Fiscal Year:	FY 2007	**Task Last Updated:**	FY 01/31/2008
PI Name:	Wolfe, Robert R. Ph.D.		
Project Title:	Nutritional countermeasures to ameliorate losses in muscle mass and function		
Division Name:	Human Research		
Program/Discipline:	NSBRI Teams		
Program/Discipline--Element/Subdiscipline:	NSBRI Teams--Nutrition, Physical Fitness, and Rehabilitation Team		
Joint Agency Name:		**TechPort:**	Yes
Human Research Program Elements:	(1) **HHC**:Human Health Countermeasures		
Human Research Program Risks:	None		
Space Biology Element:	None		
Space Biology Cross-Element Discipline:	None		
Space Biology Special Category:	None		
PI Email:	rwolfe2@uams.edu	**Fax:**	FY 501-526-5710
PI Organization Type:	UNIVERSITY	**Phone:**	501-526-5708
Organization Name:	University of Arkansas for Medical Sciences		
PI Address 1:	4301 W. Markham, Slot 806		
PI Address 2:			
PI Web Page:			
City:	Little Rock	**State:**	AR
Zip Code:	72205	**Congressional District:**	2
Comments:			
Project Type:	Ground	**Solicitation / Funding Source:**	2003 Biomedical Research & Countermeasures 03-OBPR-04
Start Date:	07/01/2004	**End Date:**	07/31/2009
No. of Post Docs:	1	**No. of PhD Degrees:**	3
No. of PhD Candidates:	0	**No. of Master' Degrees:**	0
No. of Master's Candidates:	0	**No. of Bachelor's Degrees:**	1
No. of Bachelor's Candidates:	0	**Monitoring Center:**	NSBRI
Contact Monitor:		**Contact Phone:**	
Contact Email:			
Flight Program:			
Flight Assignment:	NOTE: Received extension to 7/31/2009 per NSBRI (10/09)		
Key Personnel Changes/Previous PI:			
COI Name (Institution):	Fitts, Robert (Marquette University) Ferrando, Arny (University of Arkansas for Medical Sciences)		
Grant/Contract No.:	NCC 9-58-NPFR00403		
Performance Goal No.:			
Performance Goal Text:			

Task Description:	We have completed this project and have studied the effects of chronically elevated cortisol and hypocaloric diet throughout 14 days of bed rest on muscle protein, LBM, and muscle function. We have completed 13 subjects. Preliminary evidence indicates that combined elevation of cortisol and a hypocaloric diet throughout bed rest increases muscle resistance to the action of insulin and increases the loss of lean body mass. This investigation is relevant to both clinical and astronaut populations, as both are prone to under-nutrition during a stress state. Further, we intend to investigate nutritional and exercise countermeasures with this model to determine an optimal operational countermeasure that can be economically (in terms of crew time and payload) utilized to ameliorate muscle loss during prolonged space flight.
Rationale for HRP Directed Research:	
Research Impact/Earth Benefits:	Earth-based Implications Prolonged inactivity is inherent to trauma, serious injury, or major surgery. These events represent a significant stress to the patient such that the resultant muscle loss and weakness impairs subsequent rehabilitation. Studies reveal that the requirement for hospital intensive care often entails hypocaloric intake in the patient, thus further exacerbating the deleterious results of stress. This project is designed to investigate countermeasures which will maintain muscle mass during periods of prolonged inactivity, hypocaloric intake and stress. The proposed interventions are primarily nutritional, and are of unique design and composition so as to have a maximal benefit on a gram per gram basis. Thus, these investigations will be directly applicable and translatable to a patient populations.
Task Progress:	Progress Report Summary - Year 3 A. Major Accomplishments Space flight is a unique environment to the human physiology, and as such, induces changes in the hormonal environment that exacerbate the loss of lean mass. We hypothesized that muscular inactivity, when coupled with hypercortisolemia indicative of a stress response would result in a greater loss of muscle mass and strength. Since astronauts habitually consume a hypocaloric diet in space, we recently extended our investigations to include the combined effects of inactivity, stress, and hypocaloric feeding on muscle protein synthesis, mass, and strength. In a follow-up study, 2 groups of subjects were studied before and after 14d of bed rest. One group was subjected to the conditions of bed rest, hypercortisolemia, and hyporcaloric (80%) intake. The second group was subjected to the same conditions; however, 15g of an EAA supplement was given 3 times per day. Preliminary findings indicate that the loss of muscle mass and strength is exacerbated under these combined conditions of hypocaloric intake and hypercortisolemia. The addition of the EAA supplement appears to ameliorate these losses. Analyses are ongoing at this time. Since our move to UAMS, we have initiated further studies to investigate the addition of leucine alone to meals in order to stimulate protein synthesis over a 24 hr period, and to investigate the interaction of EAA with a minimal amount of resistive exercise. To date, we have enrolled 7 subjects and completed study of 4. Preliminary data is not yet available. Since the protocols of Drs. Wolfe and Ferrando were designed to be complementary, we have included them under one IRB protocol at UAMS. Thus, this report will detail progress in both grant projects. Our recent findings are consistent with our previous data and others (Stein) during space flight and indicate that muscular inactivity and stress (hypercortisolemia) represent strong catabolic stimuli which exacerbate losses in muscle mass and strength. This catabolism is further aggravated by the hypocaloric intake that is common during space flight. The implication for space flight is that sufficient anabolic stimuli, whether by nutritional, pharmacological, exercise, or combined means, are required to offset the reduction in muscle protein synthesis to maintain muscle mass and function.
Bibliography Type:	Description: (Last Updated: 10/23/2019)
Articles in Peer-reviewed Journals	Fitts RH, Ramatowski JG, Peters Jr, Paddon-Jones D, Wolfe RR, Ferrando AA. "The deleterious effects of bed rest on human skeletal muscle fibers are exacerbated by hypercortisolemia and ameliorated by dietary supplementation." Am J Physiol Cell Physiol. 2007 Jul;293(1):C313-20. PMID: 17409123 , Jul-2007
Articles in Peer-reviewed Journals	Paddon-Jones D, Sheffield-Moore M, Cree MG, Hewlings SJ, Aarsland A, Wolfe RR, Ferrando AA. "Atrophy and impaired muscle protein synthesis during prolonged inactivity and stress." J Clin Endocrinol Metab. 2006 Dec;91(12):4836-41. PMID: 16984982 , Dec-2006
Articles in Peer-reviewed Journals	Zwart SR, Davis-Street JE, Paddon-Jones D, Ferrando AA, Wolfe RR, Smith SM. "Amino acid supplementation alters bone metabolism during simulated weightlessness." J Appl Physiol. 2005 Jul;99(1):134-40. PMID: 15691900 , Jul-2005