

ALLERGY, GENETICS

LACTASE VARIANTS IN EUROPE – ANY CONNECTION TO ALLERGY?

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I will present this poster next Monday in San Francisco at the Annual Conference of the American Thoracic Society.

Allergy and the farming environment: Do genes play a role?

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INTRODUCTION

The farming environment has been found in several studies to protect a subset of children from allergy. Factors observed in far include such diverse conditions:

- FTS (farming) vs. non-FTS
- Frequency of contact with animals
- Fertilizer or other parasite infection
- Microclimate
- Farming equipment
- Farming environment
- Farming environment

There is no genetic difference of rural population and close by cities although there is a protective effect for each difference might arise. A genetic study described in dairy in dairy farming population and unrelated to subjects (Wjst, Am J Hum Genet 2005; 76: 763).


We now tested if there is any evidence of population stratification in European farming populations as even low-level differences could lead to false-positive or false-negative association results.

METHODS

We have chosen marker rs4235 (located on chromosome 2) to be used in age participating in the European Community Respiratory Health Survey (ECRHS) that living on a farm in childhood was associated with a reduced risk of allergic sensitization in adulthood.

We have now further refined the history of living on a farm or in a city and analyzed the -13910 variant in the lactase gene (LCT) in a subset of 1030 individuals.

The LCT -13910 CT/TT genotype is known to be under positive selection going an advantage to digest lactose and may therefore relate to milk drinking.



RESULTS

LCT -13910 CT/TT prevalence shows a large variation across Europe (Fig. 1) which closely matches the ancestral distribution of CCR6 (Fig. 2) but not that of allergy.

There was a clear north-south gradient of the LCT -13910 CT/TT genotype in the total sample.

484 SN (Farm), 484 SN (City), 478 SN (City), 478 SN (City)

An exact test of Hardy-Weinberg equilibrium showed no departure of LCT -13910 genotypes in Farm (p=0.37), City (p=0.04), and city group (p=0.36, 10-7).

This effect is not due to stratification by latitude or it may be found in the South (Athens) and the North of Europe (Bergen). On a single center level (Louvain), effects are generally weaker, probably due to an intermediate regional sampling (Table 1).

LCT -13910 status was neither associated with allergic disease (Table 1) nor genetic stratification after adjustment for various confounder and inclusion of interactions (see text).

Country	n	CT/TT %	p
UK	117	11.1	0.001
France	117	11.1	0.001
Spain	117	11.1	0.001
Italy	117	11.1	0.001
Germany	117	11.1	0.001
Poland	117	11.1	0.001
Czech	117	11.1	0.001
Slovak	117	11.1	0.001
Hungary	117	11.1	0.001
Austria	117	11.1	0.001
Switzerland	117	11.1	0.001
Netherlands	117	11.1	0.001
Belgium	117	11.1	0.001
Denmark	117	11.1	0.001
Sweden	117	11.1	0.001
Finland	117	11.1	0.001
Ireland	117	11.1	0.001
Portugal	117	11.1	0.001
Greece	117	11.1	0.001
Turkey	117	11.1	0.001
Spain	117	11.1	0.001
Italy	117	11.1	0.001
France	117	11.1	0.001
UK	117	11.1	0.001

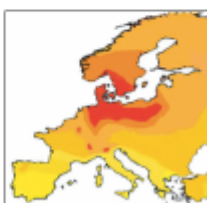


FIGURE 1. Prevalence of the LCT -13910 CT/TT genotype in European age participating in ECRHS.

abridged / revised version

The farming environment has been found in several studies to protect a subset of children from allergy. Factors discussed so far include such diverse events like LPS inhalation of barn dust, poultry contact or dog ownership, Trichiuris or other parasite infection, Acinetobacter contact, drinking unpasteurized milk or avoiding vitamin D prophylaxis. These studies usually assume that there is no genetic difference of rural population and close-by cities although there is preliminary evidence that such differences might exist. A previous study described LD decay in Scottish farming populations and unrelated U.K. subjects (AJHG 2005; 76:763). We now tested if there is any evidence of population stratification in European farming populations as even low-level differentiation could lead to false-positive or false-negative association results.

METHODS

We have shown earlier in 6251 randomly selected adults 20 to 44 years of age participating in the European Community Respiratory Health Survey (ECRHS) that living on a farm in childhood was associated with a reduced risk of atopic sensitization in adulthood. We now refined the history of being raised on a farm or in a city and analyzed the ϵ -T13910C variant in the lactase gene LCT in a subset of 5350 individuals. The LCT -13910 CT/TT genotype is known to be under positive selection giving an advantage to digest lactose and may therefore relate to milk drinking.

RESULTS

LCT ϵ -13910 CT/TT prevalence shows a large variation across Europe (FIG.1) which closely resembles the ancestral distribution of cattle (FIG.2) but not that of allergy. There was a clear rural-city gradient of the LCT -13910 CT/TT genotype in the total sample, dropping from 84.8% (farm), 80.2% rural/village) to 74.9% (city, $P=1,15 * 10^{-5}$). An exact test of Hardy-Weinberg equilibrium showed no departure of LCT ϵ -13910 genotypes in farm ($p=0.539$), however in the rural/village ($p=4,14 * 10^{-7}$) and city group ($4,96 * 10^{-7}$). LCT ϵ -13910 status was neither associated with allergic rhinitis (Table 1) nor grass sensitization even after adjustment for various confounder and inclusion of interaction terms.

