 3 – Individual Tumor Growth Curves by Group



— Control Median

- - - Group Median

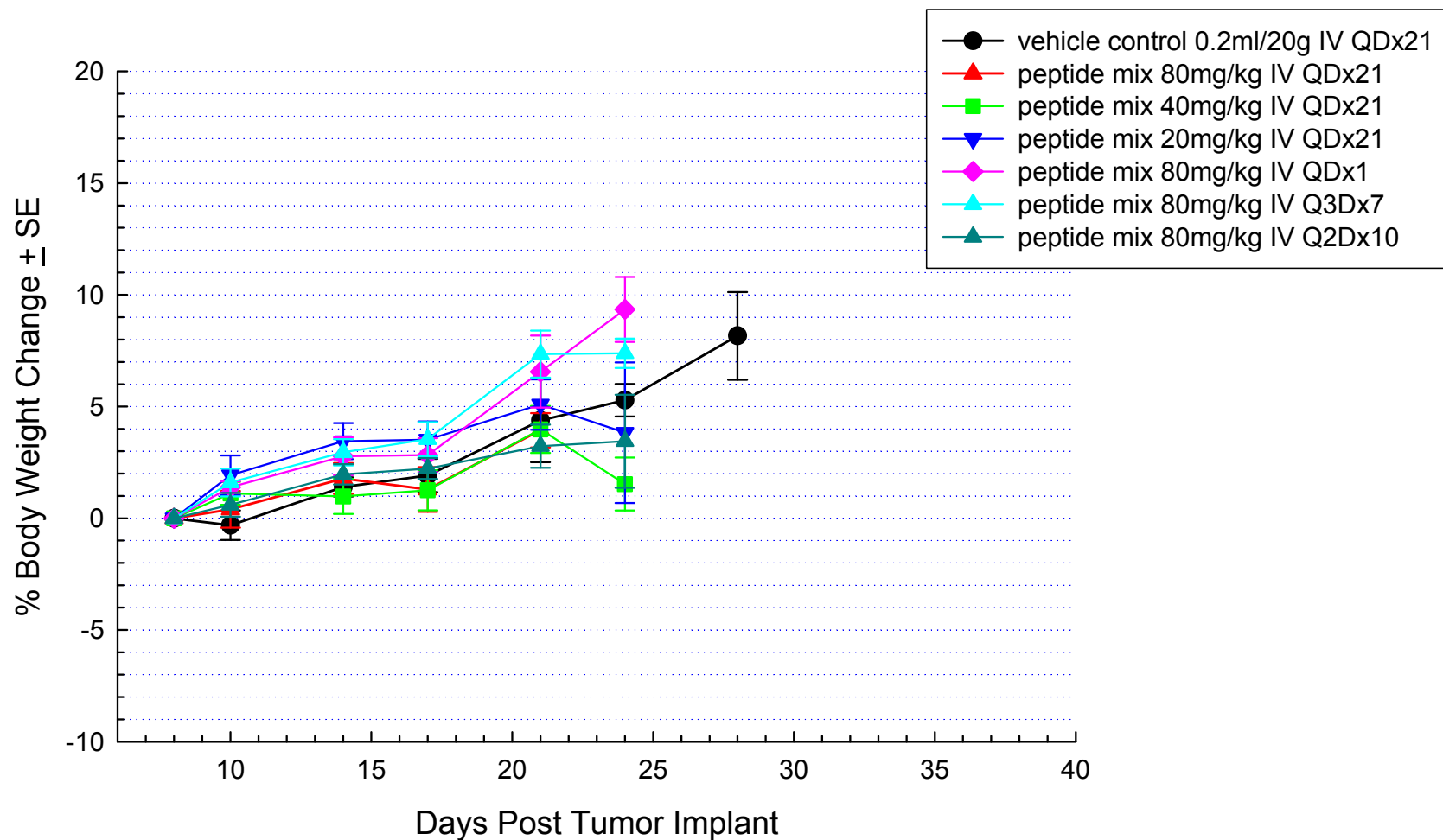


— Control Median

- - - Group Median

Figure 4 – % Body Weight Change Summary with Std. Error

MIR1058 SANA200812
Mean Body Weight Change by Group with Std. Error



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Appendix 1 – Protocol Summary

Study #SANA200812
MIR # 1058

Study Title Efficacy Evaluation of Peptide Mix Against Murine Mammary Carcinoma
Principal Scientist Mindy Stuart

Tumor = M25
Location = SC
Animal = Mouse
Strain = Balb/c

Gender = Female
Test Animals = 56
Implanted Animals = 84
Implant Date = 12/30/2008

Evaluation Size = 750 mg
Fold Growth End Point = 4 x

									Treatment Days	
Group	# Animals	Compound	Route	Schedule	Dose (mg/kg/inj)	Rx Start	Rx End	Start	End	
1	8	Vehicle I	V	QDx21	0.2ml/20g	7-Jan-09	27-Jan-09	8	28	
2	8	Peptide Mix	IV	QDx21	80.00	7-Jan-09	27-Jan-09	8	28	
3	8	Peptide Mix	IV	QDx21	40.00	7-Jan-09	27-Jan-09	8	28	
4	8	Peptide Mix	IV	QDx21	20.00	7-Jan-09	27-Jan-09	8	28	
5	8	Peptide Mix	IV	QDx1	80.00	7-Jan-09	7-Jan-09	8	8	
6	8	Peptide Mix	IV	Q3Dx7	80.00	7-Jan-09	25-Jan-09	8	26	
7	8	Peptide Mix	IV	Q2Dx10	80.00	7-Jan-09	25-Jan-09	8	26	

Drugs					
Drug Name	Vehicle	Source	Lot #	Amount Needed (mg)	Stability
Peptide Mix	PBS	Sanare	Multiple (12 peptides)	150ml	1h

Measurement Frequencies	General Procedures	
Body Weights: 2x/wk	Allow animals to acclimate for 5 days. Implant tumor fragments (30 to 70 mg) into mice high in the right axilla (just under arm). Triage mice into treatment groups when the mean tumor burden is 100mg. Distribute animals to treatment groups such that the mean body weight in each group is within 10% of the overall mean. Body weights and tumor measures are to be recorded 2x/week, clinical signs daily. Mice dosed individually by body weight on the day of treatment as described above. Animals with tumor burdens greater than 1g or found in a moribund condition will be euthanized. Hold animals for Tumor Growth Delay Endpoint and complete regression/partial regression/tumor free survivor determination. Provide weekly interim reports. Full report will be provided to the client with detailed methods, statistical multi-endpoint analysis, publication quality graphics, discussion of results and all raw data.	
Tumor Weights: 2x/wk		
Sac. Tumor Weight (g): 1g		

General Comments
The purpose of this experiment is to evaluate the efficacy of the Peptide Mixture against Mam25 murine carcinoma in Balb/c mice.

Inoculum			Thioglycolate		
Trocar	% Brei	Number of Cells Injected	Tumor Source Code	Number of Inconclusives	Total tubes
<input checked="" type="checkbox"/>			M25/34 (T, 12-4-08)	1	3

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Appendix 2 – Raw Data (Tumor Measurements and Body Weights)

Group #1 Treatment: **Vehicle** Dose: **0.2ml/20g**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day			
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	
1	6	6	17.7	6	7	17.8	7	10	17.6	8	11	17.8	9	15	19.2	11	16	18.3	13	21	20.6										
2	5	7	18.8	6	7	18.7	5	5	19.4	5	5	19.6	5	6	20.4	6	7	20.3	9.6	10.6	19.8	8,10	8,13	19.9	13	18	21.3				
3	5	8	18.8	6	8	19.1	6	10	19	6	12	19	10	11	18.1	11	15	19.8	14	17	19.2										
4	6	6	18.4	6	8	18.7	8	12	18.6	10	13	19.3	13	18	19.5																
5	5	8	18.4	5	8	18.3	7	10	18.6	10	13	19.1	12	18	20.5																
6	6	6	19.1	6	6	18.3	6	7	19.2	8	12	19.1	12	15	18.7																
7	6	7	18.7	6	8	18.5	8	8	19.1	8	9	18.6	10	13	19.4	11	15	19.8	14	16	20.4										
8	5	7	18.6	5	8	18.6	6	8	19.1	7	9	18.8	8	11	19.1	10	14	19.2	15	16	19.9										

Group #2 Treatment: **Peptide Mix** Dose: **80**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day		
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)
1	5	8	18.6	5	10	18.8	7	14	18.9	8	15	18.5	11	19	19.1															
2	6	7	19.5	6	8	19.9	8	11	20.3	11	12	20.3	13	17	20.4															
3	5	7	19.1	5	5	19	5	5	19	7	7	18.8	10	12	19.9	13	14	20.3												
4	5	6	19.1	5	6	18.9	8	10	19.7	11	11	20	12	18	20.2															
5	5	7	19.1	5	7	19.2	7	8	19.5	8	9	19.4	10	11	19.8															
6	6	8	18	6	10	17.5	7	11	18	7	12	18.7	10	17	19.2	10	22	19.7												
7	5	8	18.7	6	7	19.6	5	7	19.5	5	8	18.9	9	9	19.5	11	13	20.2	11	18	20.8									
8	6	7	20.2	6	8	20	8	11	20.1	9	11	19.6	9	13	20.1	12	13	20.3	13	14	21.3									

Group #3 Treatment: **Peptide Mix** Dose: **40**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day		
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)
1	5	8	19.2	5	8	19.2	6	8	18.8	7	9	18.8	10	11	19.5	12	18	19.8												
2	5	8	19.5	6	9	20	7	12	19.8	8	15	20.1	11	19	20.8															
3	5	7	19.1	6	9	19.5	7	11	19.7	9	12	20	13	13	20.5															
4	6	7	17.5	6	10	17.5	7	10	17.4	10	12	17.5	11	15	18.1	13	15	17.6												
5	5	6	19.5	5	6	19.3	6	9	19.2	6	10	19.4	7	12	19.5	8	13	19.6	10	20	20.1									
6	6	6	18.4	8	8	18.5	9	9	18.8	11	12	18.7	14	15	19.5															
7	4	9	19.8	5	9	20.1	6	9	20	6	9	19.6	6	9	19.9	7	10	19.6	8	13	19.9	10	15	19.9	12	17	20.7			
8	6	6	18.9	7	8	19.5	9	11	19.7	10	11	19.7	12	13	20.1	14	17	20.4												

Group #4 Treatment: **Peptide Mix** Dose: **20**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day		
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)
1	5	8	20	6	8	21.1	7	9	20.9	10	11	20.8	14	17	22															
2	6	7	19.2	6	9	19.4	8	9	19.5	9	13	19.8	11	19	20.1															
3	5	7	19.7	6	8	19.9	6	8	20.4	6	9	19.8	10	15	19.8	11	21	20.4												
4	5	6	19.7	5	8	20.7	7	10	21	8	12	20.7	9	20	21	12	22	20.5												
5	6	6	19	6	7	19.6	8	8	20.1	10	13	20.5	13	19	20.1															
6	5	8	20.3	6	8	19.9	6	9	20.2	8	8	20.5	8	10	20.5	10	12	20.5	13	13	21.3									
7	6	6	19.8	6	8	20	8	9	20.3	8	9	20.4	10	12	20.7	13	16	18.4												
8	6	7	17	6	7	17.1	7	8	17.6	8	9	17.6	12	12	18.3	13	14	20.5												

Group #5 Treatment: **Peptide Mix** Dose: **80**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day		
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)
1	6	7	18.5	7	7	18.9	7	8	19.2	7	8	18.9	9	10	19.6	11	15	20	14	20	20.6									
2	5	8	19.1	6	9	19.4	9	11	19.9	12	13	20.3	14	17	21.9															
3	5	8	20	6	9	20.1	7	9	20.1	8	9	20.2	10	11	20.8	12	14	21.1												
4	5	6	19.1	6	8	19.3	7	9	19.9	8	10	20	10	13	20.8	12	15	21												
5	4	9	19.8	5	9	20	5	12	20.1	6	16	19.9	10	25	20.6															
6	5	7	18.6	6	6	19	6	7	19.6	8	8	19.2	9	10	20.4	12	14	21.5												
7	5	7	19	5	8	19.4	8	11	19.8	10	13	19.8	12	15	20.1															
8	5	8	19.2	6	8	19.3	8	10	18.9	10	10	19.3	11	11	19.1	12	13	20.6	15	15	21.7									

Group #6 Treatment: **Peptide Mix** Dose: **80**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day		
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)
1	5	7	19	6	7	18.8	6	10	19.3	9	15	19.5	13	20	20.8															
2	6	6	17	6	6	17.6	6	6	17.6	6	8	17.4	8	10	18	10	15	18.4	11.6	17.6	18.1									
3	6	6	17	6	9	16.9	7	14	17.7	10	15	18	12	20	18.5															
4	5	6	18	5	6	18.2	5	7	18.4	5	9	18.2	9	11	18.7	10	11	19.4	11	12	19.2	12	17	19.5						
5	5	7	18.5	5	8	18.7	5	8	18.8	7	9	19.1	7	13	19.7	9	16	20	12	21	20.4									
6	5	7	17.9	6	8	18.4	6	6	18.5	6	7	18.3	7	10	18.5	7	12	18.4	10	17	19.2	11	18	20.3						
7	6	7	18.1	7	7	18.6	9	9	19.2	9	10	19.5	12	16	20.3															
8	5	7	18.5	5	8	19.1	6	10	18.7	6	11	19.1	10	12	20.1	12	14	20												

Group #7

Treatment: **Peptide Mix**

Dose: **80**

Animal	Date 1/7/09 Day 8			Date 1/9/09 Day 10			Date 1/13/09 Day 14			Date 1/16/09 Day 17			Date 1/20/09 Day 21			Date 1/23/09 Day 24			Date 1/27/09 Day 28			Date 1/30/09 Day 31			Date 2/3/09 Day 35			Date Day			
	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	Width (mm)	Length (mm)	Body Weight (g)	
1	5	7	18.8	5	8	19.4	6	8	19.1	8	9	19.1	9	10	18.9	10	13	19.6	13.6	14.7	20.6										
2	6	7	18.7	6	8	19.2	8	9	19.2	9	10	19.3	11	12	19.1	12	19	19.5													
3	5	6	18.4	6	6	18.3	7	8	18.7	8	9	18.8	10	12	18.2	12	17	17.2													
4	6	6	18.8	6	6	18.7	6	7	18.7	7	9	18.7	11	14	19.4	13	16	19.8													
5	5	8	18.2	5	8	18.3	6	8	18.4	8	8	18.9	10	12	18.9	11	13	19.1	12	14	19.4										
6	6	6	17.9	6	7	17.9	6	8	18.5	7	9	18.4	11	12	18.8	13	18	19.4													
7	5	8	17	6	9	17	7	9	17.5	8	9	17.3	12	14	18.3																
8	6	6	17	6	7	16.9	8	10	17.5	10	12	17.5	12	15	17.8																

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Appendix 3 – Raw Data (Daily Census)

LEGEND: Sacrificed (s) Dead in cage (d) Missing (m) Accidental death (a)

Group	Date 1/7/09		Date 1/8/09		Date 1/9/09		Date 1/10/09		Date 1/11/09		Date 1/12/09		Date 1/13/09		Date 1/14/09		Date 1/15/09		Date 1/16/09		Date 1/17/09		Date 1/18/09		Date 1/19/09			
	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive
1		8		8		8		8		8		8		8		8		8		8		8		8		8		8
2		8		8		8		8		8		8		8		8		8		8		8		8		8		8
3		8		8		8		8		8		8		8		8		8		8		8		8		8		8
4		8		8		8		8		8		8		8		8		8		8		8		8		8		8
5		8		8		8		8		8		8		8		8		8		8		8		8		8		8
6		8		8		8		8		8		8		8		8		8		8		8		8		8		8
7		8		8		8		8		8		8		8		8		8		8		8		8		8		8

Group	Date 1/20/09		Date 1/21/09		Date 1/22/09		Date 1/23/09		Date 1/24/09		Date 1/25/09		Date 1/26/09		Date 1/27/09		Date 1/28/09		Date 1/29/09		Date 1/30/09		Date 1/31/09		Date 2/1/09			
	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive
1	s3	5		5		5		5		5		5		5	s4	1		1		1		1		1		1		1
2	s3	5		5		5	s3	2		2		2		2	s2	0		0		0		0		0		0		0
3	s3	5		5		5	s3	2		2		2		2	s1	1		1		1		1		1		1		1
4	s3	5		5		5	s4	1		1		1		1	s1	0		0		0		0		0		0		0
5	s3	5		5		5	s3	2		2		2		2	s2	0		0		0		0		0		0		0
6	s3	5		5		5	s1	4		4		4		4	s2	2		2		2	s2	0		0		0		0
7	s2	6		6		6	s4	2		2		2		2	s2	0		0		0		0		0		0		0

Group	Date 2/2/09		Date 2/3/09		Date 2/4/09		Date 2/5/09		Date 2/6/09		Date 2/7/09		Date 2/8/09		Date 2/9/09		Date 2/10/09		Date 2/11/09		Date 2/12/09		Date 2/13/09		Date 2/14/09			
	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive	Change	Alive
1		1	s1	0																								
2		0		0																								
3		1	s1	0																								
4		0		0																								
5		0		0																								
6		0		0																								
7		0		0																								

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Appendix 4 – Raw Data (Clinical Signs, Observations, and Comments)

Date	Day	Group	Animal	Tech	Comment
3-Feb-09	35	1	2	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	1	1,3,7,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	1	4,5,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	2	5	MLS	Animal euthanized due to weeping/ulcerated tumor, no remarkable necropsy findings
20-Jan-09	21	2	1,2,4	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	2	3,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	2	7,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	3	5	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
3-Feb-09	35	3	7	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	3	1,4,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	3	2,3,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	4	6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	4	1,2,5	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	4	3,4,7,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	5	5	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	5	1,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	5	2,7	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	5	3,4,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	6	8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	6	1,3,7	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	6	2,5	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
30-Jan-09	31	6	4,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
27-Jan-09	28	7	1,5	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
23-Jan-09	24	7	2,3,4,6	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy
20-Jan-09	21	7	7,8	MLS	Animals euthanized due to tumor burden. Enlarged spleens noted on necropsy

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Appendix 5 – Consolidated Tumor Burdens

Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
4		Dose 20.00										Schedule QDx21		8	28
Animal\Day	8	10	14	17	21	24	28	31	35						
1	100	144	221	500	1666										
2	126	162	288	527	1150										
3	88	144	144	162	750	1271									
4	75	100	245	384	810	1584									
5	108	126	256	650	1606										
6	100	144	162	256	320	600	1099								
7	108	144	288	288	600	1352									
8	126	126	196	288	864	1183									
Mean	104	136	225	388	971	1198	-	-	-	-	-	-	-	-	-
SD	17	19	54	170	473	366	-	-	-	-	-	-	-	-	-
Median	104	144	233	336	837	1271	-	-	-	-	-	-	-	-	-

Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
5		Dose 80.00										Schedule QDx1		8	8
Animal\Day	8	10	14	17	21	24	28	31	35						
1	126	172	196	196	405	908	1960								
2	100	162	446	936	1666										
3	100	162	221	288	550	1008									
4	75	144	221	320	650	1080									
5	72	113	150	288	1250										
6	88	108	126	256	405	1008									
7	88	100	352	650	1080										
8	100	144	320	500	666	936	1688								
Mean	94	138	254	429	834	988	-	-	-	-	-	-	-	-	-
SD	17	28	109	253	453	68	-	-	-	-	-	-	-	-	-
Median	94	144	221	304	658	1008	-	-	-	-	-	-	-	-	-

Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
6		Dose 80.00										Schedule Q3Dx7		8	26
Animal\Day	8	10	14	17	21	24	28	31	35						
1	88	126	180	608	1690										
2	108	108	108	144	320	750	1137								
3	108	162	343	750	1440										
4	75	75	88	113	446	550	726	1224							
5	88	100	100	221	319	648	1512								
6	88	144	108	126	245	294	850	1089							
7	126	172	365	405	1152										
8	88	100	180	198	600	1008									
Mean	96	123	184	321	777	650	-	-	-	-	-	-	-	-	-
SD	16	34	111	242	568	262	-	-	-	-	-	-	-	-	-
Median	88	117	144	210	523	648	-	-	-	-	-	-	-	-	-

Group #	Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
	Dose 80.00										Schedule Q2Dx10		8	26
Animal\Day	8	10	14	17	21	24	28	31	35					
1	88	100	144	288	405	650	1309							
2	126	144	288	405	726	1368								
3	75	108	196	288	600	1224								
4	108	108	126	221	847	1352								
5	100	100	144	256	600	787	1008							
6	108	126	144	221	726	1521								
7	100	162	221	288	1008									
8	108	126	320	600	1080									
Mean	102	122	198	321	749	1150	-	-	-	-	-	-	-	
SD	15	22	73	127	224	350	-	-	-	-	-	-	-	
Median	104	117	170	288	726	1288	-	-	-	-	-	-	-	

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Appendix 6 – Consolidated Body Weights

Animal Body Weights (g)

Group #	1																												
Treatment	Vehicle											Route	IV	Rx Start Day	8	Rx End Day	28												
Dose	0.2ml/20g											Schedule	QDx21																
Animal/Day	8	10	14	17	21	24	28	31	35																				
1	17.7	17.8	17.6	17.8	19.2	18.3	20.6																						
2	18.8	18.7	19.4	19.6	20.4	20.3	19.8	19.9	21.3																				
3	18.8	19.1	19.0	19.0	18.1	19.8	19.2																						
4	18.4	18.7	18.6	19.3	19.5																								
5	18.4	18.3	18.6	19.1	20.5																								
6	19.1	18.3	19.2	19.1	18.7																								
7	18.7	18.5	19.1	18.6	19.4	19.8	20.4																						
8	18.6	18.6	19.1	18.8	19.1	19.2	19.9																						
Mean	18.6	18.5	18.8	18.9	19.4	19.5	20.0	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-			
SD	0.4	0.4	0.6	0.5	0.8	0.8	0.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
Median	18.7	18.6	19.1	19.1	19.3	19.8	19.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-				
Group #	2																												
Treatment	Peptide Mix											Route	IV	Rx Start Day	8	Rx End Day	28												
Dose	80.00											Schedule	QDx21																
Animal/Day	8	10	14	17	21	24	28	31	35																				
1	18.6	18.8	18.9	18.5	19.1																								
2	19.5	19.9	20.3	20.3	20.4																								
3	19.1	19.0	19.0	18.8	19.9	20.3																							
4	19.1	18.9	19.7	20.0	20.2																								
5	19.1	19.2	19.5	19.4	19.8																								
6	18.0	17.5	18.0	18.7	19.2	19.7																							
7	18.7	19.6	19.5	18.9	19.5	20.2	20.8																						
8	20.2	20.0	20.1	19.6	20.1	20.3	21.3																						
Mean	19.0	19.1	19.4	19.3	19.8	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
SD	0.7	0.8	0.7	0.7	0.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
Median	19.1	19.1	19.5	19.2	19.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
Group #	3																												
Treatment	Peptide Mix											Route	IV	Rx Start Day	8	Rx End Day	28												
Dose	40.00											Schedule	QDx21																
Animal/Day	8	10	14	17	21	24	28	31	35																				
1	19.2	19.2	18.8	18.8	19.5	19.8																							
2	19.5	20.0	19.8	20.1	20.8																								
3	19.1	19.5	19.7	20.0	20.5																								
4	17.5	17.5	17.4	17.5	18.1	17.6																							
5	19.5	19.3	19.2	19.4	19.5	19.6	20.1																						
6	18.4	18.5	18.8	18.7	19.5																								
7	19.8	20.1	20.0	19.6	19.9	19.6	19.9	19.9	20.7																				
8	18.9	19.5	19.7	19.7	20.1	20.4																							
Mean	19.0	19.2	19.2	19.2	19.7	19.4	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
SD	0.7	0.8	0.8	0.9	0.8	1.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					
Median	19.2	19.4	19.5	19.5	19.7	19.6	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-					

Group #		Treatment		Route		Rx Start Day		Rx End Day	
4		Peptide Mix		IV		8		28	
		Dose 20.00		Schedule QDx21					
Animal\Day	8	10	14	17	21	24	28	31	35
1	20.0	21.1	20.9	20.8	22.0				
2	19.2	19.4	19.5	19.8	20.1				
3	19.7	19.9	20.4	19.8	19.8	20.4			
4	19.7	20.7	21.0	20.7	21.0	20.5			
5	19.0	19.6	20.1	20.5	20.1				
6	20.3	19.9	20.2	20.5	20.5	20.5	21.3		
7	19.8	20.0	20.3	20.4	20.7	18.4			
8	17.0	17.1	17.6	17.6	18.3	20.5			
Mean	19.3	19.7	20.0	20.0	20.3	20.1	-	-	-
SD	1.0	1.2	1.1	1.0	1.1	0.9	-	-	-
Median	19.7	19.9	20.3	20.5	20.3	20.5	-	-	-
Group #		Treatment		Route		Rx Start Day		Rx End Day	
5		Peptide Mix		IV		8		8	
		Dose 80.00		Schedule QDx1					
Animal\Day	8	10	14	17	21	24	28	31	35
1	18.5	18.9	19.2	18.9	19.6	20.0	20.6		
2	19.1	19.4	19.9	20.3	21.9				
3	20.0	20.1	20.1	20.2	20.8	21.1			
4	19.1	19.3	19.9	20.0	20.8	21.0			
5	19.8	20.0	20.1	19.9	20.6				
6	18.6	19.0	19.6	19.2	20.4	21.5			
7	19.0	19.4	19.8	19.8	20.1				
8	19.2	19.3	18.9	19.3	19.1	20.6	21.7		
Mean	19.2	19.4	19.7	19.7	20.4	20.8	-	-	-
SD	0.5	0.4	0.4	0.5	0.8	0.6	-	-	-
Median	19.1	19.4	19.9	19.9	20.5	21.0	-	-	-
Group #		Treatment		Route		Rx Start Day		Rx End Day	
6		Peptide Mix		IV		8		26	
		Dose 80.00		Schedule Q3Dx7					
Animal\Day	8	10	14	17	21	24	28	31	35
1	19.0	18.8	19.3	19.5	20.8				
2	17.0	17.6	17.6	17.4	18.0	18.4	18.1		
3	17.0	16.9	17.7	18.0	18.5				
4	18.0	18.2	18.4	18.2	18.7	19.4	19.2	19.5	
5	18.5	18.7	18.8	19.1	19.7	20.0	20.4		
6	17.9	18.4	18.5	18.3	18.5	18.4	19.2	20.3	
7	18.1	18.6	19.2	19.5	20.3				
8	18.5	19.1	18.7	19.1	20.1	20.0			
Mean	18.0	18.3	18.5	18.6	19.3	19.2	-	-	-
SD	0.7	0.7	0.6	0.8	1.0	0.8	-	-	-
Median	18.1	18.5	18.6	18.7	19.2	19.4	-	-	-

Group #	Treatment Peptide Mix										Route IV											
	Dose 80.00										Schedule Q2Dx10											
Animal\Day	8	10	14	17	21	24	28	31	35	8	10	14	17	21	24	28	31	35	Rx Start Day	8	Rx End Day	26
1	18.8	19.4	19.1	19.1	18.9	19.6	20.6															
2	18.7	19.2	19.2	19.3	19.1	19.5																
3	18.4	18.3	18.7	18.8	18.2	17.2																
4	18.8	18.7	18.7	18.7	19.4	19.8																
5	18.2	18.3	18.4	18.9	18.9	19.1	19.4															
6	17.9	17.9	18.5	18.4	18.8	19.4																
7	17.0	17.0	17.5	17.3	18.3																	
8	17.0	16.9	17.5	17.5	17.8																	
Mean	18.1	18.2	18.5	18.5	18.7	19.1	-	-	-	-	-	-	-	-	-	-	-	-				
SD	0.7	0.9	0.6	0.7	0.5	1.0	-	-	-	-	-	-	-	-	-	-	-	-				
Median	18.3	18.3	18.6	18.8	18.9	19.5	-	-	-	-	-	-	-	-	-	-	-	-				

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Appendix 7 – Consolidated % Body Weight Change

Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
Dose 20.00		Schedule QDx21												8	28
Animal\Day	8	10	14	17	21	24	28	31	35						
1	0.0	5.5	4.5	4.0	21.0	24	28	31	35						
2	0.0	1.0	1.6	3.1	4.7										
3	0.0	1.0	3.6	0.5	0.5	3.6									
4	0.0	5.1	6.6	5.1	6.6	4.1									
5	0.0	3.2	5.8	7.9	5.8										
6	0.0	-2.0	-0.5	1.0	1.0	1.0	4.9								
7	0.0	1.0	2.5	3.0	4.5	-7.1									
8	0.0	0.6	3.5	3.5	7.6	20.6									
Mean	0.0	1.9	3.5	3.5	5.1	4.4	-	-	-	-	-	-	-	-	-
SD	0.0	2.5	2.3	2.3	3.2	10.1	-	-	-	-	-	-	-	-	-
Median	0.0	1.0	3.6	3.3	5.3	3.6	-	-	-	-	-	-	-	-	-
Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
Dose 80.00		Schedule QDx1												8	8
Animal\Day	8	10	14	17	21	24	28	31	35						
1	0.0	2.2	3.8	2.2	5.9	8.1	11.4								
2	0.0	1.6	4.2	6.3	14.7										
3	0.0	0.5	0.5	1.0	4.0	5.5									
4	0.0	1.0	4.2	4.7	8.9	9.9									
5	0.0	1.0	1.5	0.5	4.0										
6	0.0	2.2	5.4	3.2	9.7	15.6									
7	0.0	2.1	4.2	4.2	5.8										
8	0.0	0.5	-1.6	0.5	-0.5	7.3	13.0								
Mean	0.0	1.4	2.8	2.8	6.6	9.3	-	-	-	-	-	-	-	-	-
SD	0.0	0.7	2.4	2.1	4.6	3.9	-	-	-	-	-	-	-	-	-
Median	0.0	1.3	4.0	2.7	5.9	8.1	-	-	-	-	-	-	-	-	-
Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
Dose 80.00		Schedule Q3Dx7												8	26
Animal\Day	8	10	14	17	21	24	28	31	35						
1	0.0	-1.1	1.6	2.6	9.5										
2	0.0	3.5	3.5	2.4	5.9	8.2	6.5								
3	0.0	-0.6	4.1	5.9	8.8										
4	0.0	1.1	2.2	1.1	3.9	7.8	6.7	8.3							
5	0.0	1.1	1.6	3.2	6.5	8.1	10.3								
6	0.0	2.8	3.4	2.2	3.4	2.8	7.3	13.4							
7	0.0	2.8	6.1	7.7	12.2										
8	0.0	3.2	1.1	3.2	8.6	8.1									
Mean	0.0	1.6	3.0	3.5	7.4	7.0	-	-	-	-	-	-	-	-	-
SD	0.0	1.8	1.7	2.2	3.0	2.4	-	-	-	-	-	-	-	-	-
Median	0.0	2.0	2.8	2.9	7.6	8.1	-	-	-	-	-	-	-	-	-

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Appendix 8 – Group T/C Values

Calculated T/C Values (%)

Group# \ Day	8	10	14	17	21	24	28	31	35
1	100	100	100	100	100	100	100		
2	96	100	138	116	115				
3	96	129	121	151	147	140			
4	100	114	109	105	133	140			
5	90	114	104	95	105	111			
6	85	93	68	66	83	71			
7	100	93	80	90	115	142			

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Appendix 9 – Individual and Group Fold-Growth Values

Calculated Fold Growth

Group #		Treatment Vehicle										Route IV		Rx Start Day	Rx End Day
1		Dose 0.2ml/20g										Schedule QDx21		8	28
Animal\Day	8	10	14	17	21	24	28	31	35						
1	1.0	1.2	2.3	3.3	5.6	9.0	16.4								
2	1.0	1.4	0.7	0.7	0.9	1.4	5.8	10.3	17.3						
3	1.0	1.4	1.8	2.2	5.5	9.1	16.7								
4	1.0	1.3	3.6	6.0	14.1										
5	1.0	1.0	2.5	6.5	13.0										
6	1.0	1.0	1.2	3.6	10.0										
7	1.0	1.1	2.0	2.3	5.2	7.2	12.4								
8	1.0	1.1	1.6	2.5	4.0	8.0	20.5								
Mean	1.0	1.2	2.0	3.4	7.3	6.9	14.4	-	-	-	-	-	-	-	-
SD	0.0	0.2	0.9	2.0	4.6	3.2	5.5	-	-	-	-	-	-	-	-
Median	1.0	1.2	1.9	2.9	5.6	8.0	16.4	-	-	-	-	-	-	-	-
Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
2		Dose 80.00										Schedule QDx21		8	28
Animal\Day	8	10	14	17	21	24	28	31	35						
1	1.0	1.3	3.4	4.8	11.5										
2	1.0	1.1	2.8	5.8	11.4										
3	1.0	0.7	0.7	2.0	6.8	13.4									
4	1.0	1.0	4.3	8.9	17.3										
5	1.0	1.0	2.2	3.3	6.3										
6	1.0	1.3	1.9	2.0	5.9	7.6									
7	1.0	1.3	0.9	1.0	3.7	7.9	10.9								
8	1.0	1.1	2.8	3.5	4.2	7.4	9.4								
Mean	1.0	1.1	2.4	3.9	8.4	-	-	-	-	-	-	-	-	-	-
SD	0.0	0.2	1.2	2.5	4.6	-	-	-	-	-	-	-	-	-	-
Median	1.0	1.1	2.5	3.4	6.5	-	-	-	-	-	-	-	-	-	-
Group #		Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
3		Dose 40.00										Schedule QDx21		8	28
Animal\Day	8	10	14	17	21	24	28	31	35						
1	1.0	1.0	1.4	2.2	5.5	13.0									
2	1.0	1.6	2.9	4.8	11.5										
3	1.0	1.8	3.1	5.5	12.5										
4	1.0	1.4	1.9	4.8	7.2	10.1									
5	1.0	1.0	2.2	2.4	3.9	5.5	13.3								
6	1.0	2.4	3.4	6.7	13.6										
7	1.0	1.6	2.3	2.3	2.3	3.4	5.8	10.4	17.0						
8	1.0	1.8	4.1	5.1	8.7	15.4									
Mean	1.0	1.6	2.7	4.2	8.1	9.5	-	-	-	-	-	-	-	-	-
SD	0.0	0.5	0.9	1.7	4.2	5.0	-	-	-	-	-	-	-	-	-
Median	1.0	1.6	2.6	4.8	7.9	10.1	-	-	-	-	-	-	-	-	-

Group #		4												Rx Start Day		8		Rx End Day		28	
Treatment		Peptide Mix												Route		IV		Schedule		QDx21	
Dose		20.00																			
Animal	Day	8	10	14	17	21	24	28	31	35											
1	1.0	1.4	2.2	5.5	16.7																
2	1.0	1.3	2.3	4.2	9.1																
3	1.0	1.6	1.6	1.8	8.5	14.4															
4	1.0	1.3	3.3	5.1	10.8	21.1															
5	1.0	1.2	2.4	6.0	14.9																
6	1.0	1.4	1.6	2.6	3.2	6.0	11.0														
7	1.0	1.3	2.7	2.7	5.6	12.5															
8	1.0	1.0	1.6	2.3	6.9	9.4															
Mean	1.0	1.3	2.2	3.8	9.4	12.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
SD	0.0	0.2	0.6	1.6	4.6	5.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Median	1.0	1.3	2.2	3.4	8.8	12.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Group #		5												Rx Start Day		8		Rx End Day		8	
Treatment		Peptide Mix												Route		IV		Schedule		QDx1	
Dose		80.00																			
Animal	Day	8	10	14	17	21	24	28	31	35											
1	1.0	1.4	1.6	1.6	3.2	7.2	15.6														
2	1.0	1.6	4.5	9.4	16.7																
3	1.0	1.6	2.2	2.9	5.5	10.1															
4	1.0	1.9	2.9	4.3	8.7	14.4															
5	1.0	1.6	2.1	4.0	17.4																
6	1.0	1.2	1.4	2.9	4.6	11.5															
7	1.0	1.1	4.0	7.4	12.3																
8	1.0	1.4	3.2	5.0	6.7	9.4	16.9														
Mean	1.0	1.5	2.7	4.7	9.4	10.5	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
SD	0.0	0.2	1.1	2.6	5.5	2.7	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Median	1.0	1.5	2.6	4.1	7.7	10.1	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Group #		6												Rx Start Day		8		Rx End Day		26	
Treatment		Peptide Mix												Route		IV		Schedule		Q3Dx7	
Dose		80.00																			
Animal	Day	8	10	14	17	21	24	28	31	35											
1	1.0	1.4	2.0	6.9	19.2																
2	1.0	1.0	1.0	1.3	3.0	6.9	10.5														
3	1.0	1.5	3.2	6.9	13.3																
4	1.0	1.0	1.2	1.5	5.9	7.3	9.7	16.3													
5	1.0	1.1	1.1	2.5	3.6	7.4	17.2														
6	1.0	1.6	1.2	1.4	2.8	3.3	9.7	12.4													
7	1.0	1.4	2.9	3.2	9.1																
8	1.0	1.1	2.0	2.3	6.8	11.5															
Mean	1.0	1.3	1.8	3.3	8.0	7.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
SD	0.0	0.2	0.8	2.3	5.8	2.9	-	-	-	-	-	-	-	-	-	-	-	-	-	-	
Median	1.0	1.3	1.6	2.4	6.4	7.3	-	-	-	-	-	-	-	-	-	-	-	-	-	-	

Group #	Treatment Peptide Mix										Route IV		Rx Start Day	Rx End Day
	Dose 80.00										Schedule Q2Dx10		8	26
Animal/Day	8	10	14	17	21	24	28	31	35					
1	1.0	1.1	1.6	3.3	4.6	7.4	14.9							
2	1.0	1.1	2.3	3.2	5.8	10.9								
3	1.0	1.4	2.6	3.8	8.0	16.3								
4	1.0	1.0	1.2	2.0	7.8	12.5								
5	1.0	1.0	1.4	2.6	6.0	7.9	10.1							
6	1.0	1.2	1.3	2.0	6.7	14.1								
7	1.0	1.6	2.2	2.9	10.1									
8	1.0	1.2	3.0	5.6	10.0									
Mean	1.0	1.2	2.0	3.2	7.4	11.5	-	-	-	-	-	-	-	
SD	0.0	0.2	0.7	1.1	2.0	3.5	-	-	-	-	-	-	-	
Median	1.0	1.2	1.9	3.0	7.3	11.7	-	-	-	-	-	-	-	

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Appendix 10 – DYdĥXY'DfYd

2mg/ml dilution and Freeze Scheme

Peptide	MW	mg provided	ml PBS to add	conc mg/ml	conc needed for 0.000347 mmol/ml	volume of 2mg/ml needed	dilute 7.0 ml to a final volume of X	ml of PBS to add	dosing days	withdraw volume (ml)	amt remainin g	# 1.0 ml aliquots (equal molar conc)	# remaining 2mg/ml solution	Remaining mg in 2mg/ml solution
25	3125.5	31.3	15.65	2	1.084549	7	12.9086	5.9086	39	12.5	0.4086	0	8.65	17.3
26	1735.9	41.9	20.95	2	0.602357	7	23.242	16.242	39	12.5	10.742	11	13.95	27.9
27	1910.2	43.1	21.55	2	0.662839	7	21.1213	14.1213	39	12.5	8.6213	9	14.55	29.1
28	1909.3	46.8	23.4	2	0.662527	7	21.1312	14.1312	39	12.5	8.6312	9	16.4	32.8
29	2399	46.9	23.45	2	0.832453	7	16.8178	9.8178	39	12.5	4.3178	4	16.45	32.9
30	1326.5	47.2	23.6	2	0.460296	7	30.4152	23.4152	39	12.5	17.9152	18	16.6	33.2
31	1129.3	50	25	2	0.391867	7	35.7264	28.7264	39	12.5	23.2264	23	18	36
32	2223.7	35.5	17.75	2	0.771624	7	18.1436	11.1436	39	12.5	5.6436	6	10.75	21.5
33	1746.2	42.8	21.4	2	0.605931	7	23.1049	16.1049	39	12.5	10.6049	11	14.4	28.8
34	2070.3	50	25	2	0.718394	7	19.4879	12.4879	39	12.5	6.9879	7	18	36
35	1570.8	39	19.5	2	0.545068	7	25.6849	18.6849	39	12.5	13.1849	13	12.5	25
36	1886.2	43.8	21.9	2	0.654511	7	21.39	14.39	39	12.5	8.89	9	14.9	29.8
freeze remaining 2mg/ml soln in 1.0ml aliquots								5.9086	150 ml total					
peptide prep and freezing procedure.xls												freeze aliquot size =1.0 ml for the mix remaining		