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| **Fiscal Year:** | FY 2016 | **Task Last Updated:** | FY 10/26/2016 |
| **PI Name:** | Urban, Randall M.D. | | |
| **Project Title:** | Testosterone Supplementation as a Countermeasure against Musculoskeletal Losses during Space Exploration | | |
| **Division Name:** | Human Research | | |
| **Program/Discipline:** | HUMAN RESEARCH | | |
| **Program/Discipline--Element/Subdiscipline:** | HUMAN RESEARCH--Biomedical countermeasures | | |
| **Joint Agency Name:** | | **TechPort:** | Yes |
| **Human Research Program Elements:** | (1) **HHC**:Human Health Countermeasures | | |
| **Human Research Program Risks:** | (1) **Muscle**:Risk of Impaired Performance Due to Reduced Muscle Size, Strength and Endurance | | |
| **Space Biology Element:** | None | | |
| **Space Biology Cross-Element Discipline:** | None | | |
| **Space Biology Special Category:** | None | | |
| **PI Email:** | rurban@utmb.edu | **Fax:** | FY |
| **PI Organization Type:** | UNIVERSITY | **Phone:** | 409-772-1176 |
| **Organization Name:** | University of Texas Medical Branch at Galveston | | |
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| **City:** | Galveston | **State:** | TX |
| **Zip Code:** | 77555-0569 | **Congressional District:** | 14 |
| **Comments:** | | | |
| **Project Type:** | GROUND | **Solicitation / Funding Source:** | 2009 Crew Health NNJ09ZSA002N |
| **Start Date:** | 07/30/2010 | **End Date:** | 07/31/2016 |
| **No. of Post Docs:** | 0 | **No. of PhD Degrees:** | 0 |
| **No. of PhD Candidates:** | 0 | **No. of Master' Degrees:** | 0 |
| **No. of Master's Candidates:** | 0 | **No. of Bachelor's Degrees:** | 0 |
| **No. of Bachelor's Candidates:** | 0 | **Monitoring Center:** | NASA JSC |
| **Contact Monitor:** | Loerch, Linda | **Contact Phone:** | |
| **Contact Email:** | linda.loerch-1@nasa.gov | | |
| **Flight Program:** | | | |
| **Flight Assignment:** | NOTE: Risk/Gap changes per IRP Rev E (Ed., 3/25/14)<br>NOTE: Extended to 7/31/2016 per PI and NSSC information (Ed., Aug 2015)<br>NOTE: Extended to 7/29/2015, per NSSC information and L. Loerch/JSC (Ed., 8/26/13) | | |
| **Key Personnel Changes/Previous PI:** | | | |
| **COI Name (Institution):** | Durham, William Ph.D. ( University of Texas Medical Branch )<br>Sheffield-Moore, Melinda Ph.D. ( University of Texas Medical Branch )<br>Dillon, Edgar Ph.D. ( University of Texas Medical Branch ) | | |
| **Grant/Contract No.:** | NNX10AP86G | | |
| **Performance Goal No.:** | | | |
| **Performance Goal Text:** | | | |

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| **Task Description:** | The long-term goal of this proposal was to determine the therapeutic efficacy of testosterone at preserving lean muscle mass, muscle strength, and bone mineral density in healthy humans during spaceflight. We proposed to examine the interactive or additive effects of the combination of testosterone and exercise on lean body mass (LBM), muscle strength, and bone health. Our general hypothesis is that the maintenance of normal physiologic levels of testosterone during spaceflight will protect against the functional loss of muscle and bone, and will maximize the efficacy of existing resistance exercise protocols at preventing or reversing functional impairments that occur during bed rest.<br>To achieve these goals we tested the following specific hypotheses before, during, and after 70 days of bed rest:<br><br>1: Cycled testosterone replacement (weekly testosterone injections for 2 weeks, followed by 2 weeks off, etc.) in conjunction with exercise will have an additive effect in preventing loss of muscle mass and muscle strength in men representative of the astronaut population compared to exercise with placebo testosterone.<br><br>2: Cycled testosterone replacement (weekly testosterone injections for 2 weeks, followed by 2 weeks off, etc.) in conjunction with exercise will have an additive effect in preventing loss of bone mass and alterations in markers of bone metabolism in men representative of the astronaut population compared to exercise with placebo testosterone.<br><br>To address these hypotheses we investigated the following specific aims before, during, and after 70 days of bed rest:<br><br>Aim 1: To determine the effect of cycled testosterone replacement in conjunction with resistance exercise during bed rest on muscle mass, muscle strength, and fatigue in men aged 24-55 years.<br><br>Aim 2: To determine the effect of cycled testosterone replacement in conjunction with resistance exercise during bed rest on markers of bone metabolism and bone mass in men aged 24-55 years. |
| **Rationale for HRP Directed Research:** | |
| **Research Impact/Earth Benefits:** | Results from this study will further elucidate the role of testosterone in the maintenance of skeletal muscle and bone during long term bed rest and spaceflight. The benefits to life on Earth are extensive.<br>This study demonstrates that testosterone treatment in conjunction with exercise countermeasures is corrective against head down bed rest (HDBR) induced changes in body composition of healthy men. Exercise countermeasures were protective against HDBR induced declines in LBM and strength. However, the addition of low dose intermittent testosterone treatment was necessary to promote increases in LBM and protect against increases in fat mass. Furthermore, changes in leg LBM correlated directly with changes in lower body strength. Understanding the unique synergy between exercise dosing and testosterone supplementation could have important implications for both clinical outcomes and spaceflight operations. |
| **Task Progress:** | This study has been completed and all main outcome measures have been analyzed. Manuscripts are in development and will be submitted for peer-review and publication.<br>The following main outcomes occurred with the addition of testosterone countermeasure to exercise:<br><br>- Did not negatively alter hormonal or lipid profiles.<br><br>- Increased lean body mass compared to Control and Exercise plus placebo.<br><br>- Prevented an increase in fat mass that occurred in Control and Exercise plus placebo.<br><br>- Prevented loss in calf strength compared to Control and Exercise plus placebo.<br><br>Additionally, Exercise with or without Testosterone:<br><br>- Blunted declines in strength compared to Control.<br><br>- Prevented late onset declines in pelvic bone density observed in Control but had no discernible effects on bone mass in other regions. |
| **Bibliography Type:** | Description: (Last Updated: 01/11/2021) |
| **Articles in Peer-reviewed Journals** | Scott JM, Martin D, Ploutz-Snyder R, Downs M, Dillon EL, Sheffield-Moore M, Urban RJ, Ploutz-Snyder LL. "Efficacy of exercise and testosterone to mitigate atrophic cardiovascular remodeling." Med Sci Sports Exerc. 2018 Sep;50(9):1940-9. https://doi.org/10.1249/MSS.0000000000001619 ; PubMed PMID: 29570536; PubMed Central PMCID: PMC6095799 , Sep-2018 |
| **Articles in Peer-reviewed Journals** | Dillon EL, Sheffield-Moore M, Durham WJ, Ploutz-Snyder LL, Ryder JW, Danesi CP, Randolph KM, Gilkison CR, Urban RJ. "Efficacy of testosterone plus NASA exercise countermeasures during head-down bed rest." Med Sci Sports Exerc. 2018 Sep;50(9):1929-39. https://doi.org/10.1249/MSS.0000000000001616 ; PubMed PMID: 29924745; PubMed Central PMCID: PMC6095739 , Sep-2018 |
| **Articles in Peer-reviewed Journals** | Dillon EL, Soman KV, Wiktorowicz JE, Sur R, Jupiter D, Danesi CP, Randolph KM, Gilkison CR, Durham WJ, Urban RJ, Sheffield-Moore M. "Proteomic investigation of human skeletal muscle before and after 70 days of head down bed rest with or without exercise and testosterone countermeasures." PLoS One. 2019 Jun 13;14(6):e0217690. eCollection 2019. https://doi.org/10.1371/journal.pone.0217690 ; PubMed PMID: 31194764; PubMed Central PMCID: PMC6563988 , Jun-2019 |
| **Articles in Peer-reviewed Journals** | Downs ME, Scott JM, Ploutz-Snyder LL, Ploutz-Snyder R, Goetchius E, Buxton RE, Danesi CP, Randolph KM, Urban RJ, Sheffield-Moore M, Dillon EL. "Exercise and testosterone countermeasures to mitigate metabolic changes during bed rest." Life Sci Space Res. 2020 Aug;26:97-104. https://doi.org/10.1016/j.lssr.2020.03.008 ; PMID: 32718692; PMCID: PMC7387751 , Aug-2020 |