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# Why do immunology research in hemophilia?

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# Cellular Immunology

journal homepage: [www.elsevier.com/locate/ycimm](http://www.elsevier.com/locate/ycimm)

## Editorial

### Why do immunology research in hemophilia?



In this special issue of Cellular Immunology, we highlight the work of researchers investigating the immune response to factor VIII (FVIII) in hemophilia. Hemophilia is a relatively rare disease with an incidence of 1/5000 males. Why is it important to investigate the immune response in a relatively rare disease? Why study any orphan monogenic disease? The answer lies in immunology!

Hemophilia A is an x-linked disease caused by a variety of mutations (deletions, inversions, missense, etc.) in the gene for the coagulation protein FVIII. Because these patients lack FVIII, this leads to bleeding issues that can have life-long morbidity consequences, e.g. joint arthropathy resulting from repeated bleeds. We know how to treat this disease with prophylactic and therapeutic injections of human recombinant or plasma-derived FVIII to restore near-normal clotting times. However, up to 30% of hemophilia A patients produce antibodies to FVIII that neutralize the efficacy of this bio-therapeutic. These antibodies are referred to by clinicians as “inhibitors” because they inhibit the pro-coagulant function of FVIII. Clearly, many severe hemophilia A patients lack central tolerance to this human protein because they most likely never saw it during the development of the immune system: a beautiful natural example of acquired self-tolerance.

Once patients develop inhibitors, there is currently only one major therapy, referred to as “ITI”, short for Immune Tolerance Induction. Basically this involves repeated high doses of FVIII. Aside from being expensive, ITI often fails in patients with high

titered inhibitors. Clearly, novel approaches for tolerance are needed; several articles in this issue address this problem.

So many unanswered questions remain: Why do some patients never make a clinically significant immune response? Why is FVIII so immunogenic when given intravenously? How can we prevent or reverse inhibitor formation?

We offer these research and review articles as state-of-the-art answers to these “Why?” and “How” questions. I also recommend the advice of Professor E.O. Wilson [1] in his recent book “Letters to a Young Scientist”: find a niche and excel in it. Hemophilia immunology and immune tolerance approaches to monogenic diseases is such a niche.

#### Reference

- [1] E.O. Wilson, *Letters to a Young Scientist*, Liveright, W.W. Norton & Co., NY, NY, 2013. ISBN-13: 978-0871403773.

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