Procalcitonin and Calprotectin for Differentiation of Infection and Disease Flare in Systemic Juvenile Idiopathic Arthritis

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Project Summary/Abstract

A dilemma in pediatric rheumatology is distinguishing inflammatory disease flare and infection; this is particularly difficult in systemic JIA (sJIA). This diagnostic uncertainty leads to delay in appropriate immunosuppressive therapy, which causes significant morbidity and mortality.

The broad objective of this proposal is to develop better diagnostic tools to differentiate between disease flare and infection in sJIA. We will utilize the unique approach of integrating information from two complementary biomarkers, procalcitonin (PCT) and calprotectin (CP). We propose a prospective, observational cohort study to test the hypothesis that PCT and CP, taken together, will distinguish infection from disease flare with a high degree of accuracy in children with sJIA.

In the first aim, we will evaluate PCT and CP levels in patients with established sJIA and symptoms of disease flare/infection. We hypothesize that PCT will be elevated in subjects with infection, and CP will be elevated in subjects with disease flare. In our second aim, we will repeat these biomarkers at a second timepoint, after resolution of disease flare/infection. We hypothesize that the levels of PCT and CP will both return to normal, and that the change (delta) between disease flare/infection and return to baseline will be predictive of infection vs. disease flare. In the third aim, we will assess additional variables that will strengthen our biomarker model. We hypothesize that patient global health assessment and CRP level will improve the prediction of PCT and CP for flare vs. infection.

This study addresses an important unanswered clinical question, and this proposal demonstrates feasibility. As a young investigator, this study will facilitate my development into an independent investigator. This study will also increase CARRA's capacity to perform multi-site translational studies, as this will be the first large scale collection of serum from patients with sJIA during disease flare/infection and return to baseline.

Lay Summary

Juvenile idiopathic arthritis is a common pediatric rheumatologic disease, and the mainstay of treatment is immunosuppressive medication. The most problematic complication of immunosuppression is infection. Distinguishing the inflammation of immune flares with that of infections can be very challenging, particularly in systemic JIA (sJIA), where signs and symptoms are similar.

In this study, we propose using two markers in the blood, procalcitonin and calprotectin, to distinguish disease flare and infection in children with sJIA. In order to achieve this, we will draw blood from children with sJIA at two timepoints, when blood is being drawn anyway as part of standard of care. We anticipate that procalcitonin will be elevated in children with

infection, and calprotectin will be elevated in children with disease flare, so that the combination of these two markers will give very valuable information together. This will allow more accurate and early diagnosis to direct proper treatment.