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## 2013 Nutrition Risk Standing Review Panel

### Research Plan Review for: *The Risk Factor of Inadequate Nutrition*

### Final Report

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#### I. Executive Summary and Overall Evaluation

The 2013 Nutrition Risk Standing Review Panel (from here on referred to as the SRP) was impressed by the degree of progress the nutrition discipline has made with the research plan presented since the 2012 Nutrition Risk SRP WebEx/teleconference. The scientists and staff associated with the nutrition discipline have, in addition, continued their impressive publication track record. Specifically the SRP found that the novel and important progress in the ocular health research area (Gap N7.3) represents an important advance in understanding the etiology and potential countermeasures for this condition and thinks that the work will not only be valuable for vision, but may have implications for cardiovascular health, as well. The SRP also considered the bone countermeasure data presented a potentially valuable tool for investigating bone metabolism under the unique conditions of space travel, specifically the innovation of variable use of stable Ca isotopes for bone synthesis and equal contribution for bone to investigate bone metabolism, as well as, the impact of the advanced resistive exercise device (ARED) on body composition during spaceflight. Finally, the SRP considers the planned Integrated Nutrition task to be an important and necessary strategic part of the research plan.

The SRP is concerned that the risks observed in previous research on Low Earth Orbit (LEO) may not capture all the risks of longer duration flight beyond LEO. In particular, the SRP believes that there may be a much greater likelihood of an intensified chronic inflammatory response compared to the very minimal evidence seen to date and that modest effects seen in LEO, such as the reduction in appetite, may not predict an absence in longer duration flight out of LEO. The added complications of longer duration flight, greater bio-behavioral stress, radiation exposure, poorer communication, and inability to respond to unforeseen exigencies may create different risks. Thus, preparation for potential anticipated problems on long duration missions should be considered now while countermeasures can be developed even in the absence of sure knowledge as to their likelihood.

Overall, the SRP thinks that all the Gaps presently in the research plan are appropriate and relevant, but there are a few missing Gaps that will help expand the research plan.

#### II. Critique of Gaps and Tasks for the Risk Factor of Inadequate Nutrition

1. *Have the proper Gaps been identified to address the Risk?*
    - a. *Are all the Gaps relevant?*
    - b. *Are any Gaps missing?*
  2. *Have the appropriate targets for closure for the Gaps been identified?*
    - a. *Are the interim stages appropriate to close the Gaps?*
  3. *Have the proper Tasks been identified to fill the Gaps?*
    - a. *Are the Tasks relevant?*
    - b. *Are any Tasks missing?*
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4. *If a Gap has been closed, does the Rationale for Gap Closure provide the appropriate evidence to support the closure?*

**SUGGESTED NEW GAPS:**

1. Nutritional consequences of longer and more intense radiation exposure should be studied, in particular, immune function and inflammation and their interaction with nutritional systems.

**Suggested Tasks:**

- a. Analogs to look at inflammation, radiation, immune function, muscle decrements and effects on nutritional systems.
  - b. Work in LEO is informative, but prolonged spaceflight/long duration missions will have some very different features (communication delay, no service, greater radiation, greater bio-behavioral stress exposure, greater likelihood of inflammation). Plan some way of estimating this and develop a countermeasure now.
  - c. Anorexia study: Could this be part of inflammation or due to some other factor?
  - d. Consider the potential of high ambient CO<sub>2</sub> levels to produce a mild chronic respiratory acidosis.
  - e. Explore effects on immune function. The capacity to respond to vaccination with a robust anamnestic response, for example, represents an experimental paradigm that is potentially amenable to study in small numbers of astronauts. The immunologic and inflammatory correlates of fatty acid composition in plasma and erythrocyte membranes and the effects of dietary fatty acid modulation may also be worth exploring.
  - f. Explore effects on reproductive hormones (e.g., testosterone in men, estrogen and progesterone in women). Effects on gonadal steroids have not been fully characterized in LEO and there is a potential for greater effects in the setting of longer and more intense radiation exposure and associated inflammation.
2. Is the decrease of food intake adequately characterized?

**Suggested Tasks:**

- a. Without a known cause, the spaceflight associated-weight loss that is seen could be a consequence of LEO which can be countered by resistance exercise.
  - b. Explore possible exacerbation of anorexia by inflammation (or inflammation induced anorexia) and/or motion disturbances, microgravity.
  - c. Characterize the nature of reduced food intake in anticipation that it may be enhanced by spaceflight beyond LEO.
3. The effects of elevated pCO<sub>2</sub> levels in space vehicles should be explored as to their impact on acid base homeostasis and subsequent impact on muscle and bone metabolism.

**Suggested Tasks:**

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- a. Does chronic respiratory acidosis really occur (animal and human study to test)?
  - b. If so, what are the effects on muscle and bone catabolism and response to alteration in pCO<sub>2</sub> or alkalization?

## **Gaps and Tasks:**

### **N3.1: Determine the macronutrient requirements for spaceflight.**

- The SRP thinks this Gap is relevant and appropriate.

#### **Tasks:**

- Evaluate Energy Expenditure During Long Duration (>3mo) Missions – PI: TBD
- Nutritional Status Assessment: SMO-016E – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

### **N3.2: Determine the micronutrient requirements for spaceflight.**

- The SRP thinks this Gap is relevant and appropriate.

#### **Tasks:**

- Nutritional Status Assessment: SMO-016E – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Concordia: D, Immune and Metabolism – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Issues Related to Systemic Inflammatory Response – Planned Task
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Lab Analysis Point-of-Care Device Evaluation and Downselect – PI: TBD

### **N3.3: We need to determine changes in nutritional status due to spaceflight.**

- The SRP thinks this Gap is relevant and appropriate.

#### **Task:**

- Nutritional Status Assessment: SMO-016E – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

### **N4: Does mission architecture and/or available countermeasures impact nutritional status of crewmembers during spaceflight?**

- The SRP thinks this Gap is relevant and appropriate.

#### **Tasks:**

- Nutrition/Pharm Interactions – Planned Task
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

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**N6: What impact does the spaceflight environment have on oxidative damage?**

- The SRP thinks this Gap is relevant and appropriate.

Tasks:

- Characterization of Oxidative Damage During a Saturation Dive – Task Completed
- Nutritional Status Assessment: SMO-016E – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Oxidative Damage Study – Planned Task
- Evaluation of the combined effects of gamma radiation and high dietary iron on oxidative damage and antioxidant status in rats – Task Completed
- Evaluation of the effect of short duration spaceflight on hepatic nutrition, oxidative damage, and colon microflora – Task Completed
- Effects of high dietary heme iron and radiation on cardiovascular function – PI: Christian Westby, Ph.D. – Universities Space Research Association
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

**N7.1: We need to identify the most important nutritional factors for musculoskeletal health.**

- The SRP thinks this Gap is relevant and appropriate.

Tasks:

- Nutritional Status Assessment: SMO-016E – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Evaluate n-3 Fatty Acids as a Countermeasure for Bone Loss – Planned Task
- Loading-Independent Factors that Contribute to Spaceflight-Induced Muscle Loss – Planned Task
- Role of Energy Balance in Maintaining Muscle and Bone – Planned Task
- Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Spaceflight and Recovery (Pro-K) – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Bone Epidemiologic Analysis II – Planned Task
- Nutritional countermeasures to ameliorate losses in muscle mass and function – Completed Task

**N7.2: We need to identify the most important nutritional factors for cardiovascular health.**

- The SRP thinks this Gap is relevant and appropriate.
- This work will be very beneficial, especially with the one-carbon metabolism issue.

Tasks:

- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

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- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
  - Effects of high dietary heme iron and radiation on cardiovascular function – PI: Christian Westby, Ph.D. – Universities Space Research Association

**N7.3: We need to identify the most important nutritional factors for ocular health.**

- The SRP thinks this Gap is relevant and appropriate.
- ***Suggested new task:*** To identify the role of elevated ambient CO<sub>2</sub> in acidosis and in producing cerebral vasodilation with potential impact on ocular disturbances.

***Tasks:***

- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Risk of visual impairment and intracranial hypertension after spaceflight: Evaluation of the role of polymorphism of enzymes involved in one-carbon metabolism – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

**N7.4: We need to identify the most important nutritional factors for behavior and performance.**

- The SRP thinks this Gap is relevant and appropriate, but that it should be emphasized more and if not already, better integrated with the Behavioral Health and Performance Element.

***Tasks:***

- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

**N13: Can renal stone risk be decreased using nutritional countermeasures?**

- The SRP thinks this Gap is relevant and appropriate.

***Tasks:***

- Data Mining for Incidence of Renal Stone Formation Following Spaceflight – Completed Task
- Renal Stone Risk during Spaceflight: Assessment and Countermeasure Validation (Renal Stone - DSO 633) – Completed Task
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Dietary Intake Can Predict and Protect Against Changes in Bone Metabolism During Spaceflight and Recovery (Pro-K) – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

**N15: We need to identify the most important nutritional factors for oxidative damage during spaceflight.**

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- The SRP thinks this Gap is relevant and appropriate.
  - The SRP thinks that the nutrition discipline should coordinate with the Space Radiation Program Element on this research.
  - The SRP did not think the nutrition discipline was described with enough specificity on how they planned to measure oxidative damage, which may be developed in conjunction with the Space Radiation Program Element.

Tasks:

- Characterization of Oxidative Damage During a Saturation Dive – Task Completed
- Oxidative Damage Study – Planned Task
- Investigation to Determine Countermeasures to Lower Body Iron Stores to Mitigate O<sub>2</sub>/Radiation Risks – Planned Task
- Evaluation of the combined effects of gamma radiation and high dietary iron on oxidative damage and antioxidant status in rats – Task Completed
- Evaluation of the effect of short duration spaceflight on hepatic nutrition, oxidative damage, and colon microflora – Task Completed
- Space Biochemistry Profile – PI: Scott Smith, Ph.D. – NASA Johnson Space Center
- Novel Double-Hit Mouse Model to Investigate Oxidative Damage from Radiation/Hyperoxia Related to Space Exploration - Evaluation of Dietary Flaxseed as Countermeasure – PI: Melpo Christofidou-Solomidou, Ph.D. – University of Pennsylvania
- Issues Related to Systemic Inflammatory Response – Planned Task
- Evaluate n-3 Fatty Acids as a Countermeasure for Bone Loss – Planned Task
- Integrated Nutrition: Development and Provision of Functional Foods to Mitigate Bone Loss on ISS Missions – PI: Scott Smith, Ph.D. – NASA Johnson Space Center

**M23: Do factors in addition to unloading contribute to muscle atrophy during spaceflight (e.g., radiation, inflammation, hydration, redox balance, energy balance)?**

- The SRP thinks this Gap is relevant and appropriate and re-emphasizes the importance of looking at the pCO<sub>2</sub> levels, systemic respiratory acidosis, and their effects on all of these factors.

Tasks:

- Gender Effects on Muscle – Planned Task
- Role of Energy Balance in Maintaining Muscle and Bone – Planned Task
- Loading-Independent Factors that Contribute to Spaceflight-Induced Muscle Loss – Planned Task
- Redox Modulation of Skeletal Muscle Function in Microgravity – Completed Task

**N2: What is the adequate dose range of vitamin D supplementation? (This Gap is now closed)**

- The SRP thinks the rationale for closing this Gap is appropriate.

Tasks:

- Efficacy of Vitamin D Supplementation in an Antarctic Ground Analog of Spaceflight –

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Completed Task

- Vitamin D Supplement Evaluation of Dosing Requirements – Completed Task
- Vitamin D Supplementation in an Antarctic Ground Analog of Spaceflight: Study of Supplementation Protocol and Relationship to Immune System Function – Completed Task

### **III. Discussion on the strengths and weaknesses of the IRP and identify remedies for the weaknesses, including answering these questions:**

Is the Risk addressed in a comprehensive manner?

- The SRP thinks the risk is addressed in a comprehensive manner and that the nutrition discipline is doing a good job at trying to alleviate the Risk.

Are there obvious areas of potential integration across disciplines that are not addressed?

- The SRP thinks that the integration between the nutrition discipline and other areas of the Human Research Program should be more clearly described. Specifically those with the Space Radiation Program Element and the Behavioral Health and Performance Element. If these interactions are occurring, they are not clearly evident to the SRP.

### **IV. Evaluation of the progress in the IRP since the 2012 SRP meeting**

- The SRP is very impressed with the progress made in the IRP since the 2012 SRP meeting.

### **V. Additional Comments**

- The nutrition discipline may want to start looking at radiation data from acute medical treatments and possibly establish collaborations.
- The SRP suggests broadening the carotenoid contents in food.
- The SRP does not think there are enough body mass measures taken, only dual-energy x-ray absorptiometry (DXA). The SRP thinks you need magnetic resonance imaging (MRI) of the abdomen for visceral adipose tissue and magnetic resonance spectroscopy (MRS) for liver and muscle fat.

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## **VI. 2013 Nutrition Risk SRP Research Plan Review: Statement of Task for the Risk Factor of Inadequate Nutrition**

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The 2013 Nutrition Risk Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist. The purpose of the SRP is to review the Human Health Countermeasures (HHC) Element's section of the current version of the HRP's Integrated Research Plan which is located on the Human Research Roadmap (HRR) website (<http://humanresearchroadmap.nasa.gov/>). Your report will be provided to the HRP Chief Scientist and will also be made available on the HRR website.

### **The 2013 Nutrition Risk SRP is charged (to the fullest extent practicable) to:**

1. Based on the information provided in the current version of the HRP's IRP, evaluate the ability of the IRP to satisfactorily address the Risk by answering the following questions:
  - A. Have the proper Gaps been identified to address the Risk?
    - i) Are all the Gaps relevant?
    - ii) Are any Gaps missing?
  - B. Have the appropriate targets for closure for the Gaps been identified?
    - i) Are the interim stages appropriate to close the Gaps?
  - C. Have the proper Tasks been identified to fill the Gaps?
    - i) Are the Tasks relevant?
    - ii) Are any Tasks missing?
  - D. If a Gap has been closed, does the Rationale for Gap Closure provide the appropriate evidence to support the closure?
2. Identify the strengths and weaknesses of the IRP, *and* identify remedies for the weaknesses, including answering these questions:
  - A. Is the Risk addressed in a comprehensive manner?
  - B. Are there obvious areas of potential integration across HRP disciplines that are not addressed?
3. Please evaluate the progress in the IRP since your 2012 SRP meeting.
4. Please comment on any important issues that are not covered in #1, #2, or #3 above. If addendum questions are provided below, please address each of the questions as fully as possible.



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### **Additional Information Regarding This Review:**

1. Expect to receive review materials at least four weeks prior to the meeting.
2. Participate in a 2013 Nutrition Risk SRP conference call to discuss any issues, concerns, and expectations of the review process approximately three weeks prior to the meeting.
  - A. Discuss the 2013 Nutrition Risk SRP Statement of Task and address questions about the SRP process.
3. Attend the 2013 Nutrition Risk SRP meeting at NASA JSC on November 20 - 21, 2013.
  - A. Attend Element or Project presentations, question and answer session, and briefings.
  - B. Prepare a draft report that addresses each of the evaluation criteria listed in the panel charge. Debrief the HRP Chief Scientist and a representative from the HHC Element on the salient points that will be included in the final report and specifically the items in the panel charge.
4. Prepare a draft final report (within one month of the site visit debrief) that contains a detailed evaluation of the current IRP specifically addressing items #1, #2, #3, and #4 of the SRP charge. The draft final report will be sent to the HRP Chief Scientist and he will forward it to the appropriate Element for their review. The HHC Element and the HRP Chief Scientist will have 2 business days to review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP. If any misunderstandings or errors of fact are identified, the SRP will have 10 business days to address them and finalize the 2013 SRP Final Report. The 2013 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the HHC Element that sponsors the nutrition discipline and also made available to the other HRP Elements. The 2013 SRP Final Report will be made available on the HRR website (<http://humanresearchroadmap.nasa.gov/>).

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## VII. 2013 Nutrition Risk Standing Review Panel Roster

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### **Panel Chair:**

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