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Anti-Citrulline Antibody as Novel Therapeutic Drug in early Rheumatoid Arthritis

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ModiQuest developed a novel treatment for Rheumatoid Arthritis (RA), which prevents the onset and exacerbation of the disease.

For the development of this novel therapy, we focussed on more RA specific targets like Deiminated Peptide-Epitopes (DPE). Deimination is the posttranslational modification of arginine into citrulline residues induced by peptidyl-arginine deiminases that are released in the inflamed joints from dying cells. A growing number of studies indicated that these modifications could be responsible for the initial triggering of autoimmunity and the breaking of tolerance.

We identified a subset of rCit-hMabs that were capable of preventing the onset of inflammation in both CIA and CAIA animal models. When mild inflammation was present, administering the rCit-hMabs resulted in stabilization of the inflammation and prevented further increase of the inflammatory response. Histological analysis of the inflamed joints revealed, that bone damage was strongly prevented, as compared to control animals. To identify the epitopes recognized by the rCit-hMabs, we performed IP, followed by MS-analysis on post-lytically huPAD4 deiminated human 293F cells. The main DPE recognized by the rCit-hMabs was used to generate new therapeutic Mabs. Introduction of these novel rCit-hMabs in the CAIA model proved them to be potent inhibitors of the inflammatory response.

Conclusion: ModiQuest has developed a family of novel rCit-hMabs which have strong therapeutic potential in regard to preventing: 1) the onset of the inflammation, 2) joint damage during inflammation, 3) further increase of inflammation and swelling, 4) inflammation relapse and tissue/joint damage to occur.

The availability of the previously developed diagnostic test for RA, detecting RA up to 10 years before onset of the disease, makes this novel therapeutic approach of special interest for early stage RA. In a more progressive form of RA a combination therapy might be possible with existing biologicals that have different mechanisms of action.

Biography

Jos established ModiQuest Research and its sister company, ModiQuest B.V focusing on the development of novel therapeutics for autoimmune diseases in 2004. He has been involved in scientific research for more than 15 years, with over 46 publications from work at the University of Nijmegen, the Wellcome/CRC Institute in Cambridge (UK), and at the University of Minnesota, in Minneapolis (USA). Currently he also holds a guest appointment as Assistant Professor of Biomolecular Chemistry at the University of Nijmegen (The Netherlands). He has initiated and managed various combined projects of university research groups and commercial enterprises, including a new diagnostic target for rheumatoid arthritis (CCP), which has been developed into a highly sensitive early diagnostic test for RA (anti-CCP test).

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