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Endoglin Levels are Significantly Higher in Mothers of Autistic Individuals

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ABSTRACT

Endoglin (ENG) is a type I membrane glycoprotein located on cell surfaces and is part of the TGF beta receptor complex. When studying 40 different receptors on the cells of mothers of autistic individuals, parents, and controls, using immune-arrays, we found that endoglin levels were significantly higher in mothers of individuals with autism, and, because of this, we suspect that the endoglin receptor may be associated with the etiology of autism.

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Introduction

Endoglin (ENG) is a type I membrane glycoprotein located on cell surfaces and is part of the TGF beta receptor complex. Endoglin has been shown to interact with high affinity to TGF beta receptor 3 [1,2]. Endoglin itself doesn't bind the TGF beta ligands but is present with the TGF beta receptors when the ligand is bound, indicating an important role for endoglin [3].

Endoglin is involved in modulating a response to the binding of TGF-beta1, TGF-beta3, activin-A, BMP-2, BMP-7 and BMP-9. Beside TGF-beta signaling endoglin may have other functions. It has been postulated that endoglin is involved in the cytoskeletal organization affecting cell morphology and migration [4]. Endoglin has a role in the development of the cardiovascular system and in vascular remodeling. Its expression is regulated during heart development. Experimental mice without the endoglin gene die due to cardiovascular abnormalities [4].

Endoglin is expressed on adventitia of normal brain arteries and on arterialized veins in cerebral AVMs (arteriovenous malformations). The presence of endoglin on fibroblasts in the perivascular stroma suggests an active role for this protein in vascular remodeling in response to increased blood flow and shear stress [5].

When studying 40 different receptors from the cells of mothers of autistic individuals and controls, using immune-arrays, we found that maternal endoglin levels were significantly higher, and because of this we suspect that the endoglin receptor may be associated with the etiology of autism.

Materials and Methods

Subjects

Cellular Endoglin receptor was measured in 26 autistic children and 12 age and gender similar neurotypical, controls.

White blood cells from mothers of /autistic individuals (with diagnosed autism) (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)**. This study was approved by the IRB of the Health Research Institute.

Patient consent was obtained from all patients involved in this study and this study was approved by the IRB of the HRI.

Cellular phosphorylated concentrations were measured using an Immuno-array assay described 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 ELISAs and Immunoassay analysis.

Immuno-array Assays

Immuno-arrays were performed by RayBiotech, Inc, Peachtree Corners, GA. 30092 and described previously (19).

Statistics

Unpaired t-test and odds ratios with 95% confidence intervals were used for statistical analysis. Correlations were performed using Pearson Moment analysis also with 95% confidence intervals for determining statistical significance.

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Results

Endoglin receptor from white blood cells of mothers with children with diagnosed autism (n=16; mean age 32 years) and neurotypical female controls (n=12; mean age 29 years) were measured using innumo-arrays. We found that endoglin receptor was significantly increased in the mothers of autistic children (Figure 1) (p=0.02).

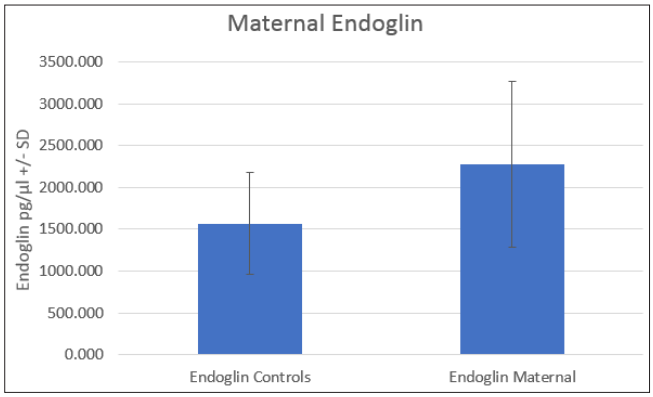

Figure 1: Endoglin levels in mothers of autistic individuals (2274+/- 988 pg/µl) is significantly higher than controls (1569 +/- 602 pg/µl) (p=0.02)

Discussion

Endoglin levels have been found to be elevated in pregnant women who subsequently develop preeclampsia [6].

The role of endoglin plays in angiogenesis and the modulation of TGF beta receptor signaling, which mediates cellular localization, cellular migration, cellular morphology, cell proliferation, cluster formation, etc., makes endoglin an important player in tumor growth and metastasis [7,8].

There may be a role for preeclampsia in the pathogenesis of ASD with low cognitive function [9]. There is also evidence that endoglin levels rise in women with preclampsia [10]. Our data shows an increase in endoglin concentration in mothers of autistic children. This suggests n association between endoglin levels and autism etiology.

Conclusion

Our data shows that mothers of autistic children have increased levels of endoglin. These increased levels may be associated with the etiology of autism.

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