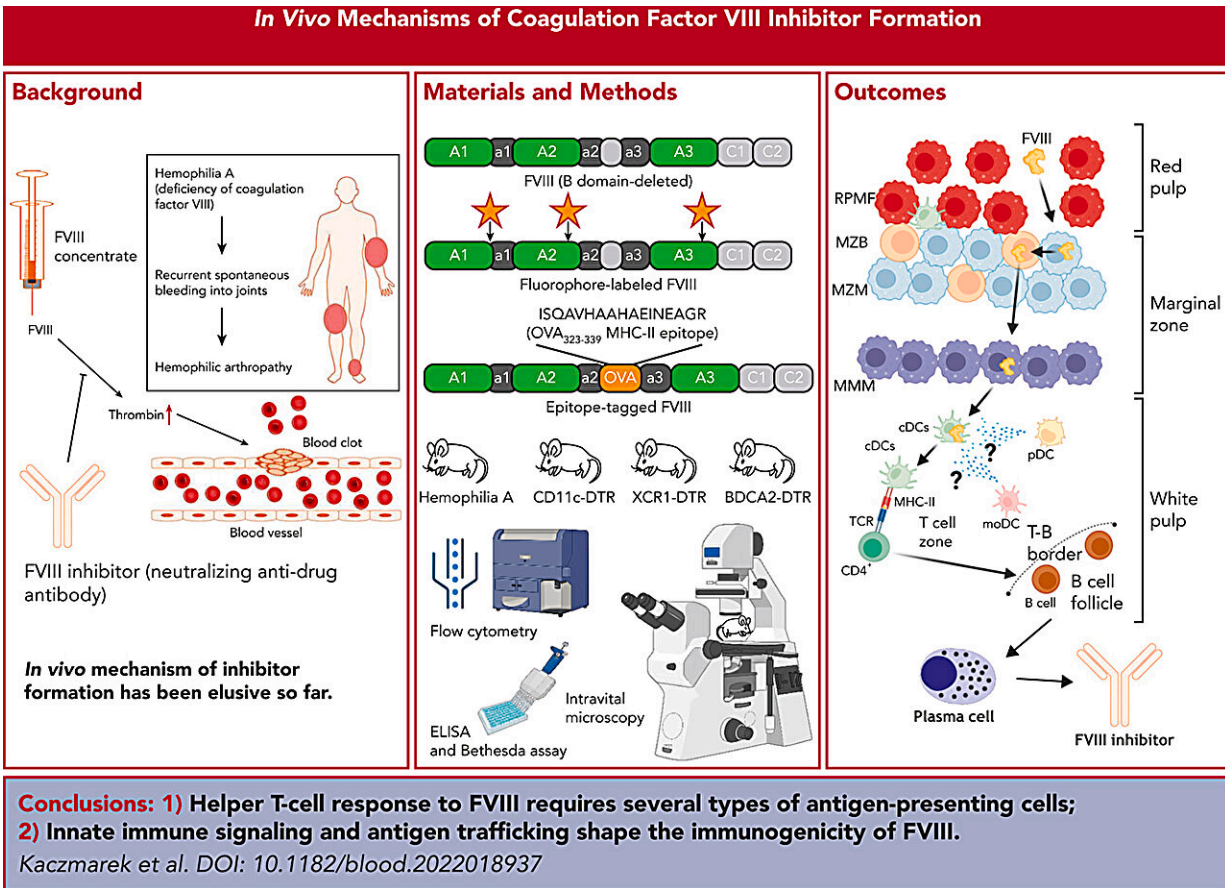


# Researchers uncover mysteries behind immune response to hemophilia A treatment

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Credit: *Blood Journal* (2023). DOI: 10.1182/blood.2022018937

Patients with the genetic disorder hemophilia A receive factor VIII protein replacement treatments to replenish this clotting protein in their

blood, thus preventing dangerous bleeding. Unfortunately, about 30% of these patients develop antibodies against the treatment and until now, despite more than 80 years of clinical experience with this complication, little has been known about its mechanism.

In a recent study published in *Blood*, researchers from Indiana University School of Medicine shed new light on the underlying causes of immune response to factor VIII, providing valuable insights that could lead to more effective and safer hemophilia A treatments in the future.

The research team led by Radek Kaczmarek, Ph.D., assistant research professor of pediatrics, and Roland Herzog, Ph.D., professor of pediatrics and director of the Gene and Cell Therapy Program at the Herman B Wells Center for Pediatric Research, studied the connections between factor VIII, [immune cells](#) and the spleen to uncover what leads to the negative response of inhibitor formation.

"Our goal was to provide a clearer understanding of how and why factor VIII inhibitors develop in individuals with this complication," said Kaczmarek. "We are hopeful that our findings will lead to more successful immune tolerance therapies for those living with hemophilia A and factor VIII inhibitors. Development of new interventions is difficult without understanding the molecular and cellular underpinnings of an issue that is being addressed. cursory understandings of factor VIII inhibitor formation have stymied progress."

The scientists discovered that T [cells](#), which play a vital role in the immune system and help trigger factor VIII inhibitor formation, rely on a specific set of other cells to move coagulation factor VIII to the regions of the spleen where T cells reside. The study also identified the immune response to factor VIII was made stronger by stimulating an innate immune sensor called Toll-like receptor 9. Furthermore, the research team noted that factor VIII not only impacts its own [immune](#)

[response](#) but may also enhance the [immune system](#)'s reactivity to other antigens, indicating intrinsic immunostimulatory properties.

"The most surprising finding in our study was that antigens may take different routes to reach T cell zones in the spleen," said Herzog. "These differences in trafficking offer a new perspective on why antigens differ in immunogenicity."

Overall, these findings collectively represent a significant step forward in unraveling the mysteries of hemophilia A complicated with factor VIII inhibitor and may help develop more tailored and efficient treatment approaches.

**More information:** Radoslaw Kaczmarek et al, Factor VIII Trafficking to CD4+ T cells Shapes its Immunogenicity and Requires Several Types of Antigen Presenting Cells, *Blood Journal* (2023). [DOI: 10.1182/blood.2022018937](https://doi.org/10.1182/blood.2022018937)

Provided by Indiana University

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