

## Higher Interleukin Receptor Levels in Mothers of Autistic Children

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### ABSTRACT

*Interleukin (IL) receptor expression has been shown to increase significantly during maternal immune activation. It has been suggested that dysfunctional Interleukin activity is associated with cortical dysplasia and ASD-like behaviors. We measured the concentration of 30 cell receptors, including 5 Interleukin receptors (IL-1R, IL-2R, IL-10R, IL-17R and IL-21R) from mothers with at least one autistic child and neurotypical, gender and age similar controls, using immune-arrays. Of the 5 Interleukin receptors, 4 (IL-1R, IL-10R, IL-17R and IL-21R) had concentrations significantly higher in mothers of autistic children, when compared to neurotypical controls.*

### Keywords

Autism, Autoimmunity, Inflammatory disorders.

### Introduction

The etiology of autism is a complex one, involving genetic and environmental factors, most likely in combination with one another [1]. Dysregulation of the immune system has been shown to be associated with a significant number of autistic individuals [2,3].

Inflammatory abnormalities have also been found frequently in autistic individuals [4-6], and autoimmunity and inflammatory disorders have been found in mothers of autistic individuals [7-9]. Maternal infection has also been linked to increased incidence of autism [10-12], and animal models of ASD have established maternal immune activation with a higher incidence of ASD [13].

Interleukin (IL) receptor expression has been shown to increase significantly during maternal immune activation [14]. Specifically, infection causes expression of IL-6, a potent inflammatory immunokine. IL-6 may cause the Th17 cells to secrete elevated levels of IL-17, and, in turn activates potentially several intracellular pathways such as ERK and MAPK. These pathways have a significant effect on developmental developmental processes [15]. It has been suggested that dysfunctional Th17 cell and IL-17A activity is associated with cortical dysplasia and ASD-like behaviors [16].

We measured the concentration of 30 cell receptors, including 5 Interleukin receptors (IL-1R, IL-2R, IL-10R, IL-17R and IL-21R) from mothers with at least one autistic child and neurotypical, gender and age similar controls, using immune-arrays. Of the 5 Interleukin receptors, 4 (IL-1R, IL-10R, IL-17R and IL-21R) had concentrations significantly higher in mothers of autistic children, when compared to neurotypical controls.

### Materials and Methods

IL receptor levels were measured using immuno-arrays. Plasma from mothers of autistic individuals (n=17; mean age 32.3 years) and controls (n=15 females with no autistic children; mean age 28.2 years) were obtained from the Autism Genetic Resource Exchange (AGRE)\*\*.

Patient consent was obtained from all patients involved in this study. This study was approved by the IRB of the Mensah Research Institute (MRI).

Cellular phosphorylated concentrations were measured using an immuno-array assay referenced below.

### Buffy Coat White Blood Cells

All experimental and control cells were obtained from whole blood using centrifugation and were all treated identically then refrigerated (4 C). Plasma and buffy coat samples were frozen at -70C and used for immunoassay analysis.

## Immuno-array Assays

Immuno-arrays were performed by RayBiotech, Inc, Peachtree Corners, GA. 30092 and described previously [17].

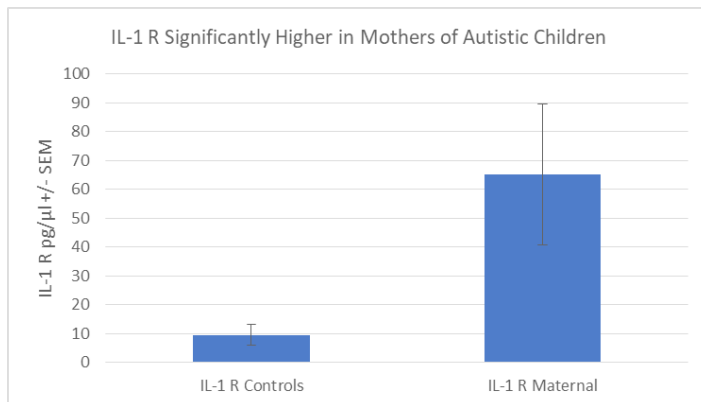
## Statistics

Unpaired t-test and odds ratios with 95% confidence intervals were used for statistical analysis.

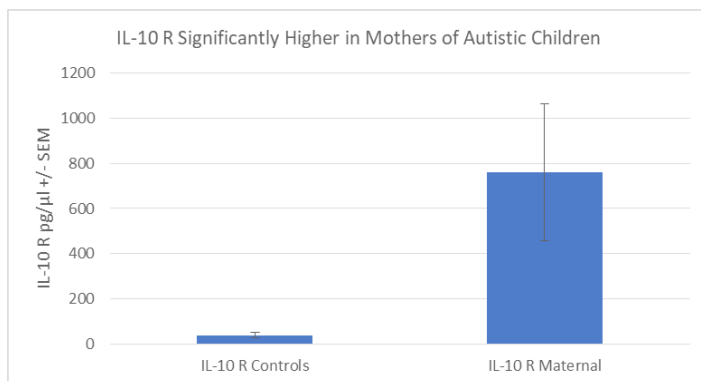
\*\*We gratefully acknowledge that all autism family serums were provided by the Autism Genetic Resource Exchange (AGRE) Consortium and the participating AGRE families. The Autism Genetic Resource Exchange is a program of Cure Autism Now and is supported, in part, by grant MH64547 from the National Institute of Mental Health to Daniel H. Geschwind (PI)

## Results

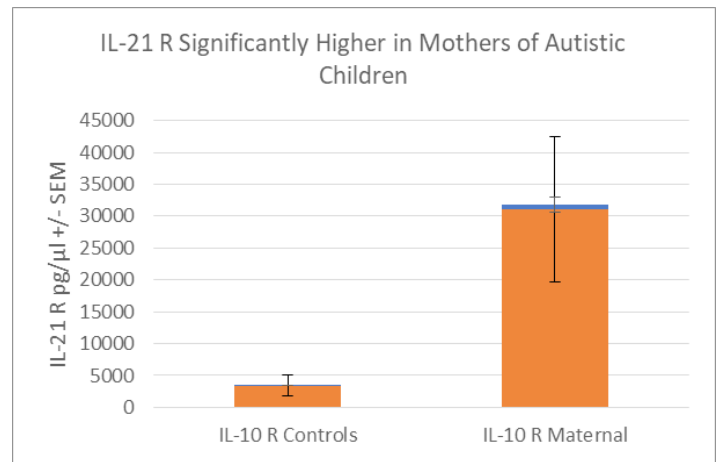
In this study, we measured the concentration of 30 cell receptors, including 5 Interleukin receptors (IL-1R, IL-2R, IL-10R, IL-17R and IL-21R) from 14 mothers of at least one autistic child and 11 neurotypical, gender and age similar controls, using immunoarrays. Of the 5 Interleukin receptors, 4 (IL-1R, IL-10R, IL-17R and IL-21R) had concentrations significantly higher in mothers of autistic children when compared to neurotypical controls (See figures 1-4 below).



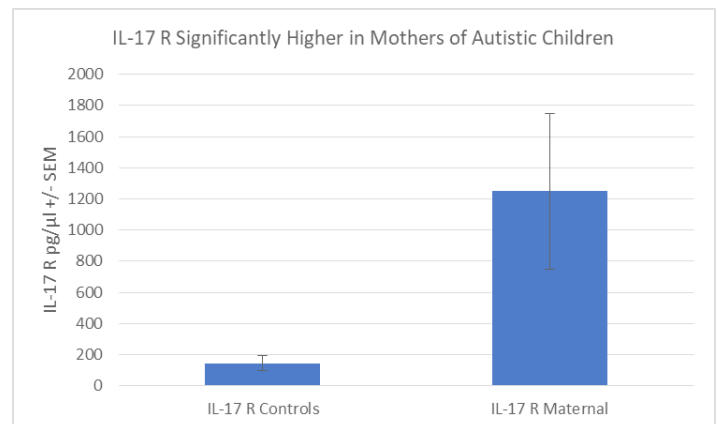
**Figure 1:** Cell IL-1 RI receptor concentration is significantly higher in mothers of autistic children (P=0.045).



**Figure 2:** IL-10Rb is significantly higher in the maternal group (p=0.034).



**Figure 3:** IL-21R is significantly higher in the maternal group (p=0.035).



**Figure 4:** IL-17R is significantly higher in the maternal group (p=0.05).

## Discussion

Our data demonstrates that a select group of Interleukin receptors have higher concentration in mothers of autistic children. To our knowledge this is the first time that these elevated receptors have been reported. We acknowledge that we have tested a small number of patients, and controls, and future studies should include larger population sizes.

Studies have shown that mothers with infections during pregnancy have a higher risk of having an autistic child [18,19]. In animal models, when mothers have an activated immune system, such as a system involved in infection, offspring have a higher incidence of behaviors found in ASD [20,21].

What role do interleukin receptors play in the etiology of autism? IL-17 levels are elevated in autistic individuals [22,23]. In animal models, mothers with activated immune systems have offspring with increased IL-17 levels [24].

Many studies indicate that dysfunctional immune response associated with abnormal pro-inflammatory and anti-inflammatory cytokines, including the interleukins, may be associated with the etiology of ASD [25].

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