ENDOCRINE SOCIETY
Hormone Science to Health

May 12, 2015

Gary H. Gibbons, MD
Director, National Heart, Lung, and Blood Institute
National Institutes of Health
Building 31, Room 5A52
31 Center Drive MSC 2486
Bethesda, MD 20892

Dear Dr. Gibbons,

The Endocrine Society appreciates the opportunity to provide comments on the NHLBI Strategic Visioning Process. Founded in 1916, the Endocrine Society is the world's oldest, largest, and most active organization dedicated to research on hormones and the clinical practice of endocrinology. The Society's membership of over 18,000 includes basic researchers, clinical researchers, and clinicians in practice. Our members conduct research on areas of central importance to the NHLBI mission, including obesity, metabolism, circadian cycles and sleep disorders, hypertension, and others. Our members have identified several compelling questions that we believe should be incorporated in the NHLBI Strategic Vision:

- What is the hormonal basis of increased atherosclerotic cardiovascular disease (ASCVD) in post-menopausal women?
- What is the genetic basis of the relationship between placental trophoblasts and angiogenesis, and how does the gravid uterus signal maternal diseases such as gestational hypertension?
- Can we target stress reduction to decrease the burden of chronic metabolic and cardiovascular disease?

Please see the appendix to this e-mail for a more detailed description of each question. We look forward to contributing to the NHLBI strategic goals of promoting human health, reducing human disease, advancing translational research, and developing the biomedical workforce and resources. Thank you for considering the Endocrine Society's comments. If we can be of any assistance in your efforts, please do not hesitate to contact Dr. Joseph Laakso, Associate Director of Science Policy at jlaakso@endocrine.org.

Sincerely,

Lisa H. Fish MD

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Hormonal Influences on Atherosclerotic Cardiovascular Disease (ASCVD)

Provide a title for your CQ or CC idea.

Hormonal influences on atherosclerotic cardiovascular disease (ASCVD)

Describe your CQ or CC (in no more than 300 words).

Cardiovascular diseases are the leading cause of morbidity and mortality for both men and women worldwide. It has been established that post-menopausal women have decreased protection from ASCVD relative to premenopausal women and men. However, the hormonal basis of protection (or lack thereof) is not clear.

Provide the Strategic Goal number to which your CQ or CC is aligned.

Goal 2: Reduce Human Disease

Provide 1-3 keywords describing your CQ or CC.

Hormone, cardiovascular, menopause

List the idea as a CQ or a CC.

What is the hormonal basis of increased atherosclerotic cardiovascular disease (ASCVD) in post-menopausal women?

Describe the impact of answering this CQ or CC.

By addressing this question, we will gain a greater understanding of hormone-based risk factors for ASCVD in women and men. Beyond expanding our fundamental knowledge of how hormones interact with cardiovascular systems, we could develop or improve therapeutic strategies for addressing risk factors for cardiovascular disease.

Describe the feasibility and challenges of answering this CQ or CC (focusing on the next decade).

Addressing this question is feasible and could be most effectively addressed through strategic initiatives sponsored by the institute. It will require a systematic approach to investigating differences in hormonal status between pre and post-menopausal women, as well as comparing them to male hormonal status. At the level of basic research, progress in this area may be slowed because researchers are not currently required to balance the studies of males and females in preclinical research involving animal models.

Physiological and Pathophysiological Angiogenesis and Placental Function in At Risk Pregnancies

Provide a title for your CQ or CC idea.

Examining the interface between physiological and pathophysiological angiogenesis and placental function in *at risk* pregnancies.

Describe your CQ or CC (in no more than 300 words).

Abnormal placental function, characterized by retarded nutrient and oxygen exchange, and abnormal hormone and angiogenic growth factor production, is linked to a number of diseases that have a strong impact on maternal and fetal health. Perhaps of highest impact is pre-eclampsia, a disease affecting 5-8% of pregnant women worldwide. Moreover, issues related to a suboptimal intrauterine environment leading to growth retardation of the developing fetus are likely linked to adult disease, making this biomedical issue very far reaching. This problem is particularly timely, given the recent initiation of the Human Placenta Project at the NICHD, and adding this compelling question to the NHLBI Strategic Vision will create important synergies.

Provide the Strategic Goal number to which your CQ or CC is aligned.

Goal 1: Promote Human Health

Goal 2: Reduce Human Disease

Goal 3: Advance translational research

Provide 1-3 keywords describing your CQ or CC.

Placenta, angiogenesis, maternal health

List the idea as a CQ or a CC.

What is the genetic basis of the relationship between placental trophoblasts and angiogenesis?

How does the gravid uterus signal maternal diseases such as gestational hypertension?

Describe the impact of answering this CQ or CC.

By addressing this question, NHLBI and partner institutes can work toward clarifying how abnormal placental function leads to maternal disease. Perhaps more importantly, working to define potential nutritional strategies to optimize blood vessel growth and function in the developing placenta may lead to improvement in preventing and treating diseases such as pre-eclampsia.

Describe the feasibility and challenges of answering this CQ or CC (focusing on the next decade).

In vivo models of gestational hypertension will help to improve our understanding of how the gravid uterus can control maternal blood pressure during pregnancy, including the impact on renal and hepatic function of high blood pressure. Animal models that have a well-defined genetic basis will be particularly useful. Coordination of scientific fields in

reproduction and hypertension should provide synergy for addressing these questions. Efficient progress will require collaboration and buy-in from NICHD and perhaps other institutes, and this is an excellent opportunity to build on the overlapping strengths within both institutes.

Chronic Stress and Cardiovascular/Metabolic Disease

Provide a title for your CQ or CC idea.

Chronic stress and cardiovascular/metabolic disease

Describe your CQ or CC (in no more than 300 words).

Chronic stress is a risk factor for obesity, cardiovascular disease, atherosclerosis, and stroke. Glucocorticoid hormones are elevated chronically in stressed conditions and are thought to contribute to the pathogenesis of metabolic and cardiovascular disease. Despite strong evidence for this, non-pharmacologic therapies to reduce stress are not currently part of standard care for the prevention or treatment of metabolic and cardiovascular disease, and no pharmacologic therapies exist at present to directly target stress systems for this indication.

Provide the Strategic Goal number to which your CQ or CC is aligned.

Goal 2: Reduce Human Disease

Goal 3: Advance translational research

Provide 1-3 keywords describing your CQ or CC.

Hormone, stress, metabolic, cardiovascular

List the idea as a CQ or a CC.

Can we target stress reduction to decrease the burden of chronic metabolic and cardiovascular disease?

Describe the impact of answering this CQ or CC.

Understanding how stress contributes to cardiovascular and metabolic disease could lead to additional therapies targeting stress reduction for their prevention. The long-term impact of studies to establish and reduce the negative impact of stress on health could include better outcomes for stress reduction programs at work and strategies to reduce stress at home.

Describe the feasibility and challenges of answering this CQ or CC (focusing on the next decade).

Clinical trials to evaluate the efficacy of non-pharmacologic therapies targeting stress reduction are already feasible including such interventions as exercise, improved sleep, mindfulness, and social interaction. Some of these have been evaluated on a small scale,

but future clinical trials should include long-term follow up and be sufficiently populated for their outcomes to influence patient care. Pharmacologic therapies targeting the stress system have not yet emerged as options for prevention and treatment, and pose a greater challenge. They will require investigation into the mechanisms of stress effects on chronic disease as well as intelligent drug design to minimize systemic side effects.