Immune Memory to Influenza Hemagglutinin and Antigenic Drift

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Background/Objective
The selective pressure driving antigenic change in Influenza viruses is thought to originate from the human immune response. This view is difficult to reconcile with the polyclonal nature of the antibody response acting simultaneously at multiple sites on the hemagglutinin glycoprotein.

Method
We have characterized the B-cell repertoire from one of two donors whose serum showed reduced neutralizing activity on the recently evolved clade 6B pandemic H1N1 viruses.

Result
While the response was markedly polyclonal, a majority of the clones failed to recognize the clade 6B viruses, while retaining neutralization of the viral strain to which the donor would have been exposed in childhood. Virus variants selected in vitro with representative monoclonal antibodies revealed that a single amino acid replacement in the Sa antigenic site, characteristic of the clade 6B viruses, was responsible for resistance to neutralization by multiple monoclonal antibodies and the serum from both donors.

Conclusion
These results show that a highly focused polyclonal antibody response can be recalled by exposure to hemagglutinins that share minimal surface epitopes with the priming virus, and this can be linked to current antigenic drift in pandemic H1N1 influenza viruses.