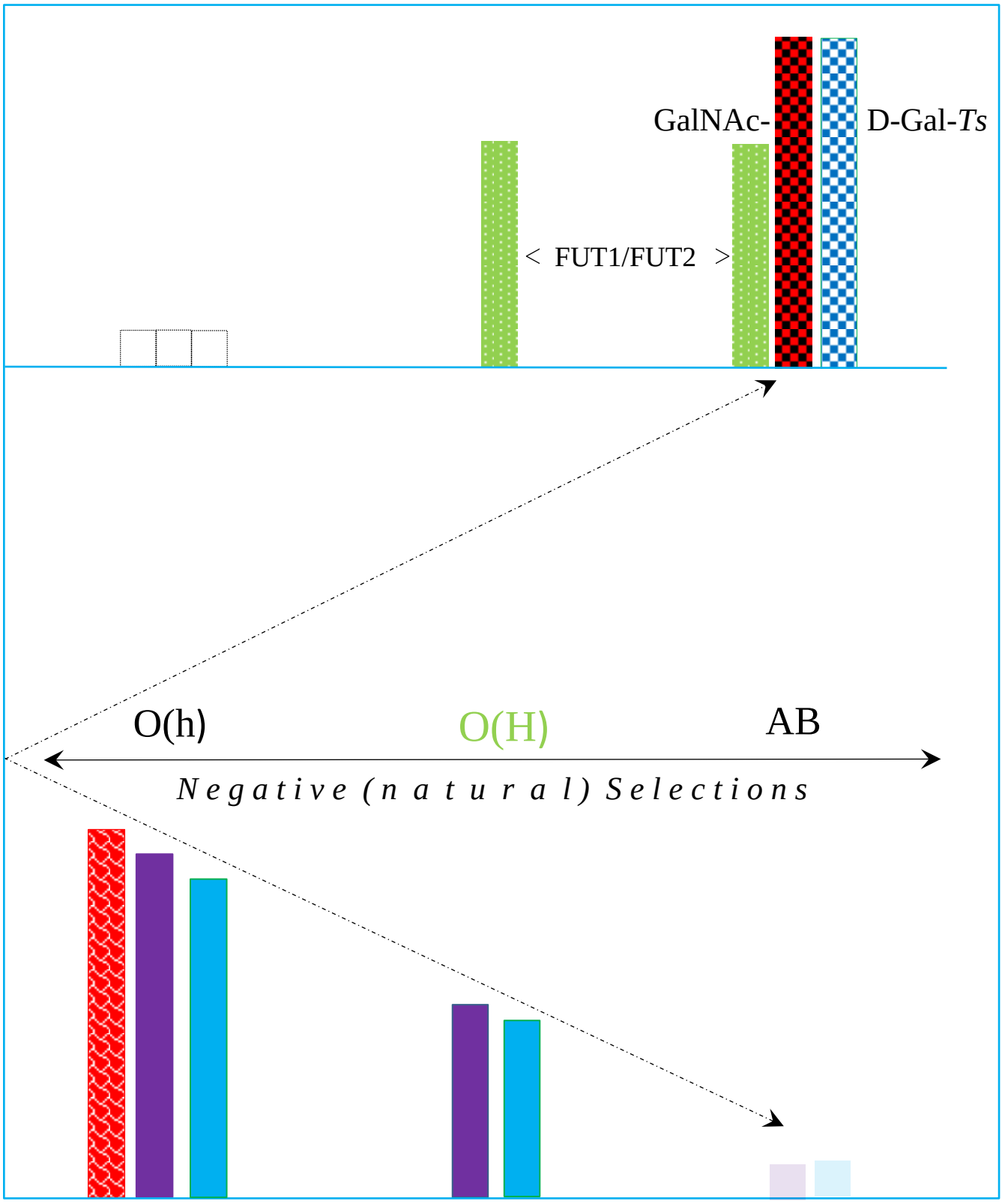
**Virtual relationships between the degree of ABO(H) phenotype-specific glycosylations and corresponding innate antibody levels**



# The relationships between the ABO(H) blood group-specific glycosylations and the levels of corresponding innate antibodies

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The human ABO(H) blood group phenotype formation is performed on both cell surfaces and plasma proteins, in which the anti-A and anti-B isoagglutinin activities, exerted by the nonimmune IgM molecule in blood group O(H) plasma, are downregulated through blood-group phenotype-specific, glycosidic accommodation of plasma proteins in the non-O blood groups A, B and AB.[1] [2] This accommodation may be performed by soluble plasma glycotransferases [3] on the secretory immunoglobulin molecule or occurs in molecular connection with the intracellular, complex ABO(H) blood synthesis in the *Golgi* apparatus. It is here potentially performed via a single *O*-glycosidic enzymatic step, which creates a blood group A, B or AB mucin-type epitope and releases a secretory IgM, consequently lacking the corresponding anti-A or -B isoagglutinin activities. In blood group OH), in which blood group A and B glycosylations do not occur, the polyreactive IgM molecule exerts both anti-A and anti B isoagglutinin activities. The lack of any ABO(H) blood group glycosylations or phenotype formation, as shown by the rare O(h) or *Bombay* type, which originates from consanguinities, is associated with strongly elevated isoagglutinin levels and an unusual anti-H reactivity, acting over a wide range of temperatures, with an amplitude at 37 °C, while the male infertility of this group is assumingly caused by autoimmunological impairment of germ cell maturation and/or performances.[4] In contrast, blood group AB which likely due to evolutionary selective diseases forms the smallest among the ABO(H) blood groups, precludes any isoagglutinin formation and represents the other extreme of phenotype diversity. Thus, the non-phenotype O(h) or *Bombay* type and blood group AB appear to mark two opposite directions of negative (natural) selection and demonstrate how phenotype and isoagglutinin production form an evolutionary functional unity, in which the degree of phenotype diversity and innate immunity behave inversely proportional and demonstrate again the central evolutionary and immunological position of the human blood group O(H)[2, 5]

Comment: Because statistical data are not available from the *Bombay* type due to its small population size, the isoagglutinin levels are estimated according to existing reports and the hypothetical serological profile of the classic *Bombay* type (h/h; se/se),[4] which is characterized by complete lack of ABO(H) blood group glycosylations.

**References**:


1. Arend, P. ABO (histo) blood group phenotype development and human reproduction as they relate to ancestral IgM formation: A hypothesis. *Immunobiology* **221**, (2016).

2. Arend, P. Early ovariectomy reveals the germline encoding of natural anti-A- and Tn-cross-reactive immunoglobulin M (IgM) arising from developmental O-GalNAc glycosylations. (Germline-encoded natural anti-A/Tn cross-reactive IgM). *Cancer Med.* **6**, (2017).

3. Nagai, M., Davè, V., Kaplan, B. & Yoshida, A. Human blood group glycosyltransferases. I. Purification of n-acetylgalactosaminyltransferase. *J. Biol. Chem.* **253**, 377–9 (1978).

4. Arend, P. ABO phenotype-protected reproduction based on human specific α1,2 L-fucosylation as explained by the Bombay type formation. *Immunobiology* (2018). doi:https://10.1016/j.imbio.2018.07.015

5. Arend, P. Position of human blood group O(H) and phenotype-determining enzymes in growth and infectious disease. *Ann. N. Y. Acad. Sci.* **1425**, 5–18 (2018).