

Duquesne University

Annual Progress Report: 2007 Formula Grant

Reporting Period

July 1, 2010 – December 31, 2010

Formula Grant Overview

The Duquesne University received \$84,549 in formula funds for the grant award period January 1, 2008 through December 31, 2010. Accomplishments for the reporting period are described below.

Research Project 1: Project Title and Purpose

Expanded Health Belief Model and Adherence to Mammography Screening in Women - The purposes of this study are to describe and examine the variables associated with the Expanded Health Belief Model (EHBM) and adherence to mammography screening in women with rheumatoid arthritis (RA), and to explore the extent to which the EHBM variables can predict adherence to mammography screening in women with RA compared to women without RA.

Duration of Project

1/1/2008 - 12/31/2010

Project Overview

The broad objective of this project is to gain a better understanding of the Expanded Health Belief Model (EHBM) variables and their ability to predict adherence to mammography screening in women with rheumatoid arthritis (RA) and without RA. The specific aims of this study are to: 1) describe the EHBM variables including perceived susceptibility and severity, perceived benefits and barriers, cues to action, self-efficacy and adherence to mammography screening in women with RA; 2) explore potential predictors of adherence to mammography screening in women with RA; and, 3) compare predictors of adherence to mammography screening in women with RA to women without RA.

Design: A descriptive, correlation design will be used in this project to examine the EHBM variables including perceived susceptibility and severity, perceived benefits and barriers, cues to action, and self-efficacy and to gain a better understanding of potential predictors of adherence to mammography screening in a group of women with RA compared to a group of women without RA.

Sample and Settings: Women with RA and women without RA will be recruited for this project from two different settings within the Western Pennsylvania Health System. Results of a power

analysis using a moderate effect size of .40 indicated that a total of 300 women or 150 women per group will be needed to achieve a power of .80 and an alpha of .05 using a two tailed test of significance.

Women with RA will be recruited from a rheumatology practice and women without RA will be recruited from a small community hospital Emergency Department (ED). Only women between 40 and 70 years of age with a diagnosis of RA, who are fluent in English and have at least an 8th grade education, and do not have a current diagnosis of breast cancer will be included in the RA group. Women in the comparison group will only be included in the project if they are 40 to 70 years old, have never been diagnosed with RA or breast cancer, are fluent in English, and have at least an 8th grade education.

Instruments: Several questionnaires will be used to collect data including the Demographic Data Form, The Breast Cancer Knowledge Test (BCKT), Benefits and Barriers Mammography Screening Test-Champion, the Short Form-36 (SF-36), the Beck Depression Inventory, 2nd edition (BDI-II), and the Mammography Screening Self-Efficacy Scale (MSSS).

Principal Investigator

Karen K Paraska, PhD, CRNP
Assistant Professor
Duquesne University
529 Fisher Hall
600 Forbes Avenue
Pittsburgh, PA 15282

Other Participating Researchers

David Helfrich, MD, Jonathan Landis, MD - employed by West Penn Allegheny

Expected Research Outcomes and Benefits

Barriers to mammography screening are present in women in the general population as well as in women with disabilities such as rheumatoid arthritis (RA). Women with RA have specific disease related variables such as physical limitation and depression that may prevent adherence to mammography screening. There may however be other variables that prevent mammography screening in women with RA. Although components of the EHBM are well established in healthy women, no studies to date have examined the extent to which RA related variables contribute to underutilization of mammography screening in women with RA.

An estimated 178,480 women are expected to be diagnosed with breast cancer in 2007. Recommended screening for breast cancer includes an annual mammogram in women age 40 and above (American Cancer Society, 2005). RA affects 1% of the United States, or 2.1 million Americans. It can affect anyone at any age, but 70% of people with RA are women. Efforts are needed to improve the quality of care for RA patients and to increase physician awareness of co-morbid diseases among patients with RA and other chronic diseases. In one group of women

analyzed with RA, only 32% of the sample received a mammogram during the past year (Kremers et al. 2003).

This research project will aid in identifying specific factors that may contribute to the low mammography screening rate in women with RA. It is necessary to know the extent by which EHBM variables predict adherence to mammography screening in women with RA in order to develop interventions that will promote adherence to mammography screening and thus, help prevent breast cancer in this population of women. This project is significant to nursing and will provide valuable insight into the delivery of health care services to reduce health risks and transfer research advances to community use, with the prevention and reduction of disease.

Summary of Research Completed

No further research was conducted during this period. Additional statistical analysis was done, including a multivariate analysis. The results are summarized in the table below. This information was used further to prepare an early investigator NIH R01 application.

Multivariate Associations with Mammogram in Past Year

Because 94% of the sample had health insurance and because insurance is correlated with barriers, we did not include it in the multivariable models, although based on the univariate model, it does appear to be associated with having a mammogram in the past year. Benefits and efficacy are correlated and have a collinear relationship with mammogram in the past year, so in the multivariate model, we only include efficacy. In the overall model, RA was associated with a greater likelihood (OR = 1.5) of having a mammogram in the past year, but not statistically significantly. Physician recommendation and higher efficacy were associated with a higher likelihood of having a mammogram in the past year; barriers were associated with a lower likelihood of having a mammogram in the past year.

Variables associated with mammogram in past year differed between RA and ED patients. For RA patients having a higher depression score was associated with a lower likelihood of having a mammogram in the past year, and higher efficacy was associated with a higher likelihood of having a mammogram in the past year. The odds ratio for physician recommendation could not be calculated in this model because no one without a physician recommendation had a mammogram. For the ED patients, physician recommendation was associated with a higher likelihood for having a mammogram in the past year and barriers were associated with a lower likelihood of having a mammogram in the past year. (Table 1)

Table 1. Multivariate Logistic Regression Models for Mammogram in Past Year

	Total		RA		ED	
	OR	P-Value	OR	P-Value	OR	P-Value
RA	1.5	.4	-	-	-	-
Age	1.03	.3	1.03	.5	1.02	.5
Physician Recommendation	15.2	<.001	-	-	7.04	.009
BDI	1.00	.9	.87	.03	1.00	.7
Efficacy	1.01	.005	1.01	.01	1.01	.092
Barriers	.89	.028	.94	.4	.81	.02

Notes Overall:

- 1) Because only 5% of participants didn't have insurance, and because insurance is correlated with barriers, we didn't include this variable in the multivariate models.
- 2) Because benefits and efficacy are correlated and have a collinear relationship with mammogram, we only include efficacy in the model.

Notes about RA:

- 1) Of the 1 African-American, 0 didn't have mammogram
- 2) Of the 1 person with no insurance, 0 had a mammogram
- 3) Of those 8 w/out a physician recommendations, 0 had a mammogram

Research Project 2: Project Title and Purpose

Development of a Bone-Regenerative Scaffold - The goal of this project is to develop a novel therapy to aid in the formation of bone by first developing a ceramic scaffold on which stem cells will attach, grow, and form bone; and by second attaching to the scaffold a hormone (melatonin) that has the ability to enhance the formation and function of these bone-forming stem cells.

Duration of Project

1/1/2008 - 12/31/2010

Project Overview

The goal of this project is to develop a novel therapy to aid in the formation of bone by way of the following Specific Aims: 1) To develop a calcium aluminate ceramic scaffold that facilitates bone formation that is non-toxic and 2) To determine the efficacy of this calcium aluminate ceramic scaffold on forming bone in a rat.

The hypothesis that underlies this proposal is that a novel use of a biomaterial called calcium aluminate along with melatonin will enhance the formation of bone in a rat model.

For Aim 1, new technologies and products combined with novel drug therapies are needed to treat injuries and bony defects in cranial and maxillofacial tissues, as well as critical fractures

and bone/joint replacement. Ideal treatments would provide off-the-shelf materials that serve as strong, biodegradable scaffolds that have the ability to contain biological factors such as hemostatic agents, analgesics, antibiotics, drugs, hormones, and/or cells to stabilize, protect, and promote tissue repair. Here, we have investigated a potential biomaterial, calcium aluminates (CA), which has a number of desirable properties including high mechanical strength, controllable porosity, ease of formation, and room temperature strength development that gives this material physical advantages over currently available bone graft and implant technologies. In addition, typical chemical moieties present in the various forms of CA offer attractive ionic and/or covalent binding sites for attachment of biological factors (i.e., melatonin) that can enhance tissue formation and repair.

Regarding Aim 2, preliminary data using a mixed phase material of $\text{Ca}_3(\text{Al}(\text{OH})_6)_2$, $\text{Ca}(\text{AlO}_2)_2$, and CaAl_4O_7 , is effective at supporting cell adhesion, proliferation and differentiation of adult mesenchymal stem cells into osteoblasts *in vitro*. In a rat skull defect (8mm) study, the calcium aluminate material implanted in the defect proved to be non-toxic over the course of four weeks and effectively filled the defect better than the control or commercial material, Vitoss[®]. We propose to test a novel drug therapy including the development of a calcium aluminate ceramic scaffold to induce bone formation in the rat and will be adding novel biological agents (melatonin) to see if they improve bone formation in the rat.

Principal Investigator

Paula A. Witt-Enderby, PhD
Professor of Pharmacology and Toxicology
Duquesne University
421 Mellon Hall
600 Forbes Avenue
Pittsburgh, PA 15282

Other Participating Researchers

Ellen S. Gawalt, PhD, Vicki L. Davis, PhD, Rachelle N. Palchesko, BS, Bill Clafshenkel - employed by Duquesne University
James Rutkowski, DDS - self-employed

Expected Research Outcomes and Benefits

Americans today enjoy greater longevity (77.6 years) than any other generation and are undergoing implanted prosthetic joint and dental implant procedures on a routine basis. Also, many of our injured soldiers lose limbs and require extensive prosthetic surgery. Often times these patients require bone grafting procedures to accommodate placement and retention of these prosthetic joints, limbs, and teeth. The use of bone grafts often necessitates that additional time is allotted for complete bone formation and frequently the final results are less than what was expected. Over one million bone grafting procedures are completed each year in the United States alone. Autogenous bone grafts are obtained from a second surgical site or allograft bone grafts are obtained from cadavers. Each of these sources presents with multiple problems.

Autogenous grafts can lead to morbidities (pain, infection, functional restrictions) associated with the donor surgical sites. Allograft bone grafts present with the concern of infectious disease transmission and possible irregularities in processing donor bone grafts that lead to recalls of materials that may have already been implanted in the patient. Because of these real-world concerns the medical and dental professions plus patients would benefit greatly if a synthetic graft material were available that would negate the need for using autogenous grafts or cadaver-derived bone grafts. It would be beneficial if the synthetic material could also be supplemented with pharmacological agents [melatonin and Platelet-Rich Plasma (PRP)] that would reduce both healing time and complications plus provide greater predictability. Additionally, it would be helpful if the grafting material could be a pliable material that would harden shortly after placement and therefore assuring that the graft stays in the intended location when the clinician closes the surgical site. All of these attributes would translate into a significant benefit for the professions and patients.

Summary of Research Completed

In the last remaining months of this project, the toxicity, osteoconductivity and osteoinductivity of the material was tested by assessing the differentiation of human adult mesenchymal stem cells seeded on calcium aluminates measured by alkaline phosphatase activity; alkaline phosphatase is one indicator of osteoblast function. Human adult mesenchymal stem cells (hAMSCs) were stimulated to grow and differentiate on unmodified CAs in the presence of growth medium (OS-). Increases in alkaline phosphatase (ALP) activity occurred when cells were grown in growth (OS-) medium (Fig. 1). These data show that the CA scaffolds were non-toxic to hAMSCs and they support their growth and differentiation into osteoblasts.

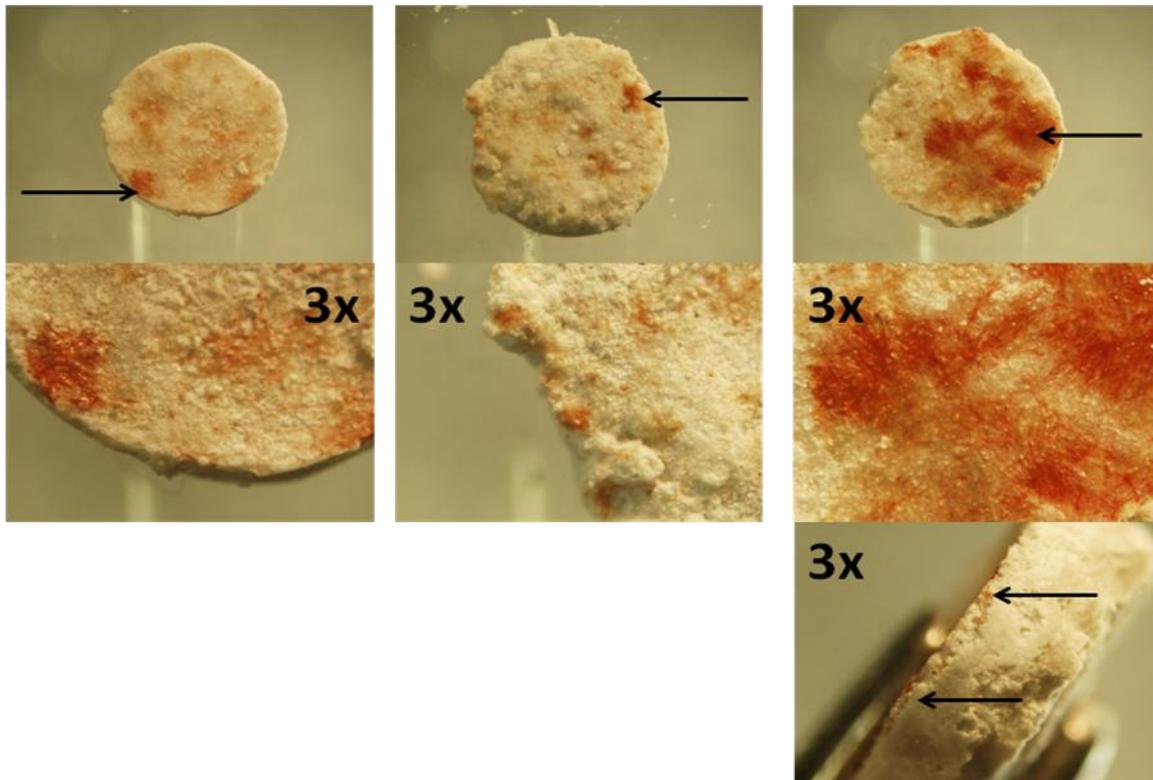


Figure 1. *Alkaline phosphatase activity on scaffolds after 14 days in culture.* Human mesenchymal stem cells (20,000 cells/mL/well of a 48-well plated) were seeded initially onto 8mm x 8mm CAs (unmodified). After 24h, the scaffolds containing hAMSCs were transferred to wells containing fresh OS- in a 24-well plate and allowed to grow. Growth medium (OS-) was replaced every third day for up to 14 days after which the cells were stained for ALP activity and then fixed in 10% formalin at 4°C. Arrows highlight ALP staining.