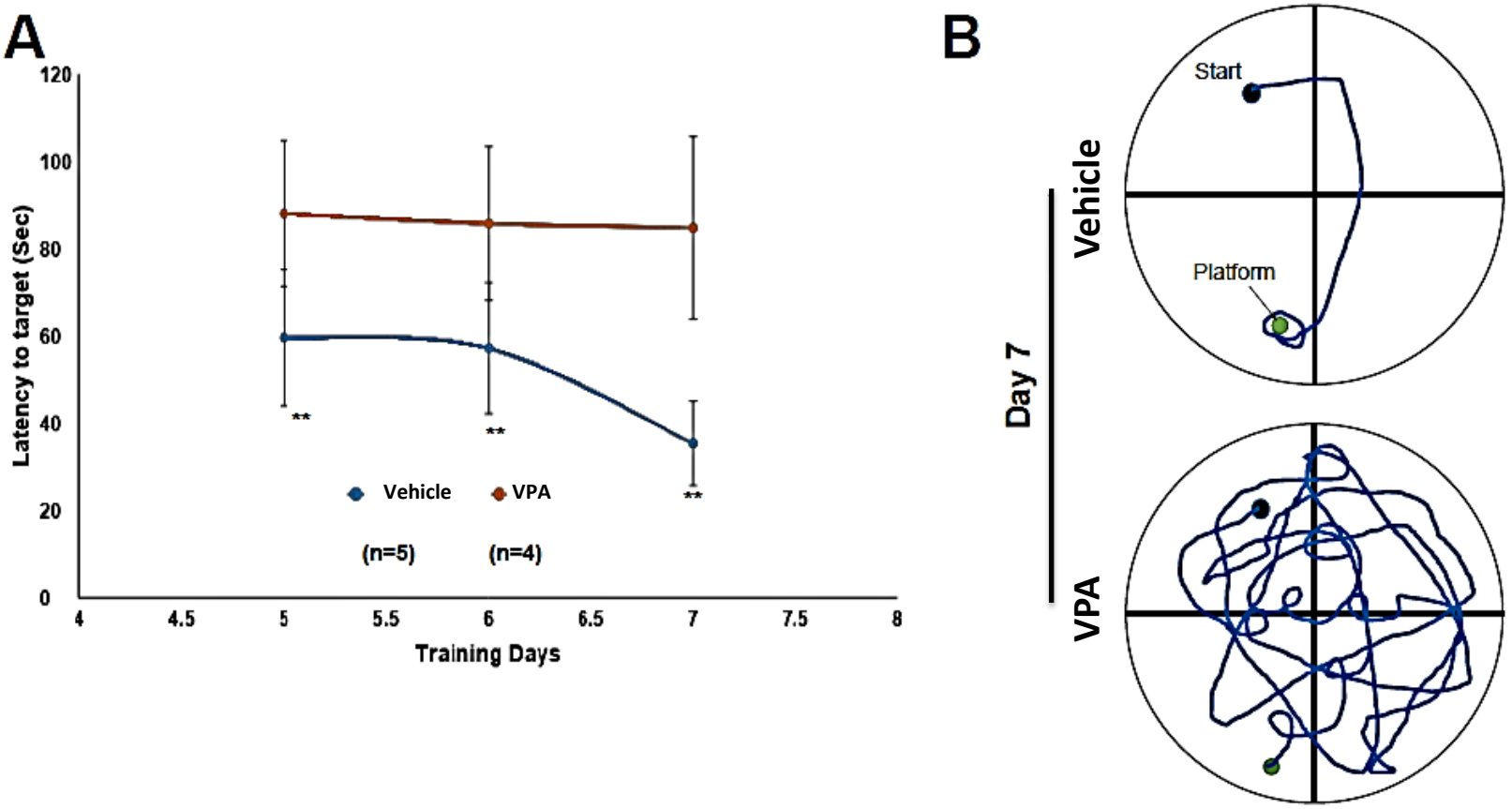


Figure S1: Identification of ASD-Like Abnormalities in VPA-Exposed Mice by Morris Water Maze Test: Neonatal VPA-exposed mice (7 days of age) were given 4 trials/day to find the target platform, when starting from the four cardinal points around the circumference of the pool. **A:** Latency to find the platform in ASD and control mice. **B:** Representative searching tracks by swimming mice.

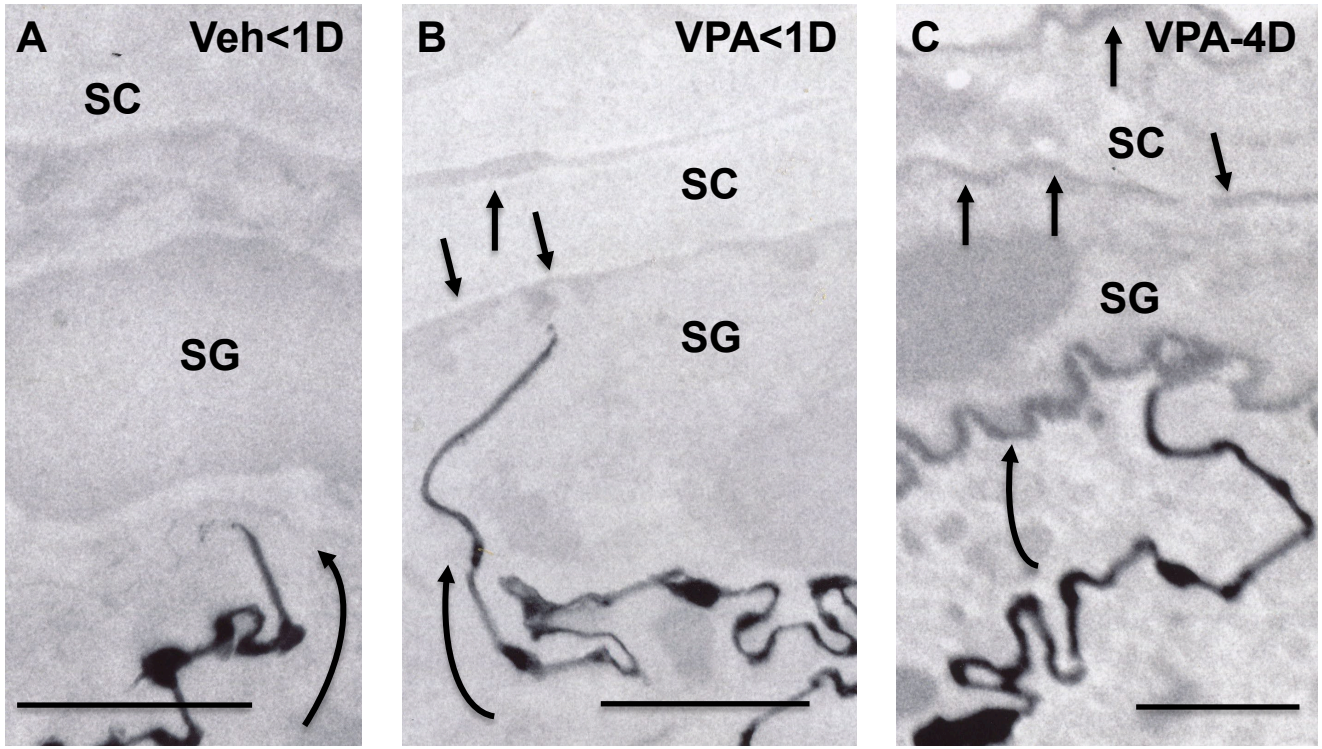


Figure S2: Demonstration of Epidermal Permeability Barrier Abnormality in VPA-Exposed Mice. Permeability barrier assessment with low molecular weight, water-soluble tracer, lanthanum nitrate (curved arrow depicts outward movement of tracer) leaking into SC interstices, non-curved arrows depict tracer in SC interstices. Mag Bar = 1 μm.

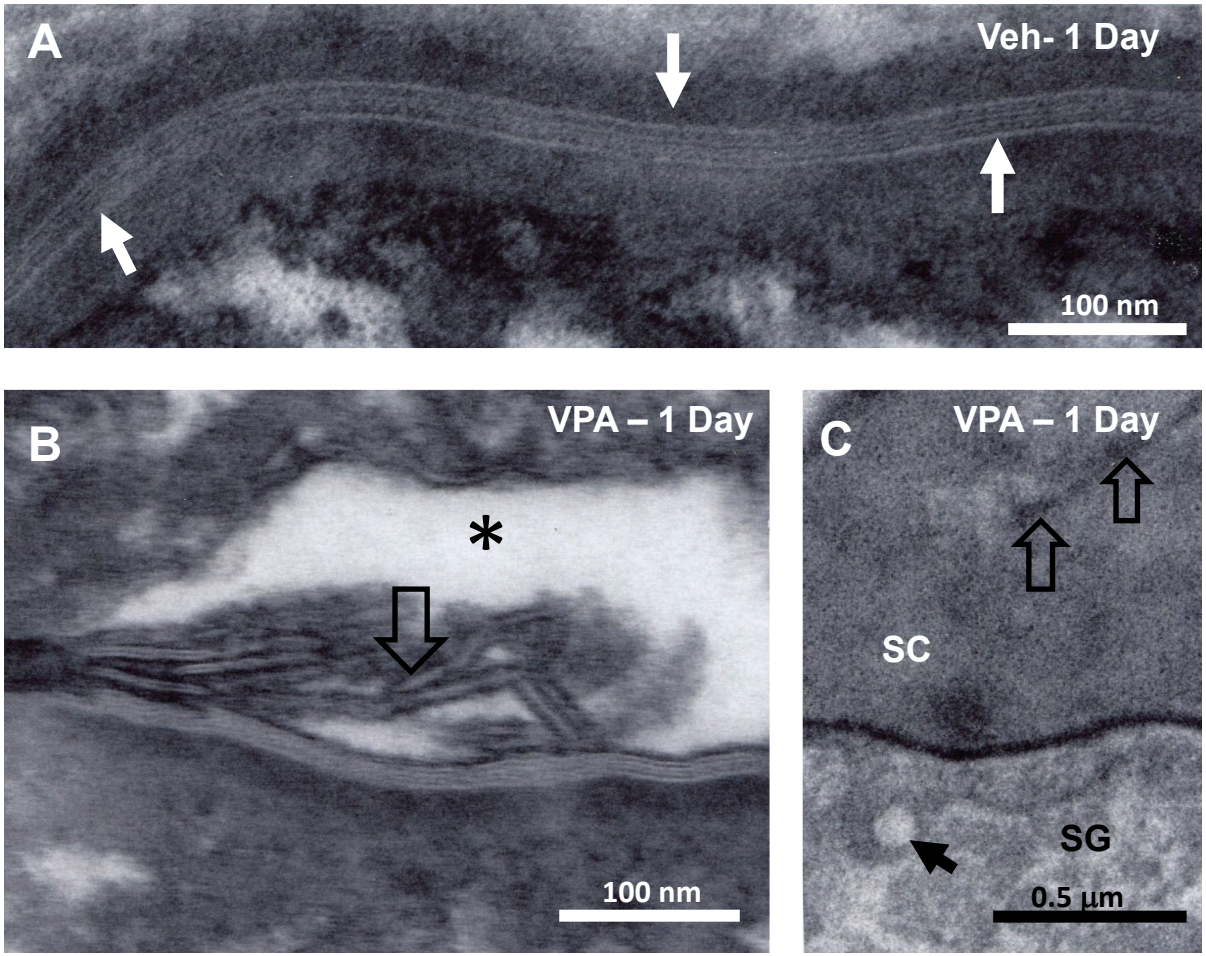


Figure S3: Basis for Impaired Cutaneous Barrier Function in VPA-Exposed Mice. A: Normal extracellular bilayers (arrows) in stratum corneum (SC) of Veh-treated mice. **B:** Abnormal lamellar bilayer organization (asterisk; open arrows) in VPA-exposed mice. **C:** Impaired secretion in VPA-exposed mice, evidenced by a reduction in secreted lamellar body contents at stratum granulosum (SG)-SC interface, as well as entombed (non-secreted) lamellae in SC cytosol (open arrows).

Figure S4: Representative H&E stained brain sections (400X total magnification) from 1 day (1D) and 4 day (4D) old mice from Veh (A&B) or VPA (C&D)-treated female mice. Scattered microglia (white arrows) and neutrophils (yellow arrows) are present within white matter parenchyma. Very few mast cells or other inflammatory cells are observed.

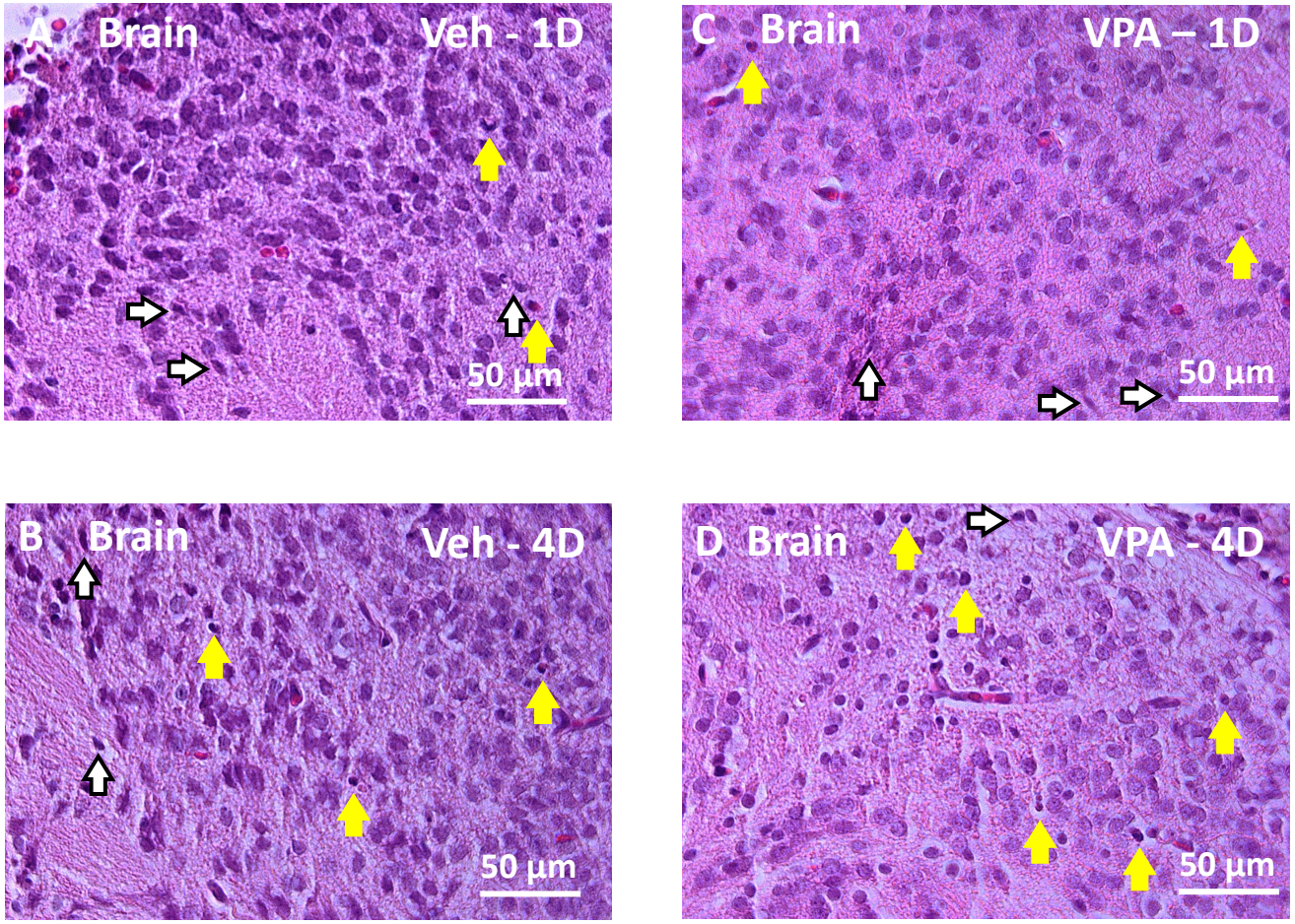


Figure S5: Sequential Changes in Additional Th-2 Cytokine Levels. **A-D:** Higher levels of TNFα and IL-13 in skin in comparison to brain at birth in VPA-exposed mice. **E+F:** Comparable levels of IFNγ in skin and brain at birth.

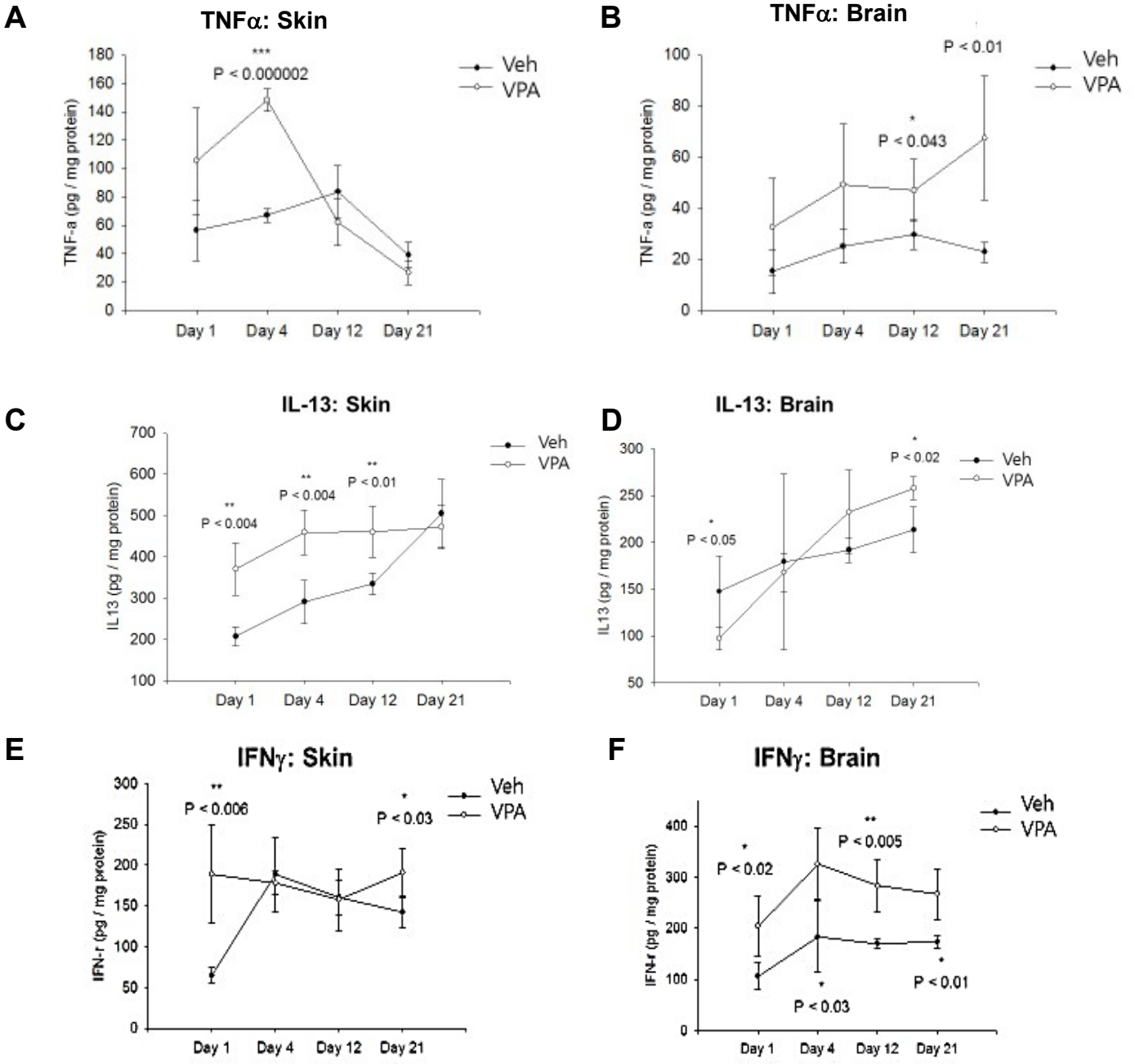
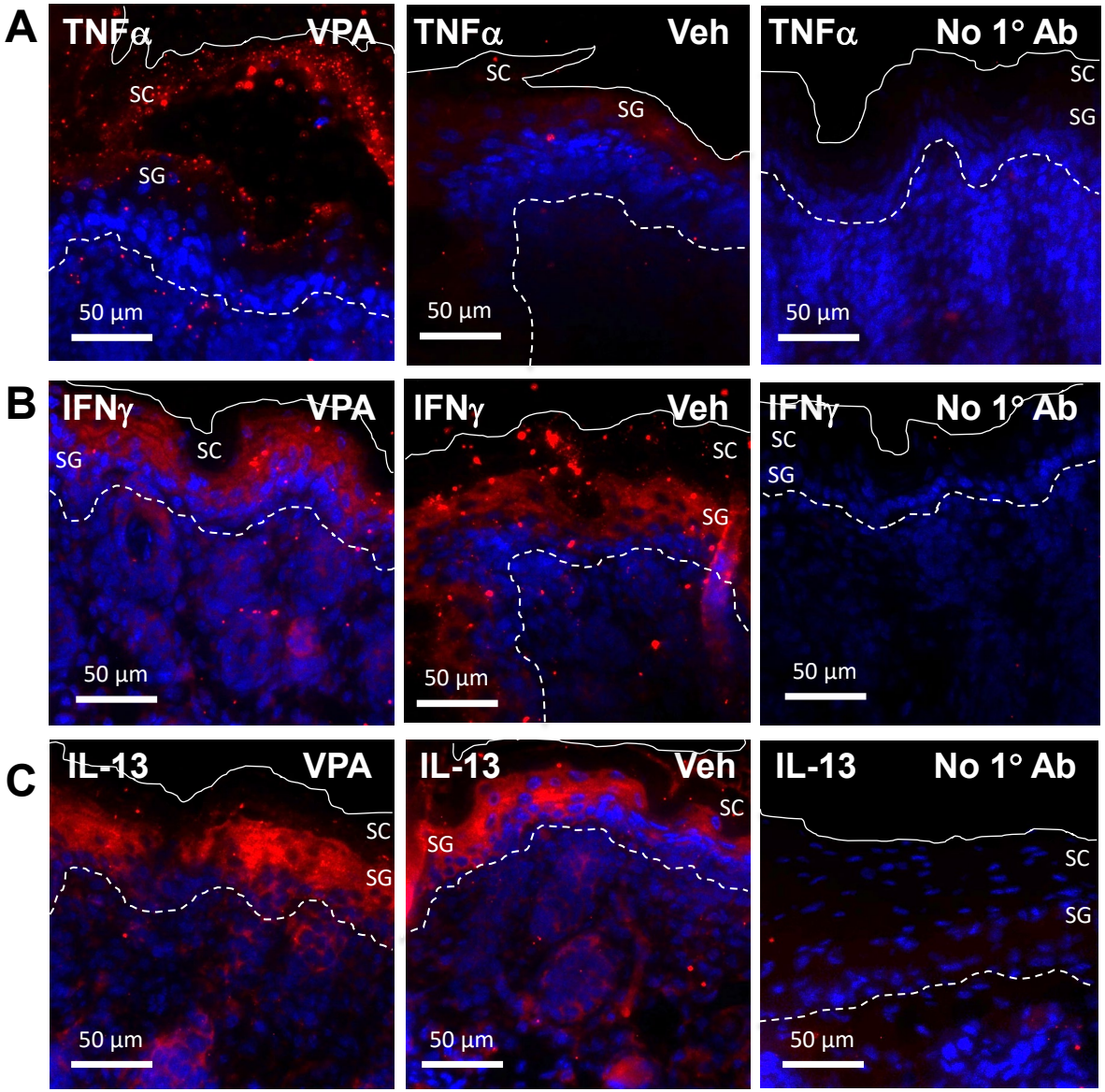


Figure S6: Immunofluorescence Localization of TNFα, IFNγ and Il-13 in Skin. A-C: Paraffin-embedded skin sections (5μm) from 1-day old VPA- and vehicle (Veh)-exposed mice were labelled with rabbit anti-mouse TNFα, IFNγ or IL-13 primary antibodies (vs. no primary antibody), followed by Alexa Fluor 594 (red) conjugated donkey anti-rabbit secondary antibody, and visualized by confocal fluorescence microscopy. DAPI (blue) was used as a nuclear counterstain. Dashed lines indicate dermo-epidermal junction, and solid lines indicate the uppermost layer of the stratum corneum (SC). **D:** Quantitation of IFNγ immunostaining in skin of 1- and 4-day-old VPA- vs. vehicle (Veh)-exposed neonates.



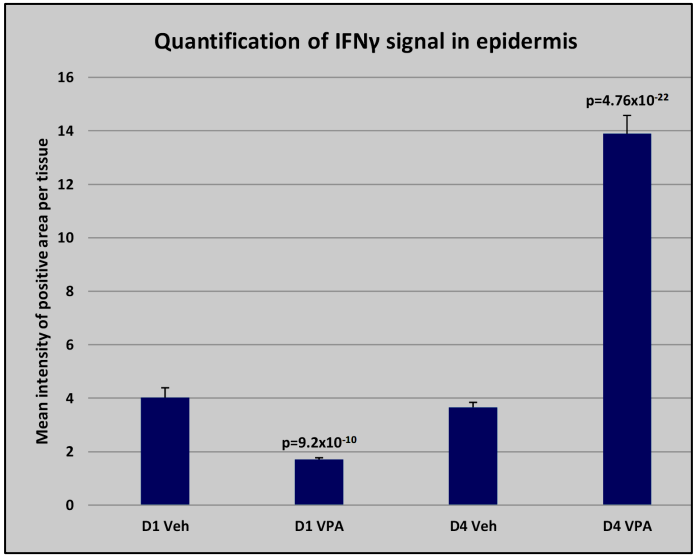


Figure S7: Epidermal Functions in ASD Subjects: Cutaneous barrier function (assessed as transepidermal water loss [TEWL]) and skin hydration (assessed by corneometry) were measured in 25 ASD volunteers (average age = 19). Though the differences between the three groups as a whole did not reach statistical significance, barrier function and skin hydration declined in a subset of volunteers with ASD, even in absence of concurrent AD or history of prior AD.

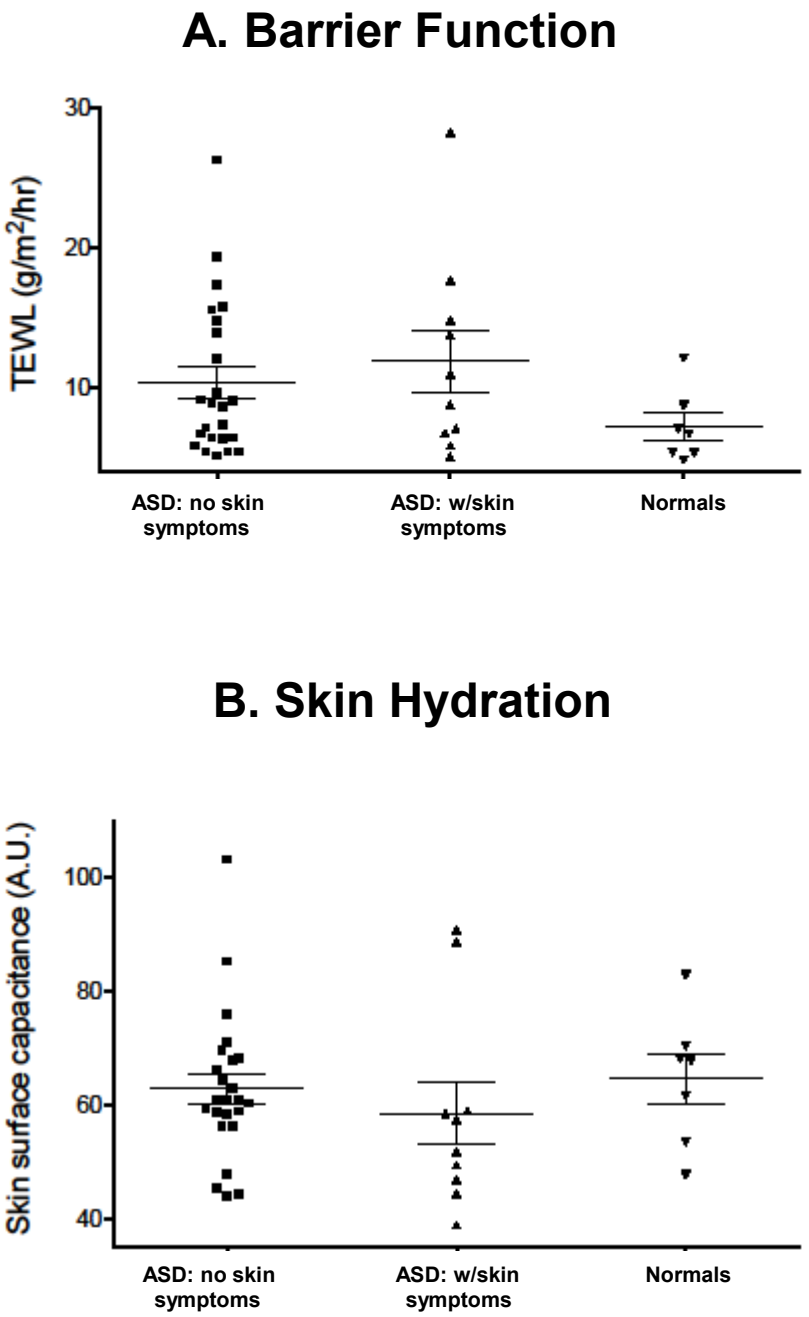


Figure S8: Proposed Sequence for Barrier-Induced Provocation of Cytokine Cascade in AD That Could 'Drive' ASD