

A Scenario for the Origin of Blood Group Antigens

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INTRODUCTION

A long time ago, in the unpublished manuscript of a book on evolutionary biology, I put forward a hypothesis for the origin of blood group antigens that correlates with recent medical findings in relation to the ABO blood group system. My scenario is based upon interactions between invading organisms (whether viral, bacterial, protozoan, or multi-cellular) and their hosts.

It is now well known that pathogens and parasites can insert DNA sequences into their hosts' genomes (or otherwise genetically manipulate them) in order to enhance their own survival, and it is becoming more and more obvious that human beings are just as susceptible to these strategies as are other species.

I suggest that such genomic reprogramming events could have been the basis of the evolution of blood group antigens, as the latter are disadvantageous to those individuals possessing them: the malaria parasite *Plasmodium vivax* gains entry to human red blood cells by means of the Duffy antigens, while the presence of all other blood group substances makes it impossible for the host to mount an immune response to the corresponding surface proteins of invading organisms, which the host is forced to treat as 'self'.

Such a scenario gives rise to a completely new perspective, for hitherto it has been assumed that all proteins are of endogenous origin and serve host functions. Furthermore, it has important implications to therapeutic measures, as an alien DNA sequence can be targeted without fear of adverse consequences to the host. In fact, researchers are at present hoping to confer resistance to HIV in some individuals by inactivating the *CCR5* gene, which encodes the receptor that HIV uses to enter certain immune cells (1).

On the basis of this hypothesis, the Table shows how the existing relationship between the presence of antigens and the respective naturally occurring antibodies in the ABO blood group system can be explained. Significantly, several studies conducted over the last few years correlate with the

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Table: Relationship between antigens and antibodies in the ABO blood group system

Blood group	Reaction
Group AB	unable to resist two different genomic attacks; therefore, acquired A and B antigens and developed neither anti-A nor anti-B (or had to shut down the production of both antibodies)
Group A	unable to resist one genomic attack; therefore, acquired A antigen and developed only anti-B
Group B	unable to resist the other genomic attack; therefore, acquired B antigen and developed only anti-A
Group O	resisted both genomic attacks; therefore, acquired neither antigen and developed both anti-A and anti-B

relative fitnesses suggested in the Table, for they show that, compared with group O individuals, the non-O groups not only have a decreased overall postoperative survival, whatever the type of surgery involved (2), but are also at increased risk of such conditions as coronary heart disease (3).

The latter study is of particular relevance to my scenario, as it demonstrates that the increased risk of coronary heart disease for group AB is more than the combined increased risks for groups A and B [*ie* 23%, 5%, and 11%, respectively] (3).

Also relevant is the fact that it is now known that group A is associated with higher levels of low-density lipoprotein (LDL) cholesterol, which can clog up arteries, and group AB is linked to inflammation, which may adversely affect the function of blood vessels, while people with blood type O have higher levels of a compound that has a beneficial effect on blood flow and clotting.

CONCLUSION

In conclusion, I should like to point out that my hypothesis for the origin of blood group antigens has important impli-

cations to Darwin's theory of evolution by means of natural selection, which was the subject of an earlier paper of mine entitled *A New Perspective on Evolution* (4), for in the first edition of *The Origin of Species* (1859), Darwin wrote: "If it could be proved that any part of the structure of any one species had been formed for the exclusive good of another species, it would annihilate my theory, for such could not have been produced through natural selection" (5). (This passage appears unaltered in the sixth (and final) edition of *The Origin*, published in 1872). Moreover, it is now obvious that Darwin's criterion for the refutation of his mechanism of natural selection applies to most, if not all, host/parasite relationships, a fact that is graphically illustrated by recent work on the leprosy bacillus, *Mycobacterium leprae*, which reprogrammes adult Schwann cells in its host and converts them into stem cells (6).

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