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Cultured lymphocytes from autistic children and non-autistic siblings up-regulate heat shock protein RNA in response to thimerosal challenge

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Abstract

There are reports suggesting that some autistic children are unable to mount an adequate response following exposure to environmental toxins. This potential deficit, coupled with the similarity in clinical presentations of autism and some heavy metal toxicities, has led to the suggestion that heavy metal poisoning might play a role in the etiology of autism in uniquely susceptible individuals. Thimerosal, an anti-microbial preservative previously added routinely to childhood multi-dose vaccines, is composed of 49.6% ethyl mercury. Based on the levels of this toxin that children receive through routine immunization schedules in the first years of life, it has been postulated that thimerosal may be a potential triggering mechanism contributing to autism in susceptible individuals. One potential risk factor in these individuals may be an inability to adequately up-regulate metallothionein (MT) biosynthesis in response to presentation of a heavy metal challenge. To investigate this hypothesis, cultured lymphocytes (obtained from the Autism Genetic Resource Exchange, AGRE) from autistic children and non-autistic siblings were challenged with either 10 μ M ethyl mercury, 150 μ M zinc, or fresh media (control). Following the challenge, total RNA was extracted and used to query “whole genome” DNA microarrays. Cultured lymphocytes challenged with zinc responded with an impressive up-regulation of MT transcripts (at least nine different MTs were over-expressed) while cells challenged with thimerosal responded by up-regulating numerous heat shock protein transcripts, but *not* MTs. Although there were no apparent differences between autistic and non-autistic sibling responses in this very small sampling group, the differences in expression profiles between those cells treated with zinc versus thimerosal were dramatic. Determining cellular response, at the level of gene expression, has important implications for the understanding and treatment of conditions that result from exposure to neurotoxic compounds.

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1. Introduction

Autism is defined as a specific clinical syndrome subject to the following criteria: (a) impairments in social relatedness; (b) impairment of speech and/or language; (c) restricted, repetitive, and stereotyped patterns of behaviors, interests, and activities. The number of families seeking referrals for social services for

autistic children has risen significantly in recent years. In 2004, the CDC issued an “Autism Alert”, announcing that the reported prevalence of autism spectrum disorders had risen to alarming levels, currently affecting approximately one in every 166 American children (Anon., 2006). There is an ongoing debate about whether these increases are related to improved diagnosis or actual increases in prevalence. At the same time, many parents have reported that regression into autism occurs shortly after injection with any number of childhood vaccines—including hepatitis B, DPT, or MMR. Adding to the controversy is the observation that, until recently, many childhood vaccines manufactured as multi-dose vials were preserved with thimerosal, a compound that is ~50% ethyl

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