

Do Sharks have a New Antibody Lineage?

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Sharks are the most primitive animals to have an advanced adaptive immune system. Their long evolutionary history (~400 million years) is reflected in a diverse array of shark antibodies, including the unique IgNAR (Ig new antigen receptor) isotype. IgNARs are heavy chain homodimers, there is no associated light chain and binding affinity mainly resides in two complementarity determining regions. Given that sharks also possess heavy-light chain antibodies, the question has been: did IgNARs evolve from the conventional antibody/T-cell receptor format, or do they represent an entirely separate antibody lineage?

Structural studies presented here including recent reports of the first three-dimensional crystal structures for IgNAR variable domains [1] and of the IgNAR-antigen complex structure [2] have provided significant insight into IgNAR evolutionary origin and antigen-binding strategy. Comparison of IgNAR structures to that of a range of immune molecules showed the best agreement with members of the cell adhesion family. We hypothesise that the IgNARs are an evolutionarily distinct antibody lineage, separate from heavy-light chain antibodies and T cell receptors.

[1] Streltsov V.A, Varghese J.N., Carmichael J.A., Irving R.A., Hudson P.J., Nuttall S.D., *PNAS*, 2004, **101**, 12444. [2] Stanfield R.L, Dooley H., Flajnik M.F., Wilson I.A., *Science*, 2004, **305**, 1770.

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