

**Title of proposed program:** Enhanced Physical and Mental Health by Decreasing the Burden of Stress

**Submitting Source:** NIH

**What is the major obstacle/challenge/opportunity that the Common Fund should address? What would the goals of the program be?** The challenge is to identify those individuals most vulnerable to stress, create interventions to enhance resilience and, for those impacted by traumatic stress, reverse the life-long change produced by trauma. The goal is to identify ways to prevent the debilitation of stress-induced effects either by reversing the cumulative response to stress or by enhancing resilience. The opportunities with the highest immediate impact and feasibility are:

- Reverse long term consequences of traumatic stress. Mounting evidence indicates that traumatic stress produces epigenetic changes. Medications and behavioral interventions can be developed to reverse these changes. In the case of early life stress, interventions to mitigate the adverse effects of stress on development can be created.
- Identify vulnerability to stress. Biomarkers of stress can be developed in order to identify those most vulnerable to stress. Genetic susceptibility and early indicators of stress exposure could identify those most likely to suffer the consequences of stress. Preventive measures can then be implemented to reduce long term effects.
- Promote resilience. Enhancement of resilience to stress will prevent the cumulative burden of stress and prevent adverse consequences of unanticipated traumatic events.

**Why is a trans-NIH strategy needed to achieve these goals? What initiatives might form the strategic plan for this topic?** Since stress impacts such a broad spectrum of biological functions, investigating or treating one biological endpoint, i.e. glucocorticoid release, will not ameliorate stress-induced consequences. Stress produces cascading effects such as the effects of hormonal secretions on cognitive function, cardiovascular activity and immune response. Only by integration of multiple measures across the entire organism will the full impact and appropriate interventions be identified. An integrated consortium of investigators must be able to address the multiple inputs, the parallel processing, and diverse central and peripheral responses to stress.

**If a Common Fund program on this topic achieved its objectives, what would be the impact?**

Medications or interventions to mitigate stress would impact across many disease processes and maladaptive behaviors. The consequences of adverse early life experiences, trauma, or stress of chronic disease could be diminished and the burden of accumulated life stress would be reduced. The benefits of a diminished stress response would be reduction of a wide range of diseases initiated or exacerbated by stressors. In addition stress-induced behavioral patterns such as impulsivity, depression, addiction relapse could be ameliorated.