LAY ABSTRACT

Immunoglobulin A nephropathy (IgAN) is the most common chronic inflammatory disease of the glomerulus of the kidney. IgAN progresses to end stage renal disease in over 30% of patients, requiring hemodialysis and kidney transplant. The pathogenesis of the disease is incompletely understood, and there are no proven treatments.

Signaling lipids, or eicosanoids, are derived from essential fatty acids (EFA). EFA, which include omega-3 and omega-6 fatty acids, are essential because they cannot be synthesized in the body, and must therefore be obtained from the diet. Fish oil, which is an excellent source of omega-3 fatty acids (ω3FA), as well as isolated ω3FA, have proven effects on modulating renal function. Animal studies show that fish oil and ω3FA improve renal function and reverse IgAN, but the success of these fatty acids in human trials has been inconsistent, and the mechanisms of action are not understood. There is preliminary evidence that IgAN patients may have EFA deficiencies.

It is hypothesized that there is a detectable disturbance in the ω3FA status of IgAN patients, and that the presence of this metabolic disturbance plays a causative role in disease development via downstream effects involving eicosanoids in the kidney. Furthermore, it is hypothesized that the disturbed ω3FA and eicosanoid status in these IgAN patients is involved in mediating the effectiveness of treatment with fish oil/ω3FA.

The specific aims of this project are to determine the ω3FA and eicosanoid status of IgAN patients compared with controls, before and after supplementation with fish oil. This project will reveal specific lipid metabolic disturbances in IgAN, and determine non-invasive metabolic biomarkers that will be used to assess metabolic status, detect responsiveness to fish oil, and monitor treatment progress in IgAN. By determining the quantitative changes in ω3FA and eicosanoids that are associated with IgAN and fish oil treatment, the data from this project will also reveal specific metabolic pathways that contribute to the development, progression, and prevention of IgAN. These data will establish the necessary groundwork for obtaining funding for a large NIH trial investigating the metabolic assessment and diagnosis of IgAN, and mechanisms of action leading to disease progression and reversal.