

Evolution of Lactase Persistence

Alan R. Rogers

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Outline

- ▶ Domestication of cattle
- ▶ Lactose and lactase
- ▶ Distribution of lactase persistence
- ▶ The gene
- ▶ Evidence for natural selection

Conventional wisdom

Something must have happened to weaken the selective pressure drastically. We cannot escape the conclusion that man's evolution towards manness suddenly came to a halt.

—Ernst Mayr 1963

Natural selection has almost become irrelevant in human evolution. There's been no biological change in humans in 40,000 or 50,000 years. Everything we call culture and civilization we've built with the same body and brain.

—Stephen Jay Gould 2000

Domesticated Cattle

- ▶ Earliest fossils: ~ 8000 BP (Near East)
- ▶ Maybe 9000 BP (Sahara)
- ▶ Uses
 - ▶ Draft animal
 - ▶ Meat
 - ▶ Blood (like the Masai)
 - ▶ Sour milk
 - ▶ Why not fresh milk?

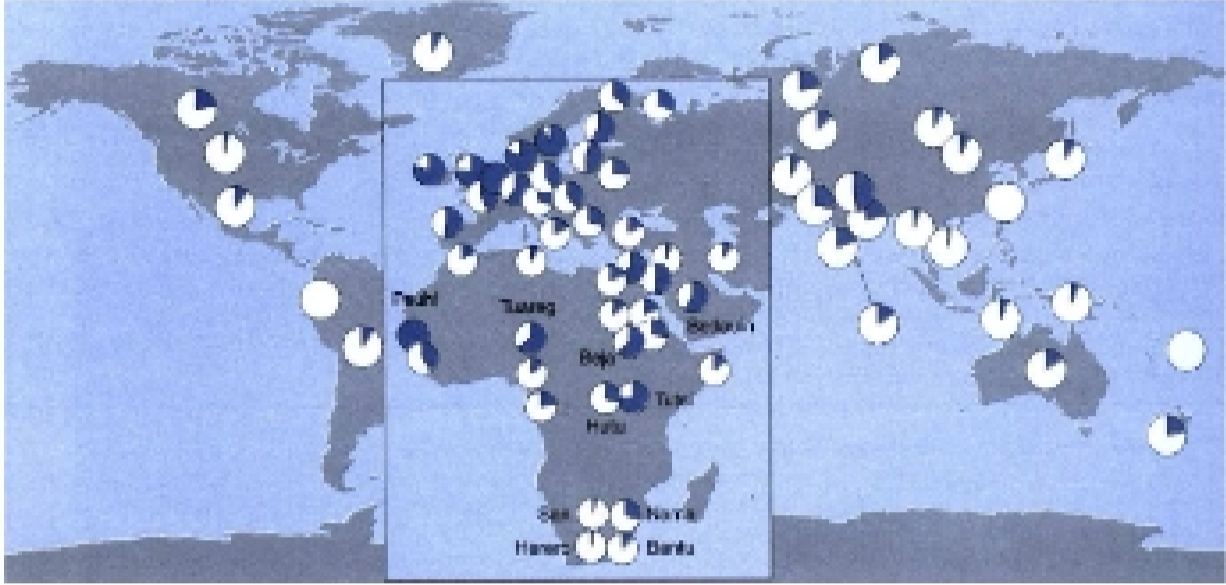
The trouble with fresh milk

- ▶ Contains the sugar *lactose*
- ▶ Digesting lactose requires the enzyme *lactase*
- ▶ Most humans don't produce it after age 5.
- ▶ Fresh milk gives them gas and diarrhea.
- ▶ 8000 years ago, all humans had this problem.

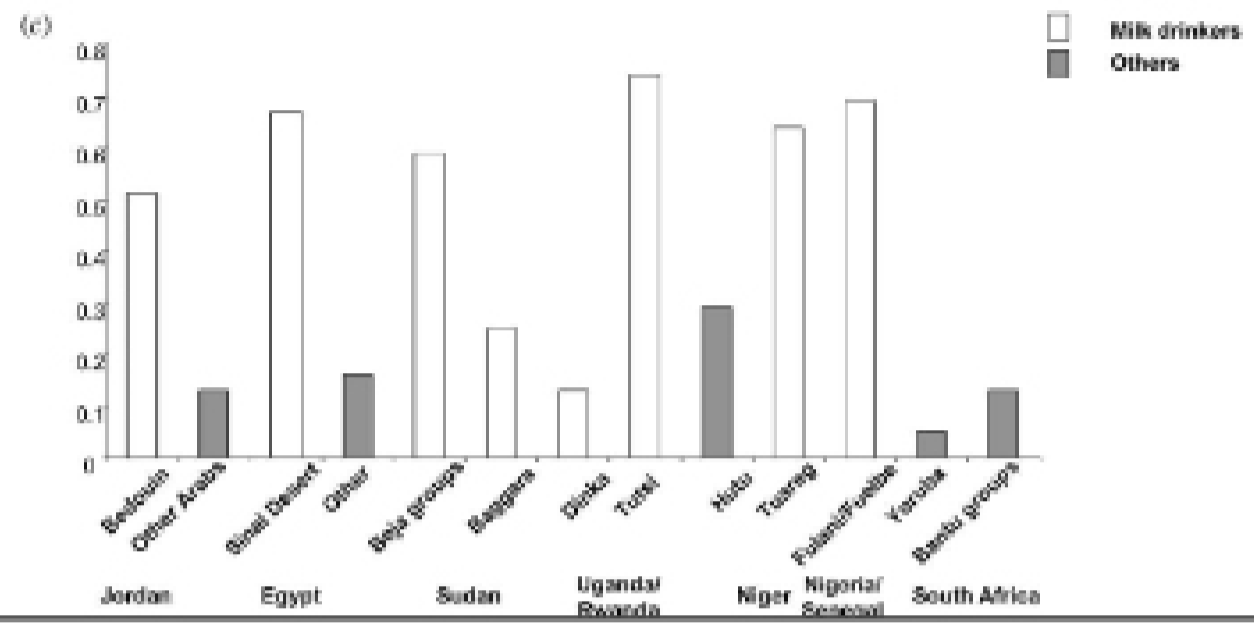
Lactase persistence

- ▶ Some modern humans produce lactase throughout life.
- ▶ Digest fresh milk as adults.
- ▶ Caused by mutation near lactase gene.
- ▶ When and where?

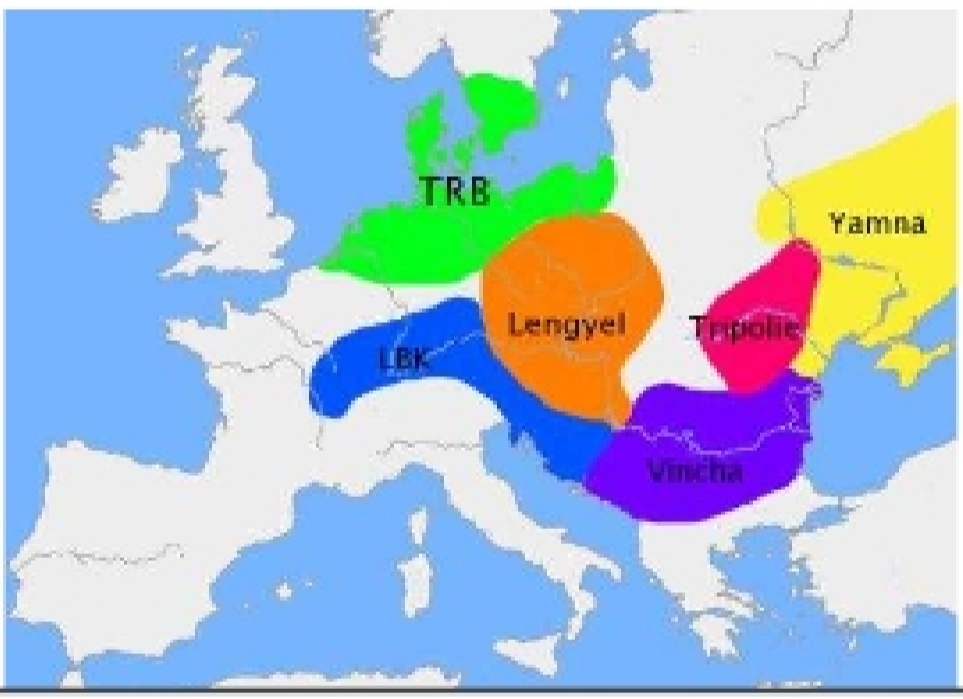
Distribution of lactase persistence (dark blue)



Within countries, lactase persistence more common in populations that drink milk

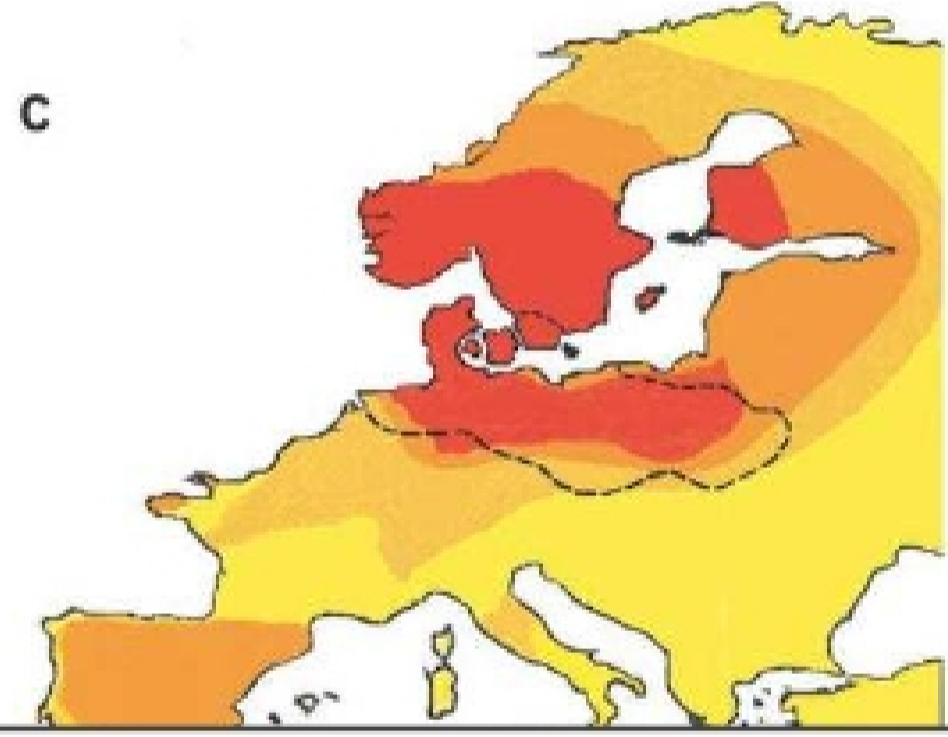


Green: Funnelbeaker Culture



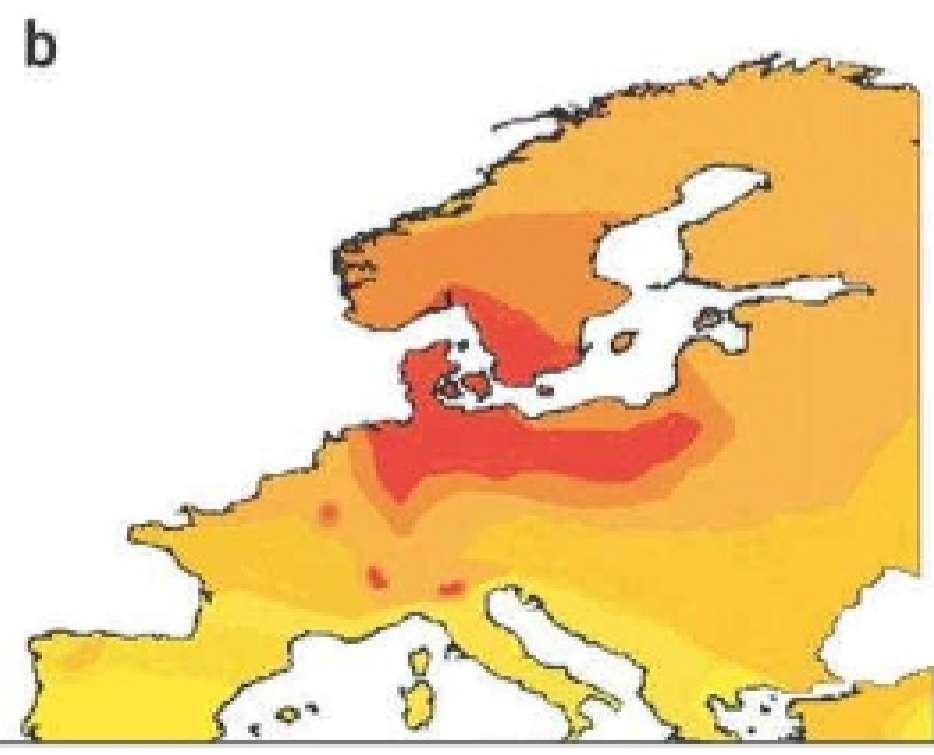
- ▶ 3500 BC
- ▶ Cattle
- ▶ Weaned calves early
- ▶ Dairy?

Lactase persistence in Europe



- ▶ Modern Europeans
- ▶ Dashes: Funnelbeaker culture

Diversity of proteins in cow's milk



- ▶ Human-cow co-evolution?
 - ▶ Relaxed selection on cows?
- We don't know.

What we know so far about lactase persistence

- ▶ under genetic control
- ▶ more common in populations that drink milk
- ▶ But which is cause and which is effect?
 - ▶ Do they drink milk because they can?
 - ▶ Or did lactase persistence evolve because they drink milk?

The drift hypothesis

- ▶ Differences in lactase persistence arose by random changes in allele frequency (genetic drift).
- ▶ A slow process
- ▶ Many recombinants near persistence allele.
- ▶ Short block of LD.

Prediction of Drift Hypothesis

	X	Y	Z
1	...c.....	...g.....	...a
2	...c.....	...g.....	...t
3	...c.....	...c.....	...a
4	...T.....	...c.....	...t
5	...T.....	...g.....	...t
6	...T.....	...c.....	...t
7	...T.....	...g.....	...t
8	...T.....	...c.....	...a
9	...T.....	...g.....	...t
10	...T.....	...c.....	...a

- ▶ Persistence allele is T at site X.
- ▶ Some T chromosomes have g at site Y.
- ▶ Others have c.
- ▶ Some have "a" at site Z.
- ▶ Others have t.
- ▶ Recombination has shuffled things up.

The selection hypothesis

- ▶ Selection favors persistence allele where people drink milk.
- ▶ Allele increased rapidly within past 10,000 years.
- ▶ Little time for recombination.
- ▶ Large block of LD

Prediction of Selection Hypothesis

	X	Y	Z
1	...c.....	...g.....	...a
2	...c.....	...g.....	...t
3	...c.....	...c.....	...a
4	...c.....	...c.....	...t
5	...T.....	...g.....	...t
6	...T.....	...g.....	...t
7	...T.....	...g.....	...t
8	...T.....	...g.....	...t
9	...T.....	...g.....	...A
10	...T.....	...g.....	...t

- ▶ Persistence allele is T at site X.
- ▶ No recombinants at nearby site Y.
- ▶ Only one at site Z
- ▶ A block of nearly identical sites surrounds persistence allele at site X.
- ▶ Linkage disequilibrium (LD)

What really happened?

- ▶ In Europeans, persistence allele surrounded by a million bases of LD.
- ▶ Indicates strong selection.
- ▶ Statistical tests reject the drift hypothesis (Bersaglieri et al 2004)
- ▶ Increasing for ~10,000 years (Coelho et al 2005).

LD surrounds lactase gene in Europe

