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Toxicity of Major Histocompatibility Complex Class II Specific Monoclonal Antibodies: Audietur et Altera Pars

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Aim. To investigate whether in vivo toxicity of class II major histocompatibility complex (MHC) specific monoclonal antibodies (mAb) is contributed by mAb's constant region binding to Fc receptor (FcR).
Methods. Laboratory mice were injected intravenously (i.v.) with class II MHC-specific mAb of various isotypes and respective antigen-binding fragments, and their clinical status was observed subsequently.
Results. All anti-class II mAb of the IgG2a isotype exhibit acute toxicity, manifested in severe lethargy and a frequent death. No adverse effects were observed after the FcR-binding capability of the toxic mAb was eliminated via deletion or mutation of its Fc segment.
Conclusion. In vivo toxicity of anti-class II mAb appears to be the consequence of the crosslinking of class II+ cells with cells expressing FcR.

Key words: antibodies, monoclonal; antibodies, toxicity; Fc fragments; immunosuppression; isotype switching; MHC class II genes; mice, transgenic