AD_Imprint

Unlock the early life pathological imprinting of Alzheimer's disease via lifestyle

With the increasing number of patients diagnosed with dementia, including Alzheimer's disease (AD), unraveling the cellular and the molecular mechanisms involved in its pathogenesis and understanding how non-pharmacological treatment can benefit brain health is crucial. Evidence from human and mouse studies indicate that the intestinal microbiota, among other environmental factors, is tightly associated with controlling the innate and adaptive immune system which may influence AD development. Reduced contact with microbiota or changes in its composition, due to excessive hygiene or western-like diets low in fiber, early in infancy can imprint inappropriate immune system maturation with long-lasting consequences on the function of central nervous system (CNS). We recently uncovered that the gut microbiota upon solid food introduction at weaning induces an immune response in the intestine, termed "weaning reaction", which prevents impaired immune system reactivity in adult mice. Inhibition of this weaning reaction generation imprints the immune system to develop severe inflammation later in life, a phenomenon we called "pathological imprinting". Our preliminary results indicate that the gut microbiota-induced weaning reaction reduces the pathological susceptibility to develop AD in adult mice. As the maturation and function of neurons and microglia, the tissue-resident macrophages of the CNS, are steered by gut bacteria-derived molecules post-birth, it is plausible that adult AD development is impacted by pathological immune and neuronal imprinting mediated by weaning reaction.

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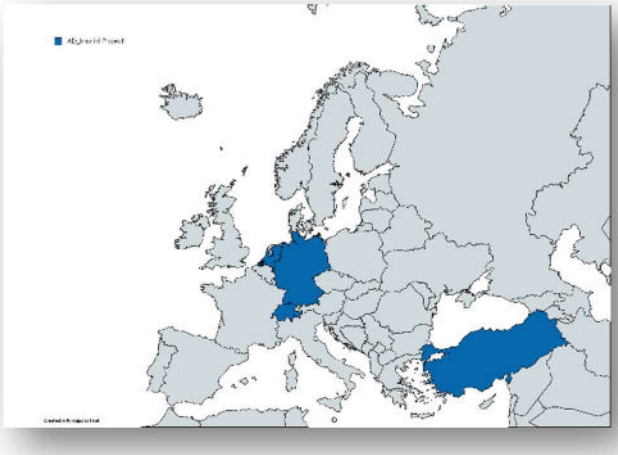

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