Subcutaneous injections of aluminum at vaccine adjuvant levels activate innate immune genes in mouse brain that are homologous with biomarkers of autism

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\textbf{Introduction}

Autism spectrum disorders (ASD) is a heterogeneous group of neurodevelopmental disorders characterized by impairment in social interaction, verbal communication and repetitive/stereotypic behaviors \cite{1,2}. A growing body of scientific literature shows that general immune dysfunction including various neuroimmune abnormalities (i.e., abnormal cytokine profiles, neuroinflammation and presence of antibodies against brain proteins) are key pathological biomarkers in ASD patients \cite{3-15}. Other key characteristics of autistic brains include abnormal neural connectivity \cite{16-19}, decreased number of cerebellar Purkinje cells \cite{20-22}, small cell size and increased cell packing density at all ages in the limbic system (the hippocampus, amygdala and entorhinal cortex) suggesting a curtailment in normal neuronal development \cite{20}.

It is also generally acknowledged that ASDs are complex disorders resulting from the combination of genetic and environmental factors with multiple gene–gene and gene–environmental interactions, although there is still uncertainty about the exact proportions of each component \cite{23}. Moreover, the molecular mechanisms of these gene–environmental interactions which result in autistic pathology remain to be discovered. Aluminum (Al) is an environmental toxin with demonstrated negative impact on human health, especially the nervous system, to which humans are regularly exposed. In particular, Al can enter the human body through various sources including food, drinking water, cosmetic products, cooking utensils and pharmaceutical products including antacids and vaccines \cite{24-33}. In addition, Al is also present in many infant formulas \cite{34}. However, compared to dietary Al of which only \textasciitilde{}0.25\% is absorbed into systemic circulation, Al from vaccines may be absorbed at over 50\% efficiency in the short term \cite{35} and at nearly 100\% efficiency long-term \cite{36}. Thus, vaccine-derived Al has a much greater potential to produce toxic effects in the body than...