



**Inserm**



**CRC**  
CENTRE DE RECHERCHE  
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PARIS UNIVERSITAS

**Alloantibodies and autoantibodies**



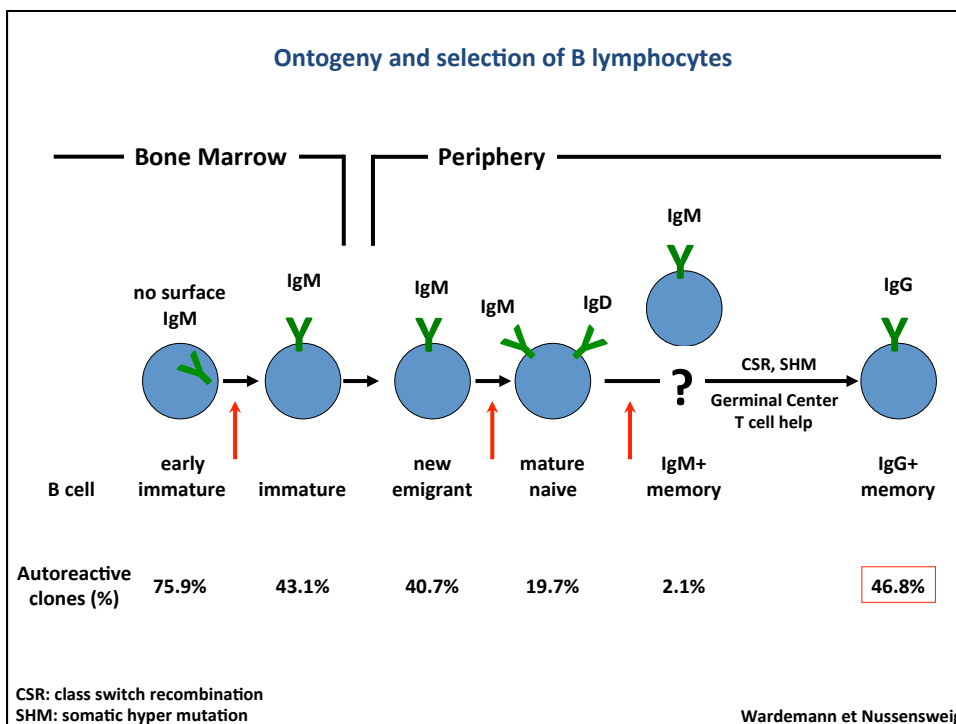
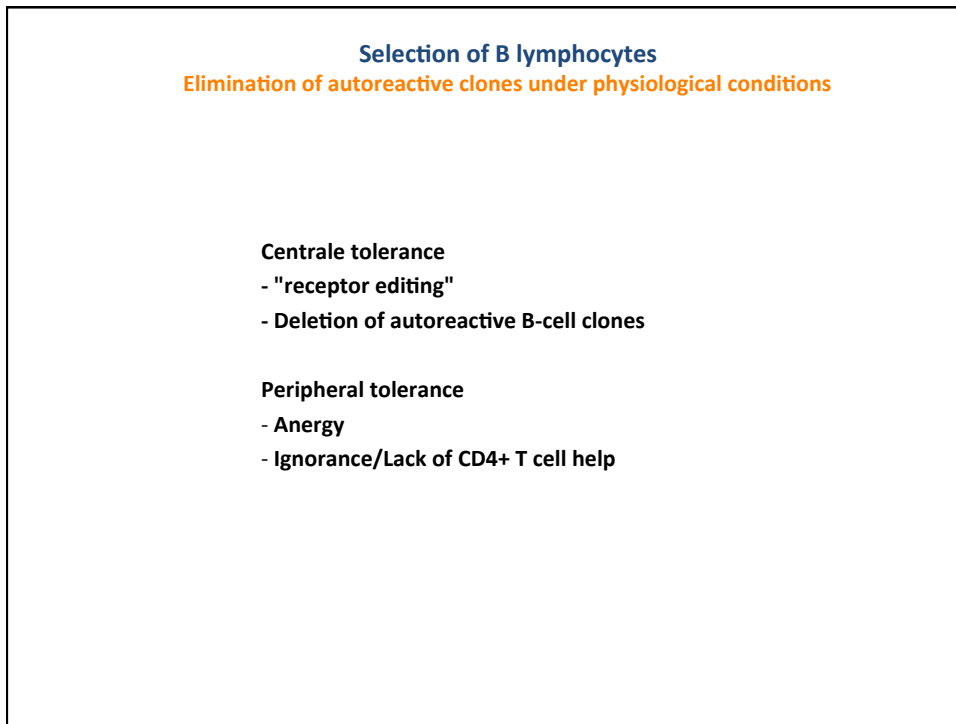
**Sébastien LACROIX-DESMAZES**

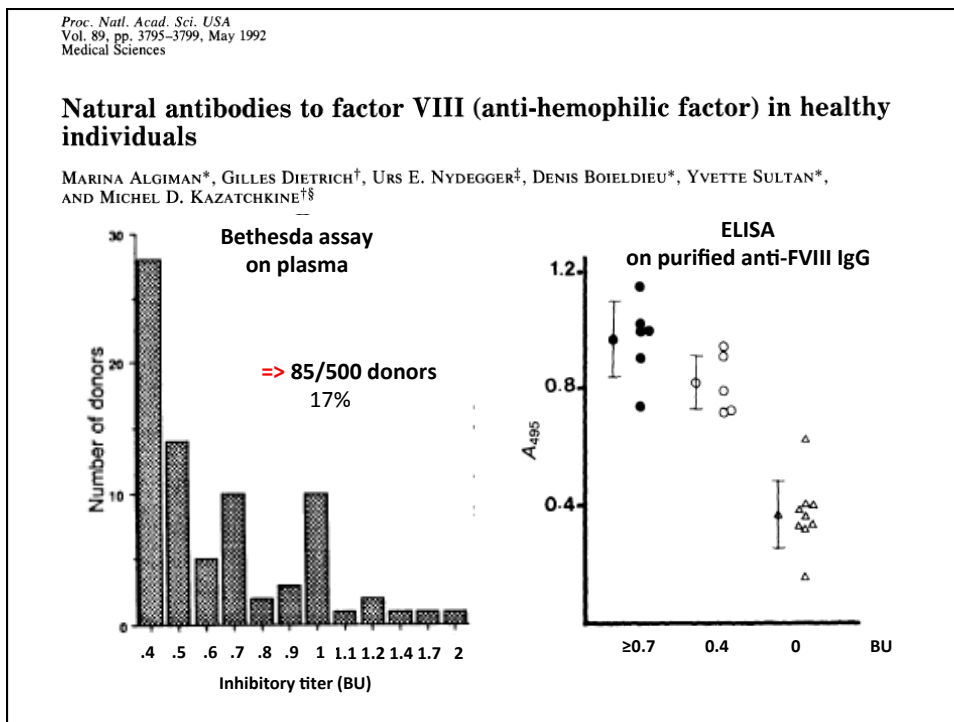
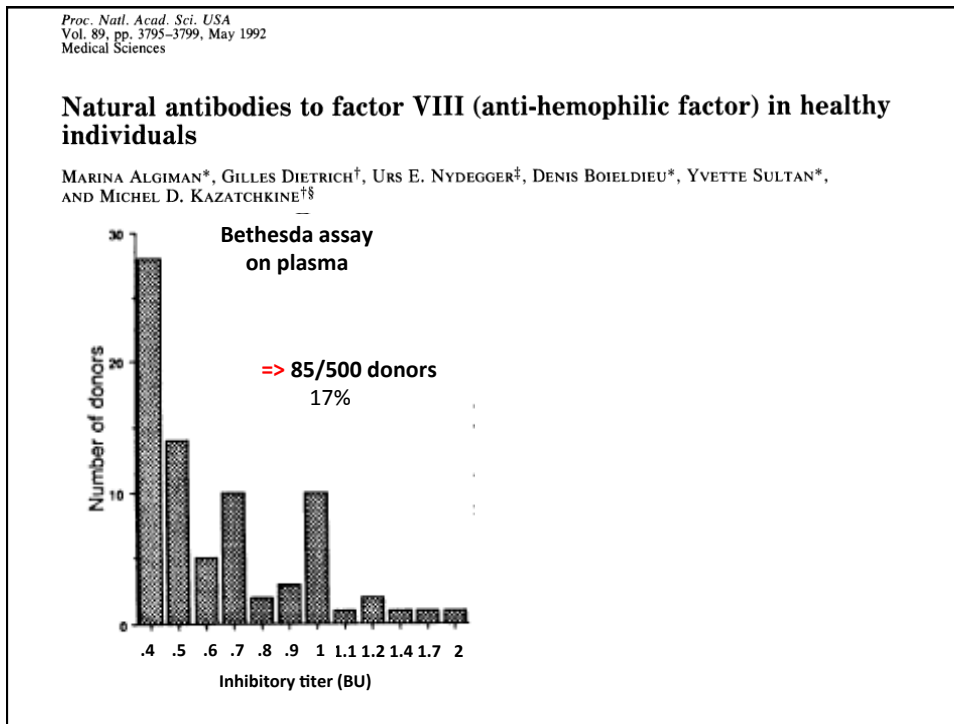
**INSERM UMRS 1138,  
Immunopathologie et  
Immunointervention Thérapeutique  
CRC - Paris, France**

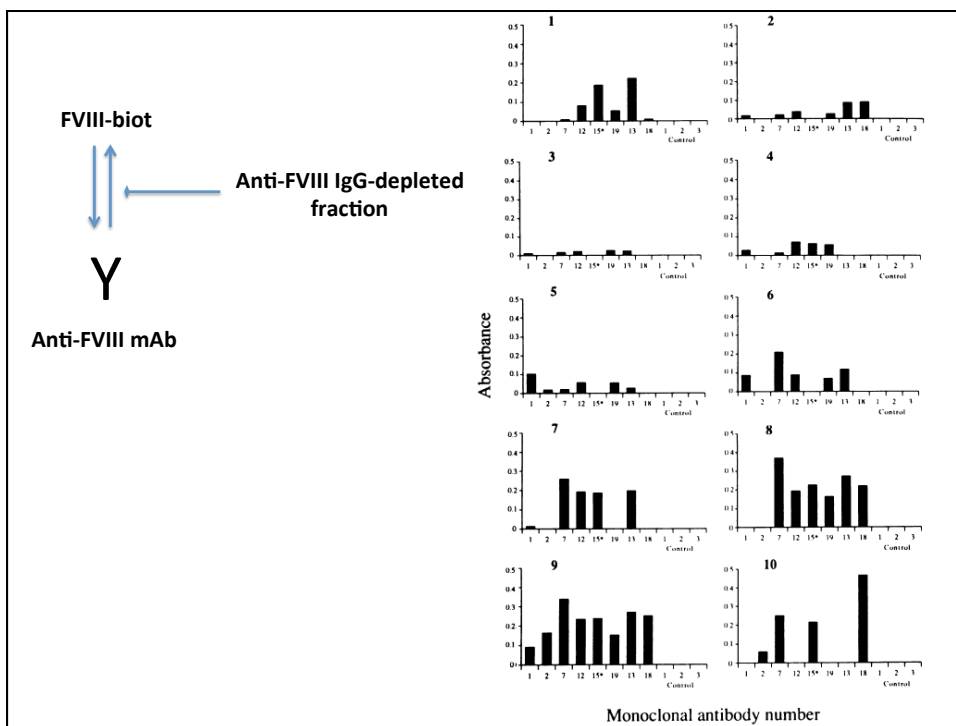
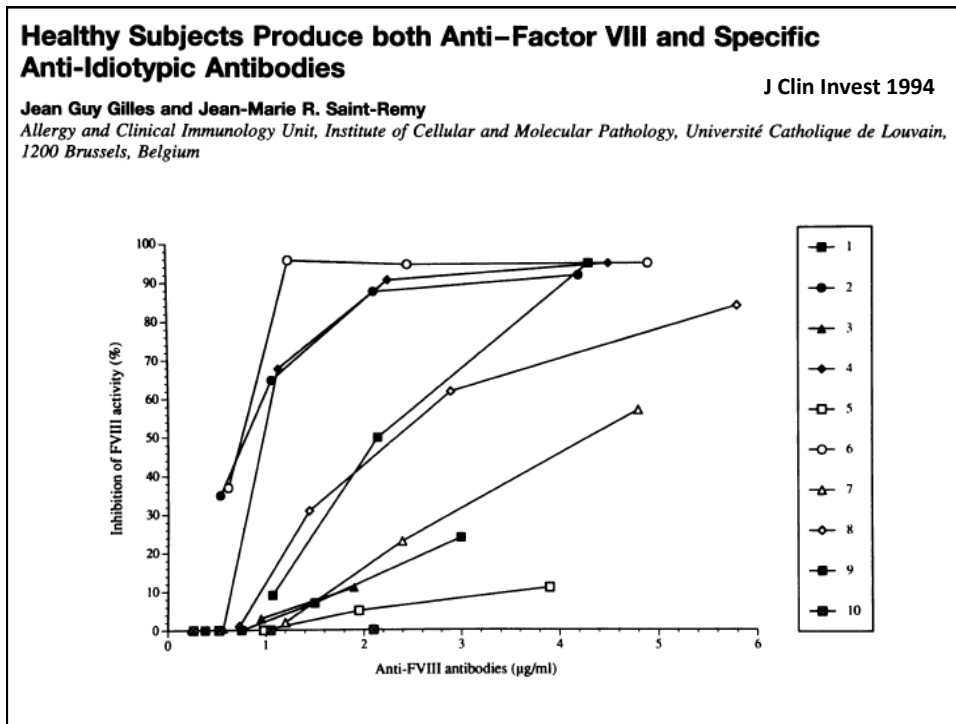
## **Horror Autoxicus**

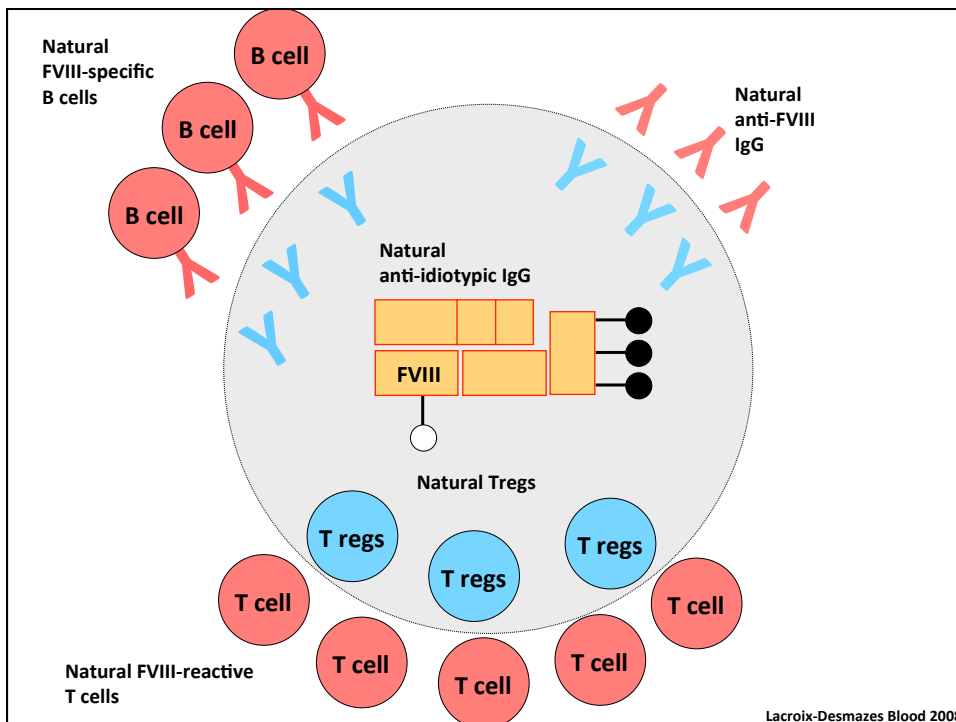
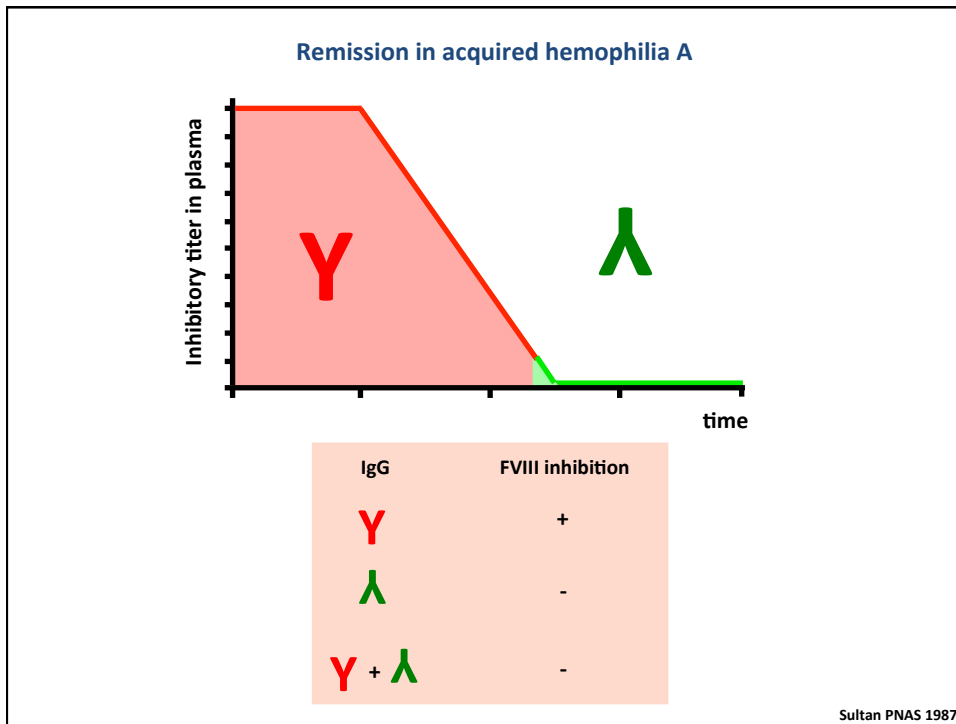
*Paul Ehrlich (1854-1915)*

Body's innate aversion to immunological self-destruction









**THROMBOSIS AND HEMOSTASIS** **Blood 2013**

**Distinct characteristics of antibody responses against factor VIII in healthy individuals and in different cohorts of hemophilia A patients**

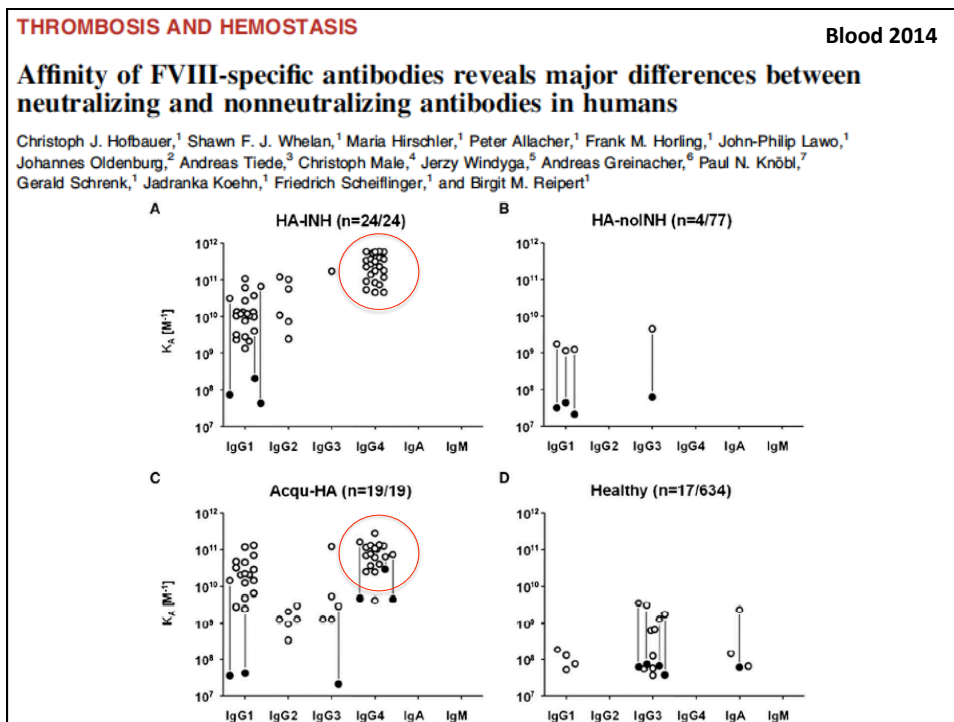
\*Shawn F. J. Whelan,<sup>1</sup> Christoph J. Hofbauer,<sup>1</sup> Frank M. Horling,<sup>1</sup> Peter Allacher,<sup>1</sup> Martin J. Wolfsegger,<sup>1</sup> Johannes Oldenburg,<sup>2</sup> Christoph Male,<sup>3</sup> Jerzy Windyga,<sup>4</sup> Andreas Tiede,<sup>5</sup> Hans Peter Schwarz,<sup>1</sup> Friedrich Scheiflinger,<sup>1</sup> and Birgit M. Reipert<sup>1</sup>

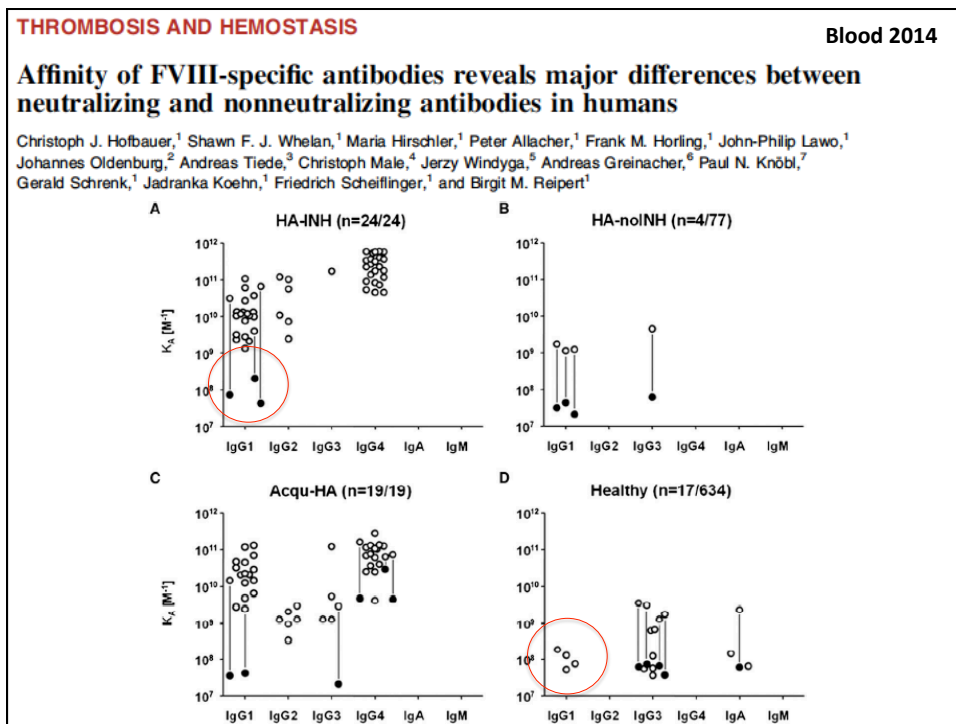
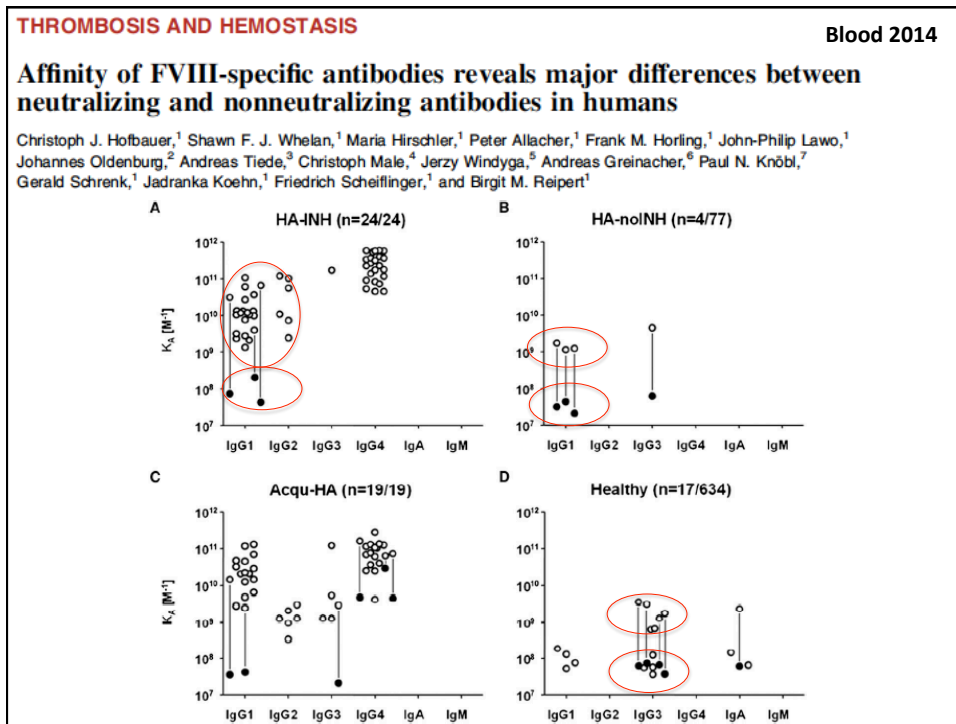
**Prevalence of FVIII-binding IgG**

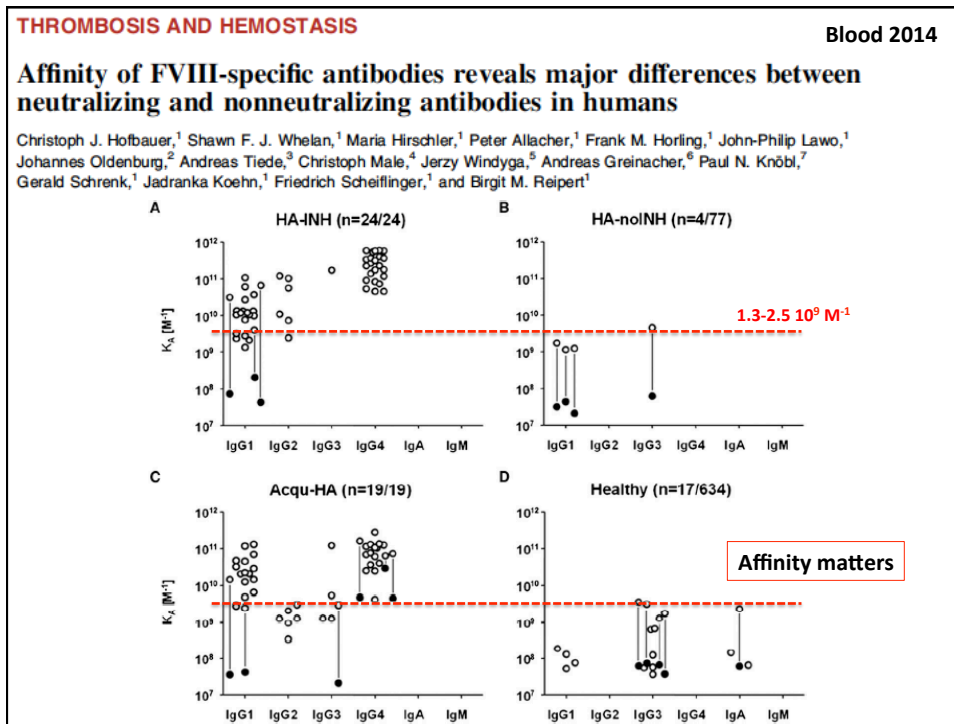
Healthy donors (#600)	19%	IgG1, IgG3, IgA	All but 1 against the B domain
Inh-negative HA patients	34%	IgG1, IgG3	
Inh-positive HA patients	100%	IgG1, IgG4	

=> suggest that FVIII-binding IgG in healthy donors are non-neutralizing

Epitope specificity matters







**Anti-FVIII allo and autoantibodies in health and disease**

**Anti-FVIII alloantibodies**

- Inhibitor-positive HA patients
- Inhibitor-negative HA PTPs
- Inhibitor-negative HA patients post-ITI

**Anti-FVIII autoantibodies**

- Acquired hemophilia A
- Healthy individuals



**Anti-FVIII allo and autoantibodies in health and disease**

**Anti-FVIII alloantibodies**

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Inhibitor-negative HA PTPs

Inhibitor-negative HA patients post-ITI

**PUPS ?**

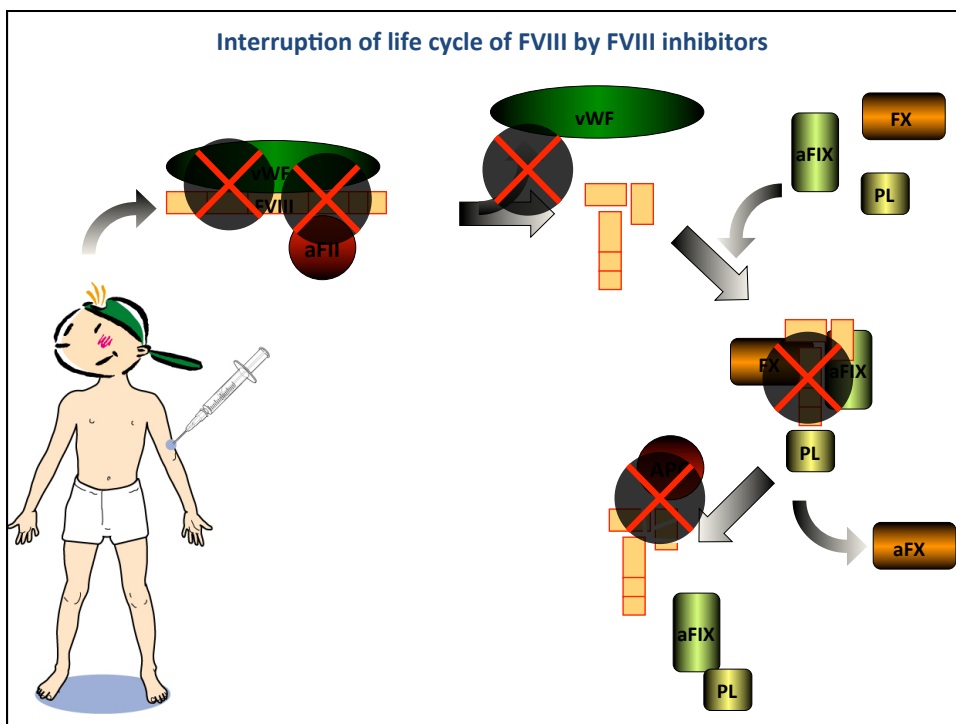
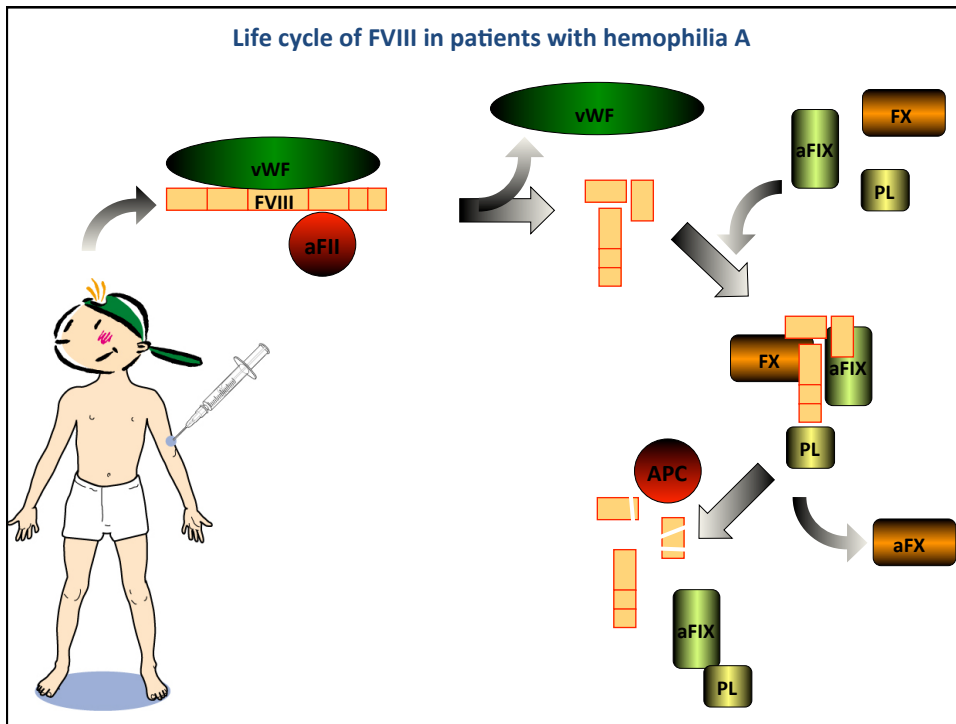
**Anti-FVIII autoantibodies**

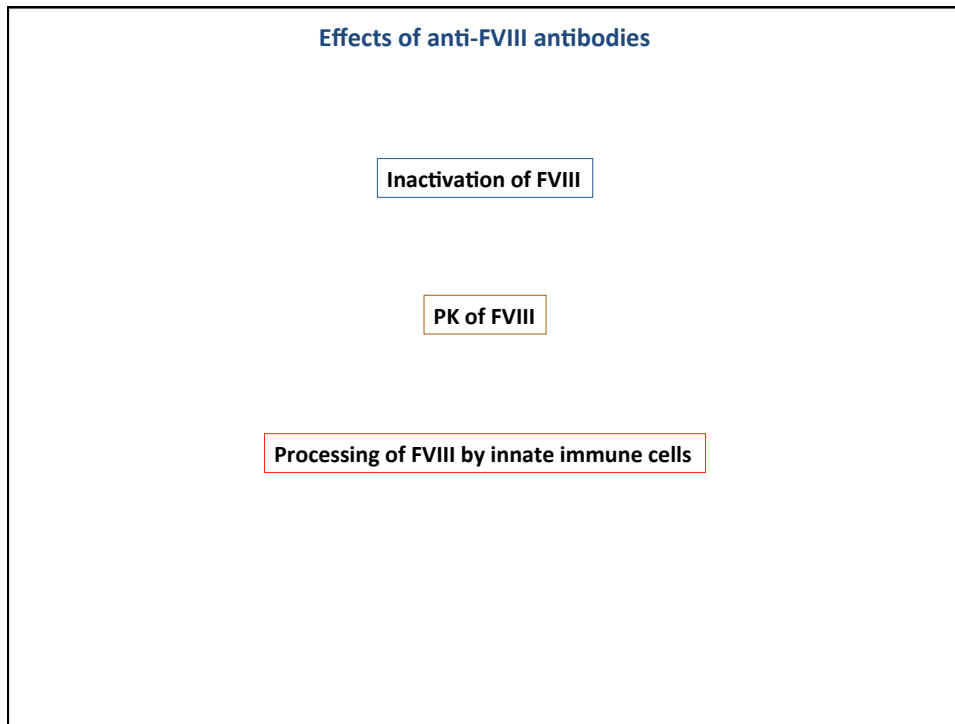
Acquired hemophilia A

Healthy individuals

**Effects of anti-FVIII antibodies**

**Inactivation of FVIII**





**ID card of anti-FVIII antibodies**

<b>Isotype</b>	<b>Binding to FcR, FcRn, to complement</b>
<b>Glycosylation profile</b>	<b>Binding to FcR, binding to other receptors (SIGLEC)</b>
<b>Epitope specificity</b>	<b>Functional epitope, B domain, VWF protected</b>
<b>Affinity (Kon/Koff)</b>	<b>As compared to other FVIII partners in coag cascade</b>
<b>Concentration</b>	

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=> Important in order to  
predict inhibitor development  
predict ITI success

