Thomas Böldicke, J Clin Cell Immunol 2018, Volume 9
DOI: 10.4172/2155-9899-C2-050

9TH EUROPEAN IMMUNOLOGY CONFERENCE ASSOCIATED WITH ANTIBODY ENGINEERING MEETING

June 14-16, 2018 | Rome, Italy

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ER-intrabody mediates knockdown of mouse IFN alpha in macrophages and dendritic cells

IFN-α activates the transcription of various IFN-stimulated genes (ISGs) in virus infected cells. Proteins encoded by ISGs block viral transport into the host cell and inhibit viral gene transcription and translation. Due to the existence of 13 different high homologous isoforms of mouse IFN-α, an IFN-α knockout mouse has not yet been established by conventional knockout strategies and CRISPR/Cas. We used an IFN-a knockdown strategy based on ER-intrabodies to inhibit IFN-a secretion in macrophages and dendritic cells, the main producers of IFN-α after virus infection. To realize this strategy an ER intrabody was constructed from an anti-mouse IFN-α rat hybridoma recognizing 5 mouse IFN-α isoforms. We follow the hypothesis that an intrabody recognizing 5 high homologous isoforms of the proteins will be able to knockdown all isoforms. The secretion of IFN-α was significantly inhibited by the intrabody in stable intrabody expressing RAW 264.7 macrophages and D1 dendritic cells as demonstrated by ELISA, Mx2-dependent luciferase assay and immunofluorescence. This antibody has the potential to knockdown IFN-α in transgenic intrabody mice. These animals must be very valuable in the future to study in detail the role of IFN-α during active- and chronic viral infections and in autoimmune diseases.

Biography

Thomas Böldicke received his PhD 1982 at the Max-Planck-Institute of Molecular Genetics, Berlin. He started his career as Post doc at the German Research Centre for Biotechnology (GBF, Brunswick) in the Department of Genetics and Cell Biology by John Collins. Now he is Senior Scientist at the Helmholtz Centre for Infection Research (HZI, former GBF) and project leader intrabodies. In 2011, he qualified as a Professor in Molecular Biology and Cell Biology at the Technical University of Braunschweig. He is an expert in generating mouse and human hybridomas and in selecting and modifying recombinant antibodies. In the last decade he focused on the construction and characterization of intracellular antibodies. He has published 35 manuscripts

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