



## Increasing the therapeutic efficacy of IgG

- This technology can greatly increase the efficacy of IgG-based therapeutics by increasing IgG effector functions through the use of longlife-IgG3.
- This technology facilitates therapeutics with increased complement activation and FcγR activation compared to current IgG-based therapeutics.
- This technology is applicable to all current and future IgG-based therapeutics.

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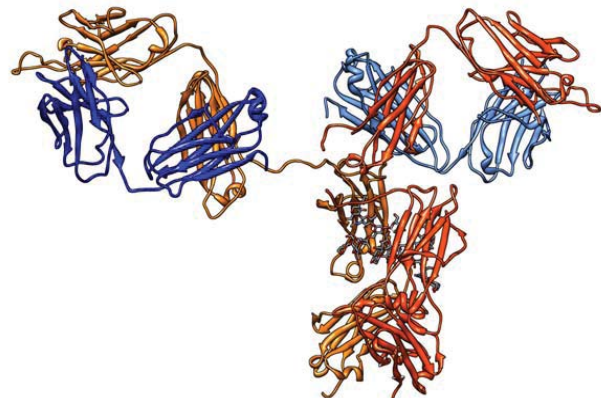
## Background

Human IgG3 displays the strongest effector functions, such as ADCC, phagocytosis or complement activation, of all human IgG subclasses, suggesting an increased therapeutic applicability over other IgG treatments. However, because of the relatively short serum half life, the effective use of human IgG3 molecules in therapy has been limited.

## The Technology

Researchers at Sanquin have recently discovered that the short half life of IgG3 is due to competition between IgG1 and IgG3 for the FcRn receptor in favour of IgG1. This results in enhanced intracellular degradation of IgG3, while IgG1 is rescued and recycled back to the serum.

Surprisingly a single amino acid substitution alleviates this competition for the FcRn receptor in favour of enhanced recycling of IgG3. Our experiments show that the serum half life of our modified human IgG3 molecules (Longlife IgG3) is increased in human patients with as much as 300%, thereby dramatically expanding the therapeutic efficacy of these molecules to levels that are comparable IgG1. We furthermore demonstrated that Longlife IgG3 retains the enhanced effector functions described for IgG3. Using this technology existing IgG based therapeutics can be adapted to significantly increase their effector functions leading to improved treatment efficacy.



Effector functions	IgG1	Longlife-IgG3
Complement	+++	++++
FcγR (ADCC/phagocytosis)	+++	++++
Half life	+++	+++

Structure and properties of Longlife-IgG3 antibodies

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## Intellectual Property

Patent application: WO/2009/089846. 9 A.D. Jul 9 A.D.  
[Direct link.](#)

## Inventors

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## Key publications

1. Bruhns P, Iannascoli B, England P et al. Specificity and affinity of human Fcγ receptors and their polymorphic variants for human IgG subclasses. *Blood*. 2009;113:3716-3725.
2. Natsume A, In M, Takamura H et al. Engineered antibodies of IgG1/IgG3 mixed isotype with enhanced cytotoxic activities. *Cancer Res*. 2008;68:3863-3872.
3. Vidarsson G, Der Pol WL, van Den Elsen JM et al. Activity of human IgG and IgA subclasses in immune defense against *Neisseria meningitidis* serogroup B. *J Immunol*. 2001;166:6250-6256.
4. Vidarsson G, van der schoot CE. Methods for increasing the therapeutics efficacy of immunoglobulin G class 3 (IGG3) antibodies. patent WO/2009/089846. 9 A.D. Jul 9 A.D.