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FARM EXPOSURE IN EARLY LIFE MODIFIES THE ASSOCIATION BETWEEN TLR6 POLYMORPHISMS ON ASTHMA

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BACKGROUND: Toll-like receptors (TLR) play a major role in the activation and modulation of the innate immune system through cytokine secretion in response to environmental microbial exposure. Although polymorphisms of TLR6 are associated with a reduced risk of asthma, their interaction with environmental factors has not been explored. We hypothesized that the association between TLR6 polymorphisms and asthma would be modified by exposure to farming environment in early life.

METHODS: We studied 1,214 participants from the Tasmanian Longitudinal Health Study (TAHS) followed from age 7 to 44 years. Two polymorphisms in the TLR6 gene (rs1039559, rs5743810) were genotyped. Participants were categorized as farmers' (n=1,050) and non-farmers' (n=102) children based on parental reported occupation in the 1968 survey. Using prospective data, asthma was classified as never, early-onset (before age 13) and late-onset (after age 13 years). The effects of interaction between TLR6 polymorphisms and exposure to a farming environment on asthma were assessed in logistic regression models.

RESULTS: The rs5743810-C allele and the rs1039559-T allele were protective against early-onset but not late-onset asthma. We found significant gene-environment (GxE) interactions between being a farmer's child and both TLR6/rs1039559 and TLR6/rs5743810 genotypes for early-onset asthma (p=0.024 and p=0.016, respectively). Stratified analyses showed significant protective effect of the rs5743810-C and rs1039559-T against early-onset asthma among farmers' children but not non-farmer's children. Furthermore, an increasing number of protective alleles of both TLR6 SNPs was associated with a reduced risk of early-onset asthma among farmer's children (OR 0.237; 95% CI 0.10-0.54).

CONCLUSION: For children exposed to farming in early life, one or more TLR6 protective alleles (rs5743810-C/ rs1039559-T) were protective against early-onset asthma. Failure to account for the GxE interaction and age at asthma onset may explain discrepant results in previous studies of these polymorphisms and asthma risk.

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