University of Pittsburgh

Annual Progress Report: 2006 Formula Grant

Reporting Period

July 1, 2010 – December 31, 2010

Formula Grant Overview

The University of Pittsburgh received $8,472,940 in formula funds for the grant award period January 1, 2007 through December 31, 2010. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Immune Assessment of a Novel Influenza Virus-Like Particle Vaccine - Public health officials predict that an influenza pandemic can cause more illnesses and deaths over a shorter period of time than any other natural health threat. The influenza virus is easily spread from person to person. Although vaccination is a useful and cost effective way to combat the threat of a flu outbreak, seasonal flu vaccines provide only partial protection, especially in the very young and the elderly. The goals of this project are to gain a deeper understanding of how the immune system responds to influenza and to develop better methods for evaluating the effectiveness of influenza vaccines.

Duration of Project

1/1/2007 - 12/31/2010

Project Overview

The broad objectives of this research project are to examine immune responses by influenza virus-like particle (VLP)-based vaccines and to develop better methods to test the effectiveness of influenza and other vaccines. This project involves two specific aims. The first aim is to compare immune responses elicited by influenza VLPs to recombinant hemaglutinin (rHA) vaccines in small animals (mice and ferrets). The second aim is to develop improved methods of testing how the immune system responds to influenza infection and influenza vaccination. Advanced technology and special instruments to test immune responses will be used in both aims. The goal is to develop improved assays for assessing influenza immune responses elicited by infection or vaccination.

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Other Participating Researchers

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Expected Research Outcomes and Benefits

Several broad areas of anticipated benefit will be derived as outcomes of this research, which will be conducted at the University of Pittsburgh Center for Vaccine Research (CVR). First, this research will enhance the understanding of immune system responses elicited by influenza vaccines in healthy adults, including elderly individuals. Second, this information will be used to develop effective influenza vaccines; it will also be used to develop new immune assays and improve existing assays for assessing influenza infection and vaccine efficacy. Third, the knowledge gained and technologies developed as a result of this research can be applied to the development of vaccines against other infectious viral diseases that affect citizens of the Commonwealth. Each of these three areas of benefit will contribute to the improved health status of Pennsylvania's citizens, particularly those most vulnerable to infectious viral diseases, like the very young and the elderly.

Summary of Research Completed

Morbidity and mortality after lethal and sub-lethal H5N1 infection in aged and adult mice: The goal of this study was to determine the efficacy of an H5N1 (hemagglutinin type 5 and neuraminidase type 1) virus-like particle (VLP)-based vaccine in aged and adult mice in combination with approved and novel adjuvants. Our research group previously analyzed the effects of seasonal influenza infections in aged and adult mice using a mouse-adapted influenza virus; however, much less is known about highly pathogenic avian influenza (HPAI) infections in aged mice. Therefore, we used an influenza virus with the hemagluttinin (HA) and neuramidinase (NA) from the influenza isolate A/Indonesia/5/2005, pseudotyped onto the mouse adapted A/PR/8/1934 backbone virus, to infect aged and adult mice.

Initially, aged (18-20 months) and adult (8-10 weeks) mice were infected with the Indo/05-PR8 virus (clade 2.1), and mortality and morbidity were compared. Aged and adult mice infected with a lethal virus dose (4 $x10^5$ plaque forming units [pfu]) rapidly lost 20 percent of their body weight over the course of the first five days postinfection and required euthanasia by day 6 (Fig. 1A). Aged mice had initial signs of sickness and enhanced morbidity compared to adult mice, as seen in their sickness scores (Fig. 1B). Following a sub-lethal infection ($1x10^4$ pfu) with the Indo/05-PR8 virus, both adult and aged mice lost approximately10-15 percent of their original weights by days 8-9 postinfection (Fig. 1C). However, aged mice had a higher sickness score than adult mice and their clinical signs were sustained for three days longer than adult mice (Fig. 1D).

Innate and adaptive immune responses in aged and adult mice:
To assess the efficacy of the immune system to control the virus, lung virus load was determined in both age groups after sub-lethal infection. At days 3 and 6 postinfection, both aged and adult mice had similar viral lung titers (approximately$1x10^6$ to $1x10^7$ pfu/g of lung tissue), but aged mice showed significantly higher virus titer at day 9 postinfection compared to adult mice (Fig 2A).

At day 6 postinfection, interferon alpha (IFNα) peaked in the lungs of both age groups, but the IFNα levels in aged animals were significantly lower compared to the adult mice ($p < 0.05$) (Fig 2B). There were no significant differences in the percentage or total number of HA_{533}Pentamer$^+$ specific $CD8^+$ T cells in the lungs of aged and adult mice (Fig.2C). In contrast, the percentage of NP_{147}Pentamer$^+$ $CD8^+$ T cells was significantly higher in adult (mean value 6 percent) than aged (mean value 3 percent) mice (Fig. 2D). At day 10, aged mice had higher numbers of lung $CD8^+$ T cells (approximately $2.1x10^6$ $CD8^+$ T cells/lung) than adult mice (approximately $0.83x10^6$ $CD8^+$ T cells/lung) and, therefore, there was no difference in the number of $NP_{147}{}^+$ $CD8^+$ T cells present in the lungs of aged and adult mice (Fig. 2D). Analysis employing interferon gamma (IFNγ) enzyme-linked immunosorbent spot (ELISPOT) technology revealed that the aged mice had fewer influenza-specific IFNγ producing T cells in their spleens compared to the adult mice (Fig. 2E).

VLP vaccine provides protection from lethal virus challenge in aged and adult mice:
To assess the efficacy of influenza VLPs as vaccine candidates, aged and adult mice were immunized without the use of an adjuvant. At week 5 following two immunizations with VLPs, all of the aged mice vaccinated with the Indo/05 VLPs had a 1:40 hemagglutinin inhibition assay (HAI) titer against the homologous Indo/05-PR8 virus. Interestingly, only three of the seven (42 percent) adult mice had an HAI titer of 1:40. Vaccinated mice were subsequently challenged intranasally with a lethal dose of Indo/05-PR8 virus. All immunized mice in both age groups were protected against a lethal challenge, whereas all non-vaccinated, naïve mice lost greater than 25 percent of their original body weight by day 6 postchallenge and had to be euthanized (Fig. 3B and 3C). Even though aged mice were protected against death following challenge, these aged mice did have signs of disease, including approximately10 percent weight loss by day 6 postinfection (Fig. 3C). These mice recovered over the course of the next 16 days but did not reach their original starting body weight. In contrast, the adult mice lost less than 5 percent of their original weight by day 6 and showed no overt signs of disease (Fig. 3A).

Alum adjuvant improves the efficacy of VLP vaccination in both age groups:
To improve the efficacy of our VLP vaccines, both adult and aged mice were immunized with VLPs (10μg) in combination with Imject Alum®, which is similar to the widely used insoluble aluminium salts used as adjuvants in human and animal vaccines. At week 5, despite the addition of Imject® Alum, only 26 percent of the aged mice had HAI titers of ≥1:40 (GMT=20), whereas 85 percent of the adult mice had HAI titers greater than or equal to 1:40 (GMT=58.56) (Fig 4A). Similarly, aged mice had a mean immunoglobulin G (IgG) endpoint dilution titer of 1:1,455 and the adult mice of 1:12,800 (Fig. 4B).

Subsequent challenge of these immunized mice with a lethal dose of the Indo/05-PR8 virus protected 100 percent of the adult and aged mice from death. Additionally, the immunized aged mice lost approximately 5 percent of their initial body weight, which is comparable to the adult mice receiving VLP vaccine without the adjuvant (Fig. 3A and 4C). Therefore, despite no detectable increase in HAI titer in the aged animals receiving the VLP plus Imject® Alum adjuvant, the protective efficacy of the VLPs was increased. Also, the adult mice immunized with the VLP vaccine plus Imject® Alum did not lose any body weight after virus challenge (Fig. 4C). In contrast, the non-immunized control mice in both age groups succumbed to the infection by day 6 (Fig. 4C).

Next, we analyzed the frequency of the recalled influenza virus specific memory CD8+ T cells after challenge of VLP immunized and naive aged and adult mice. At day 6 postinfection, the $CD8^+$ T cell response in the lungs of non-immunized mice in both age groups was low to undetectable (Fig. 4D). In contrast, adult and aged mice immunized with the VLPs plus Alum adjuvant demonstrated a slightly higher, albeit low percentage of HA_{533}-pentamer $^+$ (mean value adult: 0.3 percent and aged: 0.2percent) specific for the HA_{533} epitope in their lungs (Fig. 4D).

Dendritic cell activation by TLR3 ligand poly (I:C) in the lungs of adult and aged mice:

To evaluate the efficacy of the VLP vaccine in inducing protective immunity in aged and adult mice via the mucosal route, a synthetic toll-like receptor 3 (TLR3) ligand, polyinosinic:polycytidylic acid poly (I:C), was successfully used. Mice were immunized intranasally with VLP alone, VLP in conjunction with poly (I:C), or with poly (I:C) alone. After 24 hours, both adult and aged mice immunized with VLP alone or with poly (I:C) had a significant increase in the number of cells per gram of lung tissue compared to non-immunized mice (Fig. 5A). Curiously, the combination of VLP and poly (I:C) did not significantly increase the total number of lung cells compared to naïve mice ($p>0.05$); however, both adult and aged mice had a significant influx of conventional dendritic cells (DCs) ($CD11c^{high}$ /$CD11b^{high}$) (Fig. 5B) (aged [naïve 4.4 percent±1.9 versus VLP/poly (I:C) 10.29 percent±3.4, $p<0.05$] and adult mice [naïve 3.2 percent±1.6 versus VLP/poly (I:C) 12.7 percent±0.68, $p<0.05$]). In both age groups, the combination of VLP with poly (I:C) resulted in the largest increase in the percentage of conventional DCs in the lung compared to VLP or poly (I:C) alone (Fig 5B). The activation markers CD40 (Fig. 5C) and major histocompatibility complex class II (MHC II) (Fig. 5D) were up-regulated on the lung DC surface 24 hours after immunization, as shown by mean fluorescence intensity (MFI) flow cytometry analysis. Cell surface expression of MHCII was significantly ($p<0.05$) up-regulated in aged mice after stimulation with the VLP/poly (I:C) combination compared to naïve mice, but there was no statistically significant increase over the naïve baseline observed after poly (I:C) treatment alone (albeit a trend in activation is detectable). In adult mice, poly (I:C) immunization alone resulted in a statistically significant increase in MHCII cell surface expression compared to naïve mice ($p<0.05$) (Fig. 5C). Similarly, in adult mice, CD40 expression on the cell surface of lung DC was significantly up-regulated after poly (I:C) and VLP/poly (I:C) immunization (Fig. 5D) compared to naïve mice. Aged mice did require the combination of VLP plus poly (I:C) for a statistically significant increase ($p<0.05$) in CD40 surface expression (Fig. 5D). VLP immunization alone did not result in any MHCII or CD40 increase over baseline expression (naïve mice) in adult and aged animals (Fig. 5C and D).

Mucosal immunization provides protection against lethal challenge:
Having established that the H5N1 Indo/05 VLP vaccine in combination with poly (I:C) activates DCs in adult and aged mice, groups of mice were immunized via the intranasal route with VLP vaccines with or without poly (I:C) as adjuvant. As a control, a group of mice received poly (I:C) alone. At week 5, the adult mice that were immunized intranasally with VLPs alone had anti-HA antibodies that recognized homologous recombinant HA with a mean geometric titer (GMT) of 1:800 (Fig. 6A). In contrast, immunization with VLPs plus poly (I:C) increased the antibody titers in the adult mice to a GMT of 1:51,200. In comparison, aged mice vaccinated with VLPs alone had a GMT of 1:230, which was enhanced to a GMT of 800 with the addition of poly (I:C) (Fig. 6A). Approximately 60 percent of the adult mice had detectable HAI titers following vaccination with the VLPs alone, but all titers were less than 1:40 (GMT=11.5) (Fig. 6B). In contrast, 85 percent of the adult mice receiving the VLP plus poly (I:C) combination had detectable HAI titers, of which 47 percent were greater than 1:40 (GMT=37). Interestingly, none of the aged mice, regardless of the presence or absence of poly (I:C) as adjuvant had measurable HAI titers. As expected, immunization of aged and adult mice with poly (I:C) alone as a control did not result in detectable HAI titers (Fig. 6B).

Serum antibody responses and protection do not always correlate. Therefore, the mice were challenged with a lethal dose of Indo/05-PR8 virus to determine the protective efficacy of the intranasally administered VLP vaccine in both age groups. Aged mice receiving the VLP vaccine without adjuvant lost, on average, 15 percent of their initial body weight by day 6; and four out of six mice succumbed to the infection (Fig. 6C and 6E). In contrast, the aged mice that received the VLP vaccine in combination with poly (I:C) lost on average less than five percent of their initial body weight over the course of infection, and 100 percent of the mice survived (Fig. 6C and 6E). The adult mice receiving VLP with or without poly (I:C) all survived the challenge, and there was no significant difference in weight loss between the groups (Fig. 6D and 6E). The non-immunized control mice in both age groups lost greater than 20 percent of their body weight by day 6 and had to be euthanized (Fig. 6C and 6D).

Next, vaccine primed influenza specific memory CD8+ T cells following heterologous challenge were analyzed. Vaccinated mice were challenged with a lethal dose of the PR8 reassortant H5N1 A/VN/1203/2004 (VN/04-PR8) virus six days postinfection. VLP vaccination alone resulted in a statistically significant recall of HA_{533} specific CD8+ T cells in the adult mice after virus challenge compared to the primary response in non-immunized mice ($p<0.05$) (Fig. 7). We observed the same trend in the VLP immunized aged animals (Fig. 7). Interestingly, poly I:C treatment alone resulted in a larger percentage of HA_{533} CD8+ T cells in the lungs of the adult animals after challenge compared to non-adjuvanted mice (Fig. 7). This effect was similar, but not statistically significant, in the aged animals ($p>0.05$). The combination of VLP plus poly I:C as adjuvant resulted in significant recall of influenza specific CD8+ T cells in both age groups after VN/04-PR8 challenge compared to the primary CD8+ T cell responses in non-immunized mice ($p<0.05$) (Fig. 7).

Figure 1

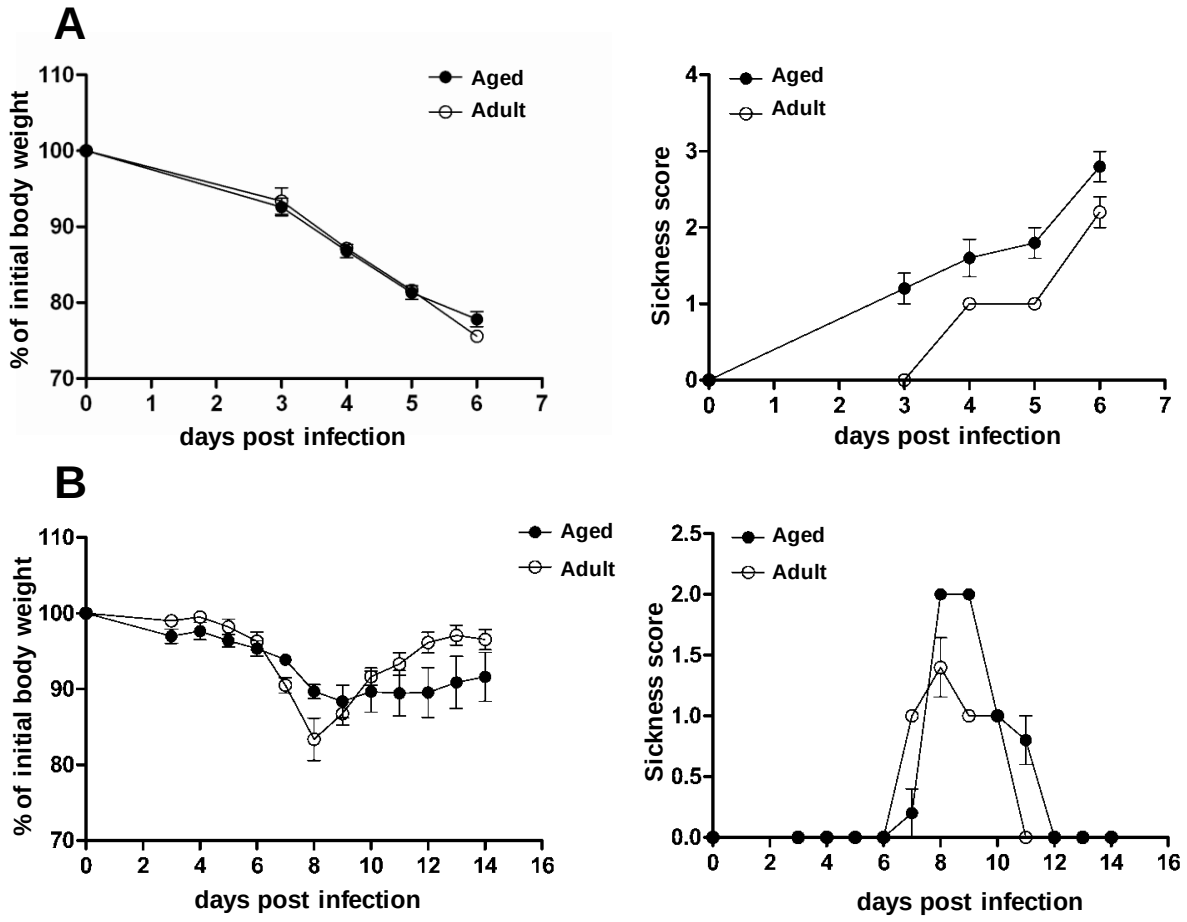

A
Aged
Adult
% of initial body weight
days post infection
Sickness score
B

Figure 2

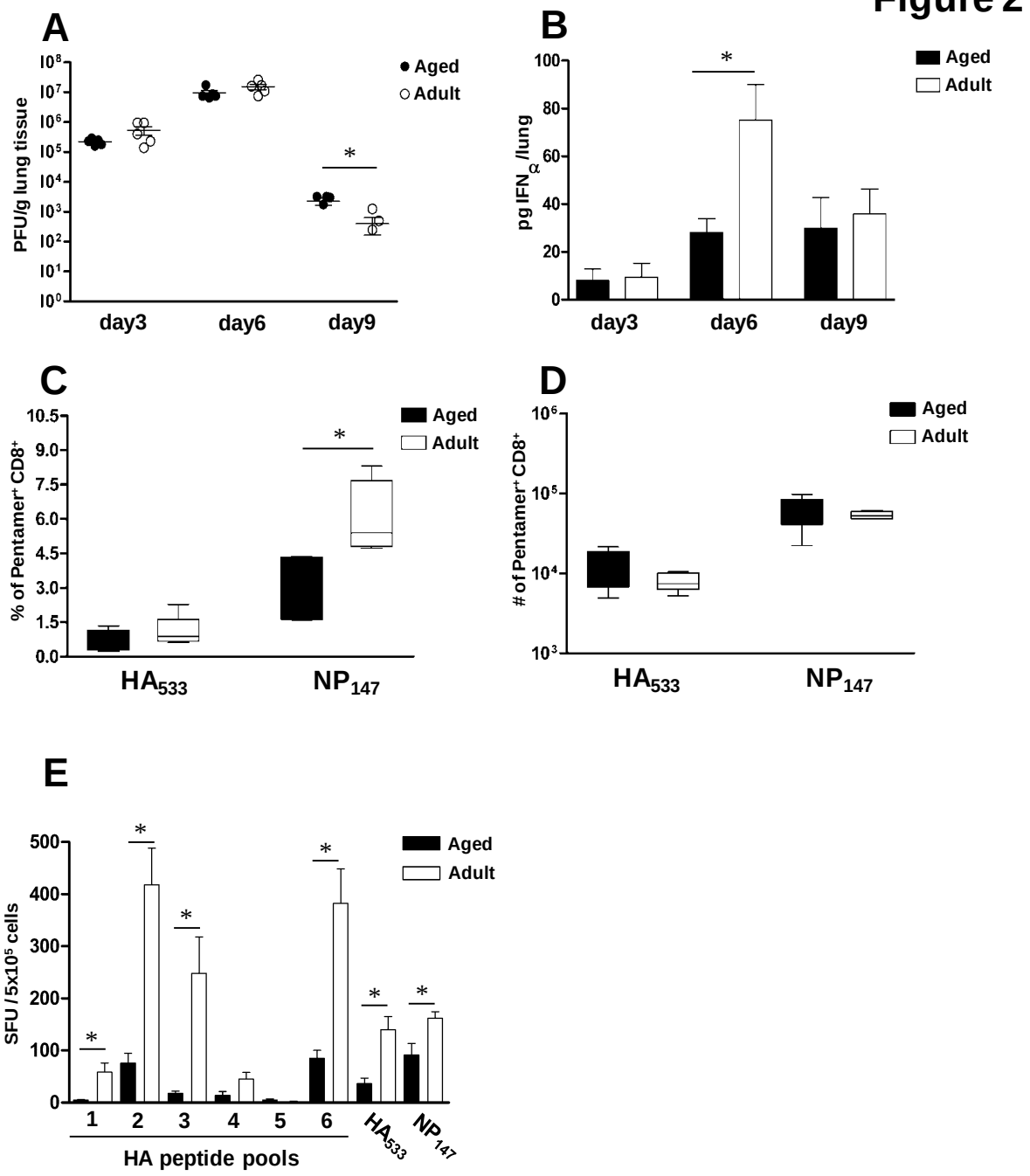

A
PFU/g lung tissue
Aged
Adult
day3
day6
day9
B
pg IFNα /lung
Aged
Adult
day3
day6
day9
C
% of Pentamer+ CD8+
Aged
Adult
HA533
NP147
D
# of Pentamer+ CD8+
Aged
Adult
HA533
NP147
E
SFU / 5x10^5 cells
Aged
Adult
HA peptide pools
HA533
NP147

Figure 3

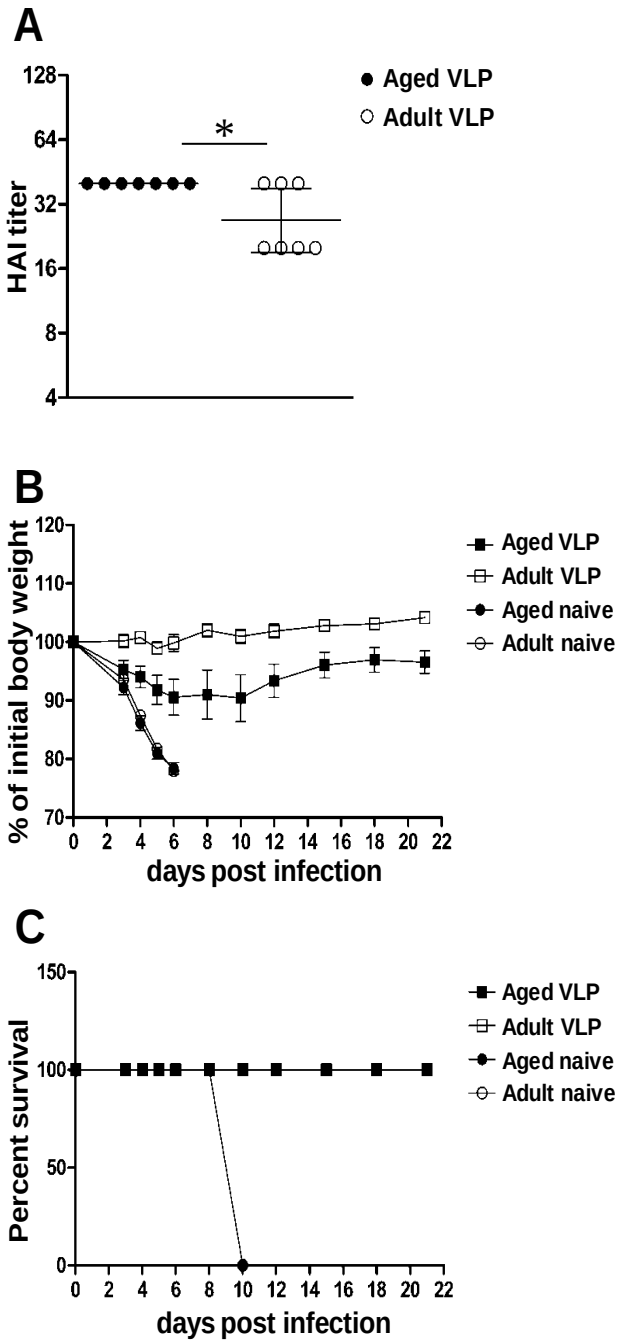

A
128
64
32
16
8
4
HAI titer
*
Aged VLP
Adult VLP
B
120
110
100
90
80
70
% of initial body weight
0 2 4 6 8 10 12 14 16 18 20 22
days post infection
Aged VLP
Adult VLP
Aged naive
Adult naive
C
150
100
50
0
Percent survival
0 2 4 6 8 10 12 14 16 18 20 22
days post infection
Aged VLP
Adult VLP
Aged naive
Adult naive

Figure 4

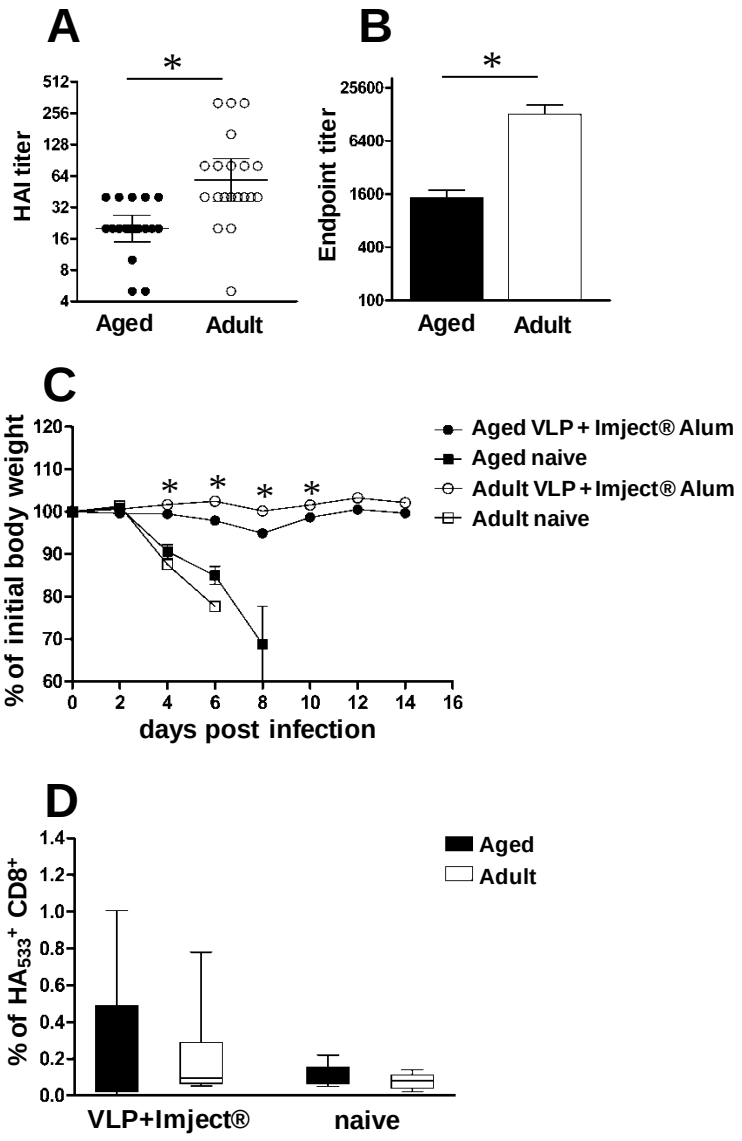

A
*
HAI titer
512
256
128
64
32
16
8
4
Aged
Adult
B
*
Endpoint titer
25600
6400
1600
400
100
Aged
Adult
C
% of initial body weight
120
110
100
90
80
70
60
0
2
4
6
8
10
12
14
16
days post infection
Aged VLP + Imject® Alum
Aged naive
Adult VLP + Imject® Alum
Adult naive
D
% of HA533+ CD8+
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0.0
VLP+Imject®
naive
Aged
Adult

Figure 5

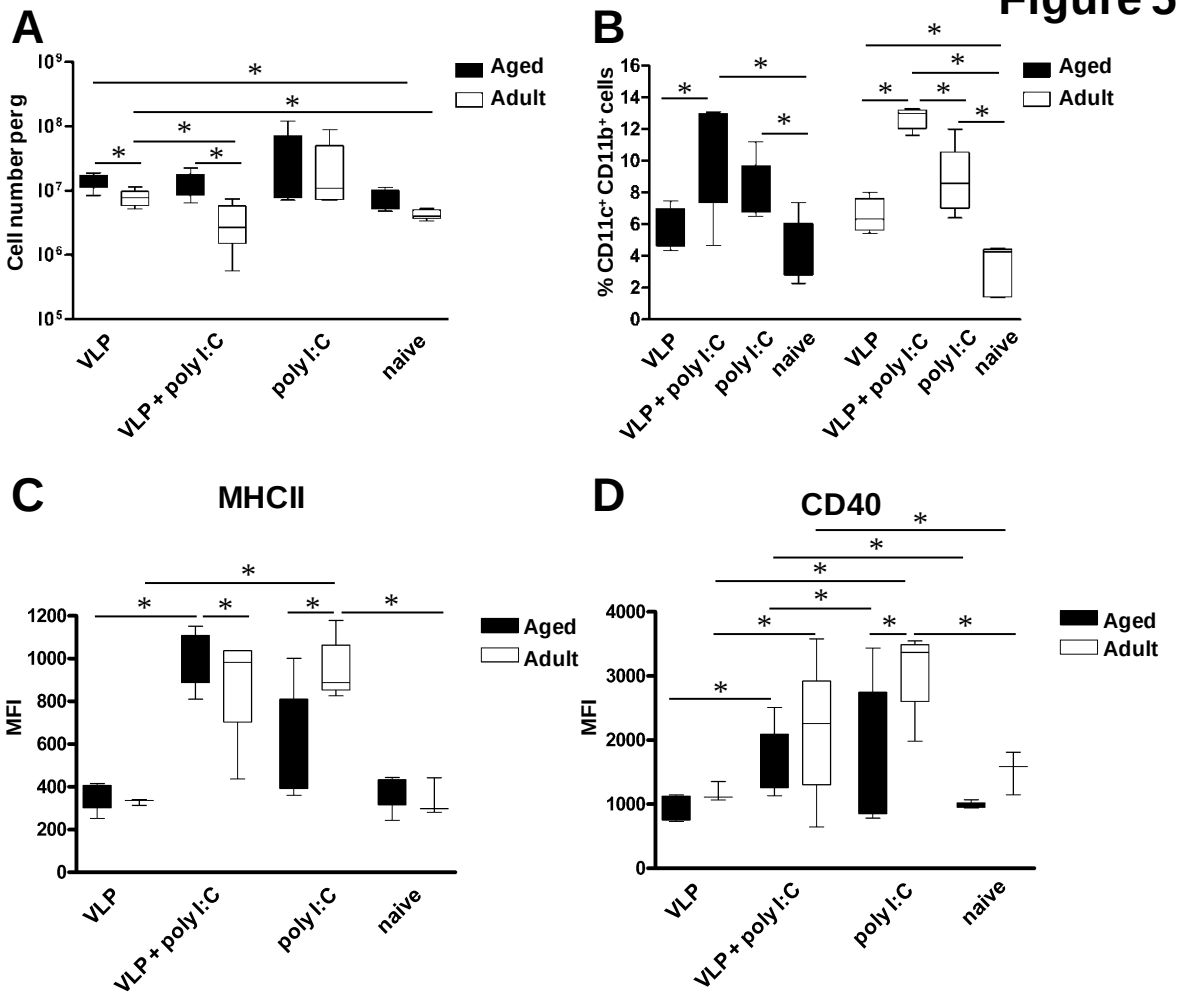
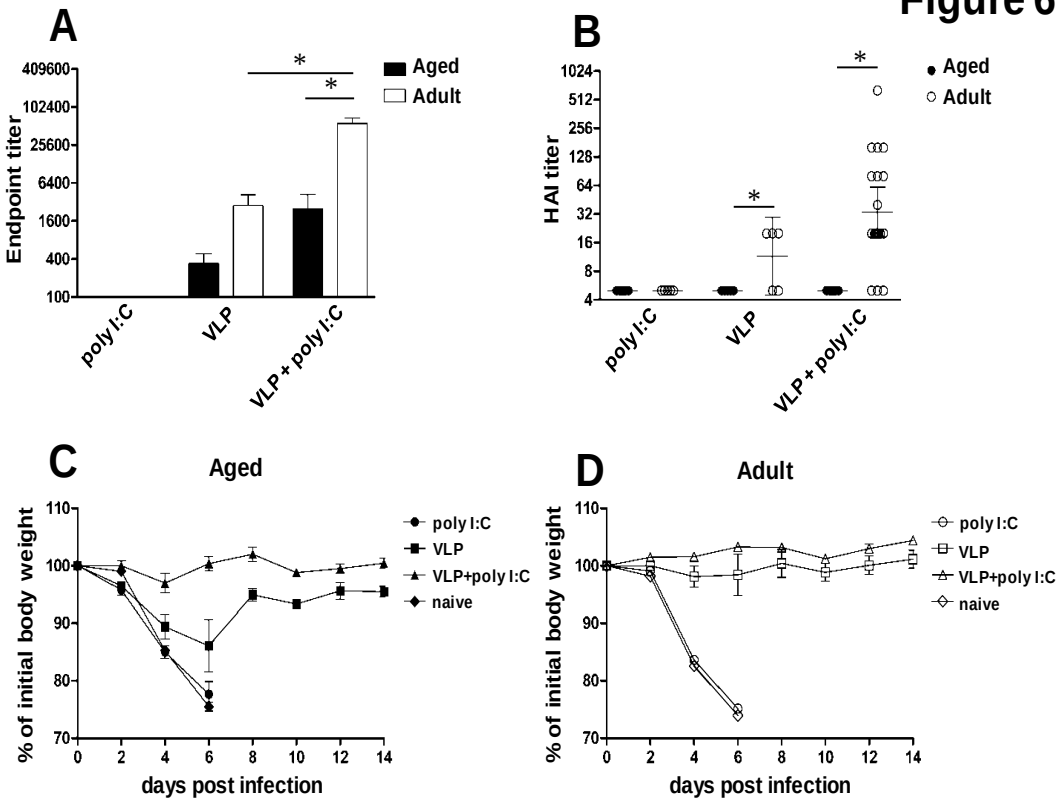

A
Cell number per g
Aged
Adult
VLP
VLP + poly I:C
poly I:C
naive
B
% CD11c+ CD11b+ cells
C
MHCII
MFI
D
CD40
MFI

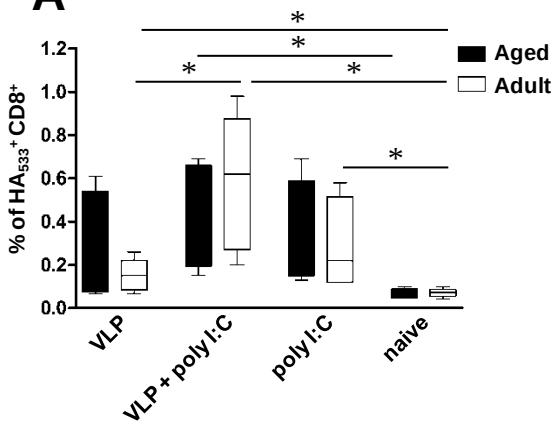
Figure 6



E

	Poly I:C	VLP	VLP + Poly I:C	Naive
Aged	0/7 (0%)	2/6 (33%)	7/7 (100%)	0/5 (0%)
Adult	0/5 (0%)	5/5 (100%)	5/5 (100%)	0/5 (0%)

Figure 7



Research Project 2: Project Title and Purpose

DNA Repair Pathways and Their Influence on Tumorigenesis - The purpose of this project is to explore novel features of three DNA repair pathways involved in mediating cellular response to DNA damage. Characterization of DNA repair has important implications for the development of cancer and for understanding certain kinds of resistance to anticancer chemotherapy. It is hoped that, through a better understanding of this fundamental process, more effective prevention and treatment strategies can be devised.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 3: Project Title and Purpose

Viruses and Cancer: Characterization of Host Cell-Virus Interactions - Kaposi's sarcoma (KS), a lymphatic endothelial cell tumor, remains a critical public health problem worldwide. While rates of this disease have declined in the United States since their peak in the late 1980s, KS is now the most commonly reported tumor in sub-Saharan countries. In the United States, specific populations remain at high risk for mortality from KS, including solid organ transplant patients who have a 40-60 percent mortality rate after contracting KS and the majority of survivors lose the transplanted allograft. Finally, while KS is currently well-controlled among acquired immunodeficiency syndrome (AIDS) patients, when these patients age it is expected that a resurgence of severe KS will occur. Therefore, developing vaccines to prevent or control this disease remains an important public health priority.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 4: Project Title and Purpose

Cancer Inflammatory and Immune Response—Novel Insights and Targets for Therapy – The experiments described in Aim 1 build upon the observation that the sera of patients with oral

carcinoma contain tumor-derived membranous microvesicles (MV) that have been shown to induce death of activated immune cells and, thus, may contribute to immune dysfunction seen in these patients. The studies will characterize MV biology, importance for diagnosis, and prognosis of tobacco-related oral cancer. The experiments in Aim 2 extend observations related to how tumor cells die, examining the release of damage-associated molecular pattern molecules (DAMPs) and their effect on inflammatory cells. The effect of DAMPs, coupled with MV, on treatment response may enhance future therapeutic strategies and improve survival rates for cancer patients.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 5: Project Title and Purpose

Mechanisms for Antiestrogen Resistance in Breast Cancer - The estrogenic signaling pathway is the target of proven and effective tamoxifen (a selective estrogen receptor modulator [SERM]) chemoprevention and treatment for breast cancer. However, it is suspected that some breast cancers contain mutations in the estrogen receptor, and the Nichols laboratory has isolated a mutation from a breast cancer that appears to be activated, not inhibited, by tamoxifen. This finding raises the question of whether expression of such a receptor converts normally sensitive breast cancer cells to antihormone resistance. By studying how cancer cells are inhibited by tamoxifen or similar SERMs and how they escape that inhibition, one can define alternative or additional therapies to minimize its effect. This new knowledge should lead to more successful combination strategies for chemoprevention, therapy, and disease-free survival for breast cancer patients.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 6: Project Title and Purpose

Oral Cancer and Chromosomal Instability: Finding Novel Cancer Prevention Targets - This

project is designed around two major aims. The first aim seeks to determine how deregulation of cell cycle checkpoints leads to genomic instability in oral cancer cells. A significant subset of oral carcinomas is associated with high-risk human papillomaviruses (HPVs), and the HPV-16-encoded E7 oncoprotein will be used as a model system for further experiments. The second aim will focus on whether attenuation of the mitotic spindle checkpoint can be used to eradicate oral cancer cells. These projects will provide the framework for future translational studies to improve preventive approaches in patients at risk for HPV-induced oral cancer as well as nonvirus-induced oral carcinomas.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 7: Project Title and Purpose

Evaluating the Effects of Stress on Spontaneous Tumor Development - The purpose of this project is to evaluate how chronic stress affects the development and progression of breast cancer in mice that spontaneously develop mammary tumors in a model that mimics the development of breast cancer in women. The investigators will also study the effects of chronic stress on the ability of these mice to mount immune responses that target a receptor on the breast tumors which is also expressed on human breast tumors and which is already known to be an antigen available for inducing immune responses in about 25 percent of women with breast cancer. These studies will provide new insights into how stress responses affect the induction of antitumor immunity to breast cancer.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 8: Project Title and Purpose

Hypermethylation of Genes in Secondary SCCHN in Relation to Smoking - Most cases of squamous cell carcinoma of the head and neck (SCCHN) are strongly associated with chronic smoking. Almost half of the survivors of first tumors continue smoking after treatment, and

many of these patients develop a second primary tumor (SPT) within two decades of initial diagnosis. The basic biological mechanisms that connect smoking and secondary SCCHN are not well understood. The Garte research team is interested in understanding these mechanisms by linking exposure to smoking with one of the more exciting recent fields of research into molecular carcinogenesis—changes in the function of genes due to hypermethylation, a specific way that cells control gene expression. The hypothesis to be addressed is that cigarette smoking is linked to hypermethylation of specific genes involved in secondary SCCHN tumorigenesis.

Duration of Project

1/1/2007 - 12/31/2007

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Infrastructure Project 9: Project Title and Purpose

Research Infrastructure: Vivarium Renovations for Barrier Facility - Despite a vivarium staff's best efforts to run a pathogen-free facility, communicable disease outbreaks will still occur. The best method to minimize these outbreaks is to develop specialized standard operating procedures (SOPs) for moving animals, personnel, and materials into the facility; moving animals between facilities; and limiting facility access for outside individuals (public and researchers). The design of the existing vivarium facility in the Biomedical Science Tower South (BSTS) prohibits rigorous SOP implementation, leaving the animals vulnerable to adventitious disease outbreaks. The purpose of this project is to renovate the existing animal facility into a barrier facility to minimize communicable disease outbreaks.

Duration of Project

7/1/2007 – 11/30/2008

Summary of Research Completed

This project ended during a prior state fiscal year. For additional information, please refer to the Commonwealth Universal Research Enhancement Annual C.U.R.E. Reports on the Department's Tobacco Settlement/Act 77 web page at http://www.health.state.pa.us/cure.

Research Project 10: Project Title and Purpose

Research Infrastructure: Caging Installation at Bridgeside Point II Vivarium Facility - Bridgeside Point II (BPII) is a new research facility at the University of Pittsburgh. At this time, final fit-out of the core vivarium facility is being completed, and this project will provide necessary caging and related sanitary equipment. Because the facility is one mile from the heart

of the main University campus, a fully equipped, on-site vivarium facility is essential for investigators working there.

Duration of Project

12/17/2009 – 12/31/2010

Project Overview

To fully outfit the newest research building at the University of Pittsburgh, appropriate vivarium equipment must be purchased and installed. The first basic need for the facility is caging designed to accommodate the needs of the animals housed within according to the standards of the Association of Assessment and Accreditation of Laboratory Animal Care International (AAALAC). These standards include the air purification systems and cage washing facilities necessary to maintain a healthy vivarium environment.

Principal Investigator

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Other Participating Researchers

None

Expected Research Outcomes and Benefits

This project will enhance research infrastructure at the University of Pittsburgh by providing an on-site vivarium facility at the newest research building, BPII. Additional research space provides the infrastructure required to expand research programs, recruit new faculty members, and accommodate the changing needs of existing investigations, all of which are essential to advance biomedical progress and, in the long run, to translate findings from animal to human studies.

Summary of Research Completed

All rodent, rabbit, and large animal caging systems have been delivered from the vendors and installed. In addition, all ancillary equipment to support the animal facilities has been installed. Biosafety cabinets and NuAire animal transfer stations have been installed. The animal facility received University of Pittsburgh Institutional Animal Care and Use Committee (IACUC) approval to open on November 12, 2010. The facility is currently in use and at approximately 14 percent capacity for large animal housing and 18 percent capacity for rodent barrier housing,

with 51 percent of the additional space allocated for expansion of existing colonies and new groups in the queue and/or in quarantine.