

Investigating the Correlation of Corticotropin-Releasing Factor (CRF) and Cardiovascular Disease

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Introduction

Stress is a common risk factor for both depression and cardiovascular disease. Neural pathways and substrates play a significant role in stress response and may provide clues as to the shared pathophysiology that links depression and cardiovascular disease. The list of neuropeptides implicated in stress-related functions is ever increasing. Of these neuropeptides, Corticotropin Releasing Factor (CRF) has been studied extensively. However, detecting neuronal proteins in human plasma and serum has remained a challenge. Most available assays are not sensitive enough to detect CRF. Here, we developed an ultrasensitive digital immunoassay to quantify CRF in human plasma samples using Single Molecule Array (SiMoA) technology. A pilot study was conducted to observe the correlation between CRF and cardiovascular risk and physiological variabilities.

Activities:

I created a digital immunoassay to quantify CRF in human plasma using Quanterix Homebrew Assay Kits. I used this assay to demonstrate the correlation between CRF concentration and the incidence of cardiovascular disease. The assay was found to be sensitive enough for final use at the capture antibody concentration of 0.5 mg/mL with 40x biotin and 150 picomolar SBG. This assay is ready for use in clinical studies targeting the neuropeptide CRF in depression and associated cardiovascular diseases. This assay helped my research group and I detect CRF in plasma samples of cardiovascular disease patients. We were able to demonstrate the specificity of the anti-CRF antibody as it did not react with another neuropeptide (NPY). In patient samples, which were categorized as lean and obese, a trend was observed indicating high CRF concentrations among obese individuals compared to those with a lean body mass. A trend was observed among BMI and CRF values, for which we plan to assess more patients in the future in order to prove our hypothesis.

Site Information:

National Institutes of Health, National Heart, Lung, and Blood Institute in Bethesda, MD

Supervisor/PI: Dr. J. Philip McCoy, Jr.

The lab that I worked in specializes in flow cytometry and immunological projects. It was an extremely interesting and rewarding experience.







CRF association with obesity and BMI: Plasma samples from an ongoing study on cardiovascular disease were analyzed (n=42) using the CRF Homebrew Assay Kit. CRF was observed to be high among obese patients and a trend correlating BMI and CRF was observed.

Impact:

This assay was used to analyze plasma samples from a female cohort. High CRF values appear to follow a trend with BMI and is associated with amygdala brain activity at borderline significance (when adjusting for age and sex). In addition, CRF concentrations were not found to correlate with vascular inflammation or psychosocial markers. In the future, this assay could have applications in early disease detection and treatment.



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