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Recent highlights of *in vivo* knockdown by intrabodies

Thomas Boldicke
Helmholtz Centre for Infection Research, Germany

Intracellular antibodies (intrabodies) are targeted into a cell expressing the corresponding antigen, binding of the intrabody to the antigen results in inhibition of protein function. The advantages of high specificity, no off target effects and targeting of post translational modifications are the reasons that such molecules are very valuable in functional genomics. Two developments will boost the intrabody technology in the future: Cytoplasmic intrabodies can be stable expressed as single domain antibodies, mostly from camels. Alternatively, the construction of human VL and VH domains is ongoing. The single domain antibody approach is an effective alternative to other approaches for selection of stable cytoplasmic intrabodies such as the Intracellular Antibody Capture Technology (IACT) based on the yeast two hybrid system and Complementarity Determining Region (CDR) grafting or introduction of synthetic CDRs in stable frameworks. ER intrabodies: Selection of recombinant antibody fragments by *in vitro* display systems mainly phage and yeast display. One cloning step is sufficient to express scFv fragments as ER intrabodies. Most promising are these intrabodies retaining proteins passing the ER. Recently we demonstrated in mice a delay of metastasis of rhabdomyosarcoma tumor cells mediated by two specific intrabodies retaining two polysialyltransferases inside the ER. Finally transgenic ER intrabody mice have been generated. An intrabody mouse expressing an anti-VCAM intrabody is not lethal in comparison to the genetic knockout counterpart. 30% of genetic knockouts are lethal; therefore intrabody knockdown mice will be very useful in case the genetic knockdown is embryonically lethal.

Biography

Thomas Boldicke has completed his PhD at the Max Planck Institute for Molecular Genetics in Berlin. He has been working for 25 years in the field of recombinant antibodies particularly intrabodies. He has published more than 20 papers in reputed journals.