ECRONICON OPEN ACCESS

EC PAEDIATRICS
Research Article

Increased ErbB3 (Erb-B2 Tyrosine Kinase 3) Receptor in Individuals with Autism

AJ Russo[1]*, Albert Mensah[2] and Judith Bowman[2]

[1]*Visiting Assistant Professor of Biology, Drew University, Madison, NJ and Research Director, Mensah Research Institute, Warrenville, Il, USA*

[2]*Mensah Research Institute, Warrenville, Il, USA*

***Corresponding Author**: AJ Russo, Visiting Assistant Professor of Biology, Drew University, Madison, NJ and Research Director, Mensah Research Institute, Warrenville, Il, USA.

Received: September 08, 2021; **Published:** November 18, 2021

Abstract

ErbB3 (Erb-B2 Receptor Tyrosine Kinase 3) also known as human epidermal growth factor receptor 3 (HER3), belongs to the HER receptor family and is a member of the EGFR family of receptor tyrosine kinases is coded by the *ERBB3* (Erb-B2 Receptor Tyrosine Kinase 3) gene. Increased synthesis of HER3 is found in many human cancers and may be associated with failure is certain cancer treatments. Using Immuno-array technology, we found that cells from autistic individuals had significantly higher levels of ERbB. This data supports the hypothesis that the HER family of receptors may be associated with the etiology of autism..

Keywords: *ErbB3 (Erb-B2 Receptor Tyrosine Kinase 3); Human Epidermal Growth Factor Receptor 3 (HER3); Autism*

Introduction

Erb-B2 Receptor Tyrosine Kinase 3 (ErbB3) belongs to the HER receptor family which also includes HER1, HER2/ and HER4. HER3 is unique in that it has none or little tyrosine kinase activity and, in cancer cells along with other kinases, especially of the Akt pathway, it often initiates cancer associated signaling [1].

Increased synthesis of HER3 is found in many human cancers and often means an increased chance of mortality, especially in solid tumors. HER expression may be associated with failure is certain cancer treatments and it may promote metastasis [2].

The human ErbB gene family members are able to bind with one another and form 28 different molecular combinations [3] ERBB2, only binds to ERbB members [4-6] because its binding site is exposed [7]. ERBB3 does not have an enzymatic domain, so it doesn't auto phosphorylate efficiently [8], even though it can be phosphorylated and start signals downstream [9].

It has been suggested that the Neuregulin 1 (NRG1)-ErbB3/ErbB4 pathway may provide a potentially rich set of drugable targets for schizophrenia [10].

Our lab has shown that EGFR levels are increased in individuals with autism (as well as other neurobehavioral disorders). This supports the hypothesis that The HER family of receptors may be associated with the etiology of autism.

Materials and Methods

Subjects

Cellular ErbB3 Receptor was measured in 26 autistic children and 12 age and gender similar neurotypical, controls.

White blood cells from individuals with diagnosed autism (n = 26; 20 male; mean age 10.7 years) and controls (n = 12; 10 male; mean age 9.8 years) were obtained from individuals presenting at the Health Research Institute (HRI)* over a two-year period. All HRI patients in this study were randomly chosen from all patients who volunteered. The autistic individuals were diagnosed using the Autism Diagnostic Interview-Revised - ADI-R and met the DSM-IV criteria.

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 -70°C 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.

Results

Using Immuno-array technology, we found that cells from autistic individuals had significantly higher levels of ERbB3 (3412 +/- 202 pg/µ/) than control cells (2113 +/- 85 pg/µl) (p = 0.022) (Figure 1).

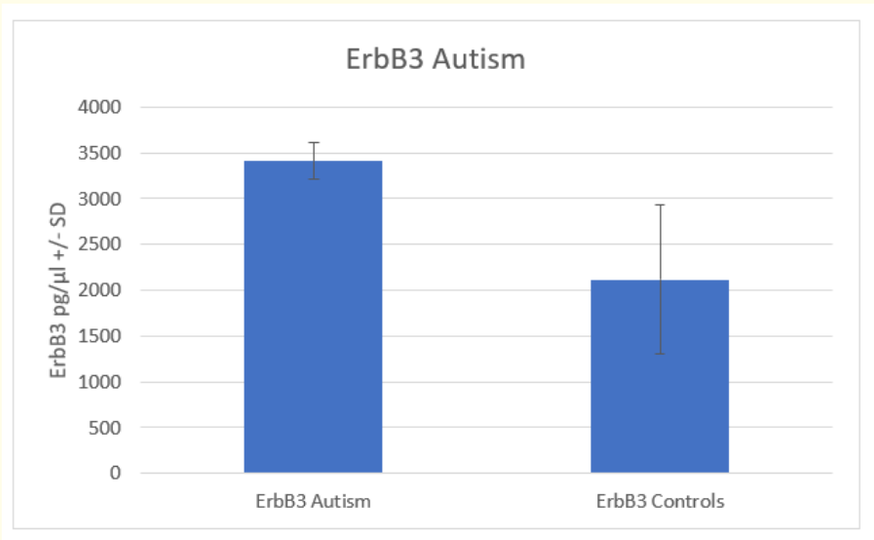

Figure 1: *ErbB3 cellular levels are significantly higher (p = 0.022) in the autistic group.*

*The Health Research Institute is a comprehensive treatment and research center, specializing in the care of individuals with neurological disorders, including autism.

Discussion

There is genetic evidence for a role for ERBB3 in cerebellar development [10]. ERBB3 is also important for the embryogenesis of selected organs and tissues, including the peripheral nervous system (PNS) [11-13].

NRG proteins are expressed in the cerebellum. They bind to ERBB3 [14,15] and may regulate morphology and cell division of reactive astrocytes by signaling downstream pathways [16].

ErbB3 is a member of the epidermal growth factor receptor (EGFR/ERBB) family of receptor tyrosine kinases. Our lab has shown that increased EGFR is associated with decreased Akt and low GABA [17].

We also found that high EGFR is associate with symptom severity in individuals with autism [18]. We hypothesize that low GABA might be associated with symptoms.

Our lab has also found that zinc therapy normalizes EGFR in autistic individuals. This suggests that autistic individuals with high EGFR may benefit from zinc therapy, which will lower EGFR and possibly improve symptoms.

Conclusion

We report a significant relationship between increased ErbB3 Receptor and autism. This supports the hypothesis that ErbB3 levels may be associated with the etiology of autism.

Bibliography

1. Kiavue N., *et al*. "ERBB3 mutations in cancer: biological aspects, prevalence and therapeutics". *Oncogene* 39 (2020): 487-502.
2. Youngseok Lee., *et al*. "Role of erbB3 receptors in cancer therapeutic resistance". *Acta Biochimica et Biophysica Sinica* 46.3 (2014): 190-198.
3. Lemmon MA and Schlessinger J. "Cell signaling by receptor tyrosine kinases". *Cell* 141.7 (2010): 1117-1134.
4. Tzahar E., *et al*. "A hierarchical network of interreceptor interactions determines signal transduction by Neu differentiation factor/neuregulin and epidermal growth factor". *Molecular and Cellular Biology* 16.10 (1996): 5276-5287.
5. Graus-Porta D., *et al*. "ErbB-2, the preferred heterodimerization partner of all ErbB receptors, is a mediator of lateral signaling". *EMBO Journal* 16.7 (1997): 1647-1655.
6. Holbro T., *et al*. "The ErbB2/ErbB3 heterodimer functions as an oncogenic unit: ErbB2 requires ErbB3 to drive breast tumor cell proliferation". *Proceedings of the National Academy of Sciences of the United States of America* 100.15 (2003): 8933-8938.
7. Burgess AW., *et al*. "An Open-and-Shut Case? Recent Insights into the Activation of EGF/ErbB Receptors". *Molecular Cell* 12.3 (2003): 541-552.
8. Tomas A., *et al*. "EGF receptor trafficking: Consequences for signaling and cancer". *Trends in Cell Biology* 24.1 (2014): 26-34.
9. Sathyamurthy A., *et al*. "ERBB3-mediated regulation of Bergmann glia proliferation in cerebellar lamination". *Development* 142.3 (2015): 522-532.
10. Paul J Harrison and Amanda J Law. "Neuregulin 1 and Schizophrenia: Genetics, Gene Expression, and Neurobiology". *Biological Psychiatry* 60.2 (2006): 132-140.

11. Erickson SL., *et al*. "ErbB3 is required for normal cerebellar and cardiac development: a comparison with ErbB2-and heregulin-deficient mice". *Development* 124.24 (1997): 4999-5011.

12. Jackson-Fisher AJ., *et al*. "ErbB3 is required for ductal morphogenesis in the mouse mammary gland". *Breast Cancer Research* 10.6 (2008): R96.

13. Riethmacher D., *et al*. "Severe neuropathies in mice with targeted mutations in the ErbB3 receptor". *Nature* 389.6652 (1997): 725-730.

14. Aono S., *et al*. "Genomic organization and expression pattern of mouse neuroglycan C in the cerebellar development". *Journal of Biological Chemistry* 275.1 (2000): 337-342.

15. Busfield SJ., *et al*. "Characterization of a neuregulin-related gene, Don-1, that is highly expressed in restricted regions of the cerebellum and hippocampus". *Molecular and Cellular Biology* 17.7 (1997): 4007-4014.

16. Chen J., *et al*. "A role for ErbB signaling in the induction of reactive astrogliosis". *Cell Discovery* 3 (2017): 17044.

17. Russo AJ. "Decreased Phosphorylated Protein Kinase B (Akt) in Individuals with Autism Associated with High Epidermal Growth Factor Receptor (EGFR) and Low Gamma-Aminobutyric Acid (GABA)". *Biomarker Insights* 10 (2015): 89-94.

18. Russo AJ. "Increased Epidermal Growth Factor Receptor (EGFR) Associated with Hepatocyte Growth Factor (HGF) and Symptom Severity in Children with Autism Spectrum Disorders (ASDs)". *Journal of Central Nervous System Disease* 6 (2014): 79-83.

19. Russo A., *et al*. "Increased Epidermal Growth Factor Receptor (EGFR) in Children with Autism Normalized with Zinc Therapy". *EC Paediatrics* 8.11 (2019): 17-23.

Volume 10 Issue 12 December 2021