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Assessment of antibody-FcRn receptor interaction using affinity CE-MS

Christoph Gstöttner[a], Dietmar Reusch[b], Manfred Wuhrer[a], Markus Haberger[b], Elena Domínguez-Vega[a]*

[a]Leiden University Medical Center, Center for Proteomics and Metabolomics, The Netherlands.

[b]Pharma Technical Development Penzberg, Roche Diagnostics GmbH, Penzberg, Germany.

The half-life of antibodies is determined by their binding to the neonatal Fc receptor (FcRn). This binding is strongly influenced by the structural features of the Fc domain and, therefore, small variations in the Fc region can severely impact their binding. Common binding techniques such as SPR, provide an overall affinity response for all different antibody proteoforms and assessment of their individual binding require tedious production or enrichment of specific proteoforms. We have developed an approach based on CE-MS to study relative affinities of antibody proteoforms with FcRn. To this end the FcRn receptor was added to the background electrolyte whereas the mixture of antibody proteoforms were injected in the CE. Differences in the mobility were observed for singly and doubly oxidized antibodies with respect to the unmodified counterparts indicating lower binding affinity. Furthermore, hyphenation with MS permitted to monitor the antibody-FcRn complex and to study the influence of receptor heterogeneity in the binding.