



Design of modified immunoglobulin preparations with induced polyspecificity for passive immunotherapy of sepsis

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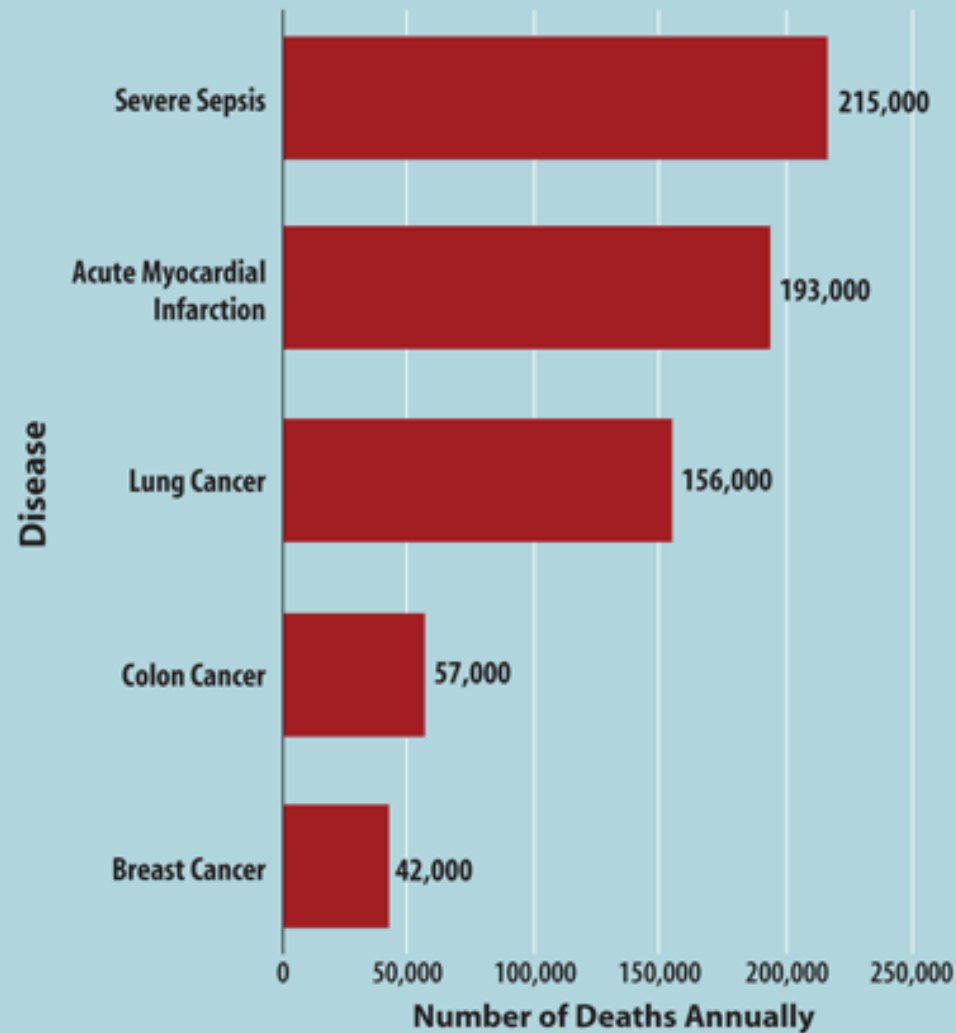
and

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How Deadly is Sepsis?

Despite advances in treatment of infectious diseases and clinical care, severe sepsis remains a major killer. U.S. mortality rates for severe sepsis exceed those for acute myocardial infarction and common cancers.



Source: www.sepsis.com

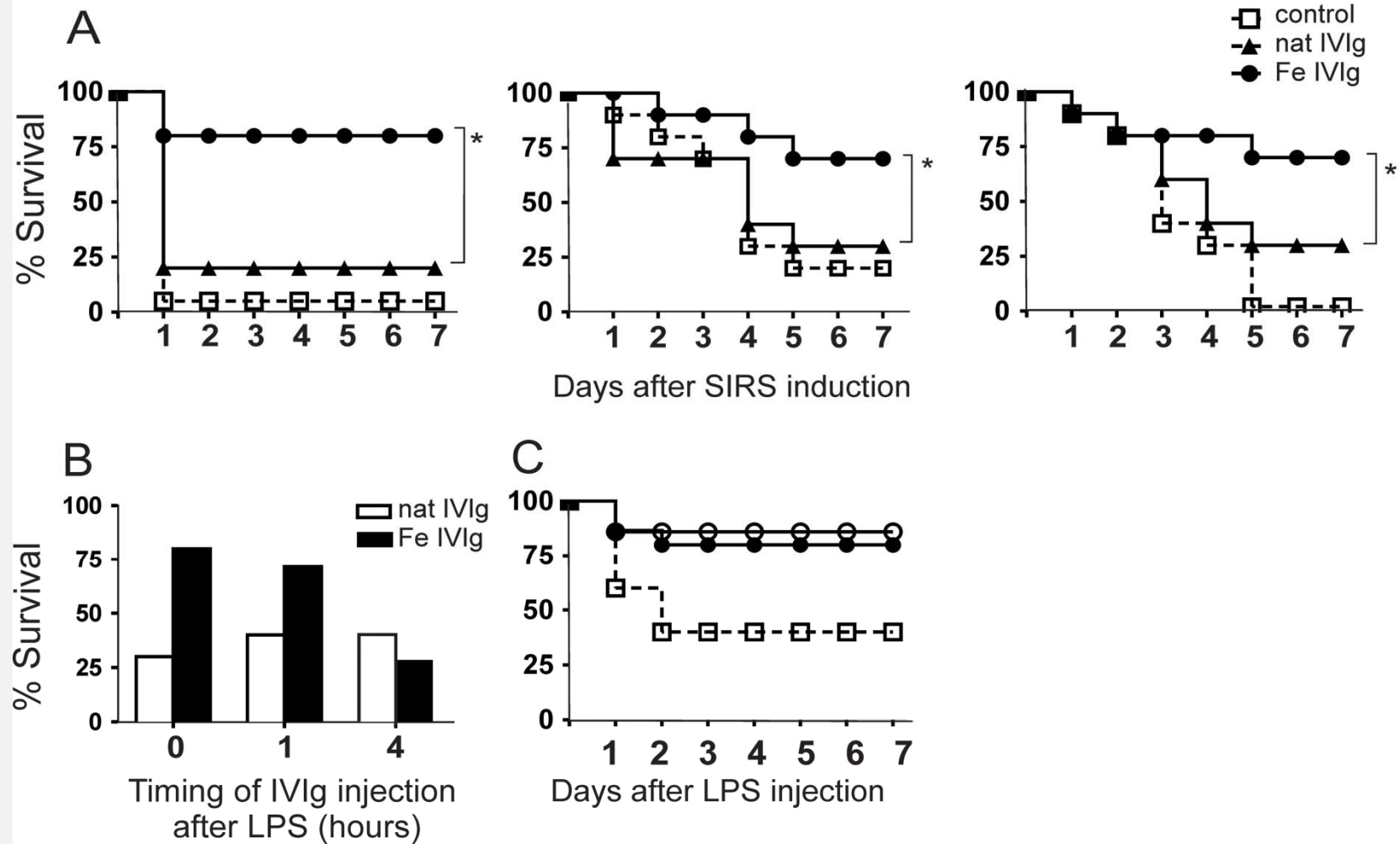
Intravenous Immunoglobulin (IVIg)

- **Therapeutic preparation of pooled normal polyspecific human IgG obtained from large numbers of healthy donors**
- **Initially used in primary and secondary immune deficiencies**
- **Effective in a number of autoantibody - mediated and T cell-mediated autoimmune and systemic inflammatory diseases**

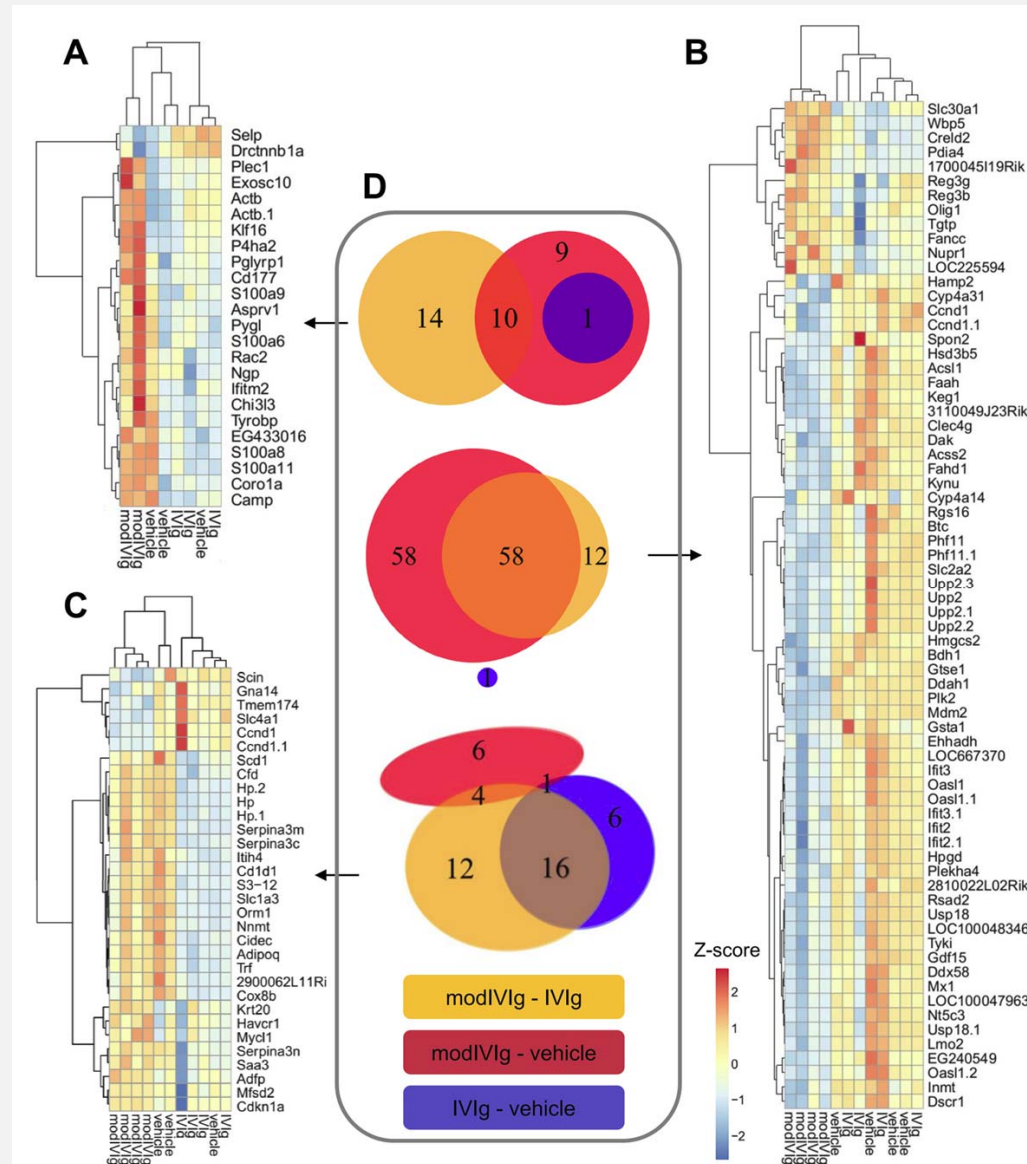
Bulgarian IVIg preparations

- **Immunoovenin (since 1981)- 60% intact IgG and 40% IgG fragments**
- **Immunoovenin-intact (since 1986) – 100% intact IgG molecules**

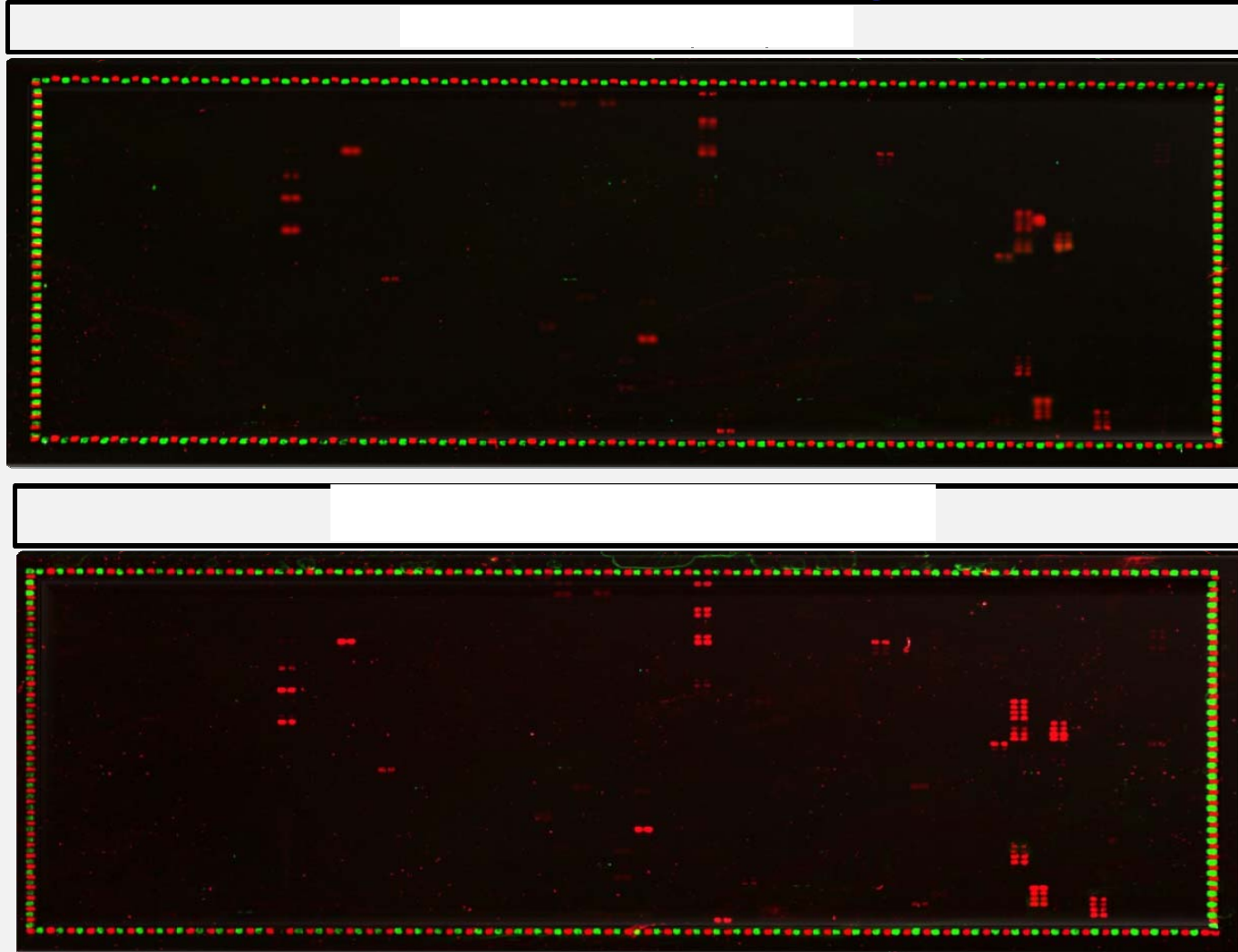
Modified IVIg is protective in experimental sepsis



Transcriptomic analysis of treated septic mice



Reactivity of native and modified IVIg to self-peptides (microarray technique)



Dissemination of results

Scientific meetings:

Results were reported at two Keystone conferences and one Gordon conference.

Publications:

1. S.v.Gunten et al. IVIg pluripotency and the concept of Fc-sialylation: challenges to the scientist. *Nat.Rev.Immunol.*, (2014), 14,1474-1475.
2. C.Schneider et al. Key features of the human IgG anti-carbohydrate repertoire revealed by integrative systems level analysis. *Nat.Immunol.* (submitted).
3. I.Djoumerska-Alexieva et al. Intravenous immunoglobulin with additionally enhanced polyspecificity improves survival in experimental sepsis and aseptic SIRS. (submitted)

Patent:

- 1 European patent - registered in 9 countries

Organization/Cooperation

- The Swiss P.I. visited us in in December 2012
- A Swiss Ph.D. student came to Sofia to learn new experimental techniques (February 2014)
- A visit of a Bulgarian Ph.D. student to Bern is planned
- At least weekly phone calls and e-mail exchanges.

Lessons learned/Problems encountered

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