New Single-Chain Variable Fragment as a drug to treat Alzheimer's Disease

THE INVENTION

New elongated Single-Chain Variable Fragments (scFv) of the antibody Bapineuzumab show their efficiency for Alzheimer's disease (AD) treatment at low dosage avoiding adverse side effects. We are seeking a company partner to commercialize this licensing opportunity.

Innovative aspects and advantatges

> We have identified 3 new ScFv elongated mutants of Bapineuzumab as a new approach to treat AD by driving $A\beta_{1-42}$ oligomers to the non-toxic pathway.

> ScFv Elongated mutants at low dosage might avoid the adverse side-effects of bapineuzumab maintaining the same level of efficiency for AD treatment.

> The ScFv Wild Type of Bapineuzumab at low dosage has shown high efficiency in the 3xTg-AD mice model (n=15).

> Elongation of ScFv to treat other diseases could be a useful tool to improve results.

IP Rights

PCT application, 16th May 2014.

Scientific Team

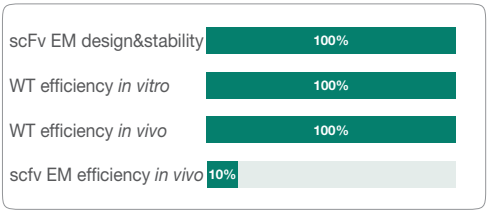
Sandra Villegas leads the scientific team specialized in Protein Folding and Stability in the field of Biomedicine. The research group belongs to the Biochemistry and Molecular Biology Department of the UAB.

Summary

At present, there is no cure for Alzheimer's disease and 44 M people suffer from it. By 2030, this figure will increase to 76 M and by 2050 could exceed 135 M people (Source: Alzheimer's Disease International). To date the most promising approach is ß (Aß) immunotherapy however Bapineuzumab (mAb) failed in phase 3 trial due to dose-related adverse side-effects.

We have designed 3 new scFv elongated mutants (scFv EM) of Bapineuzumab (*mAbs 5:5, 678-689 ,2013*). This elongation of the C-terminal region of the VL domain shows high thermodynamic stability and lower aggregation tendency (Fig 1). These mutants allow the increase of specific interaction between scFv and $A_{\beta 1-42}$ Oligomers maintain the same ability of mAb to remove $A\beta_{1-42}$ Oligomers and drive them to the *Worm-like fibrils pathway*, the non-toxic pathway. The same efficiency of the original fragment (WT) at low therapeutic dosage has been demonstrated in vitro and in vivo providing benefit (*Biochem. J. (2011) 437, 25-34; mAbs (2013) 5:5, 665-677; mAbs (2013) 5:5, 660-664*). The next efficiency results of scFv EM in vivo are expected to the end of the year.

State of Development



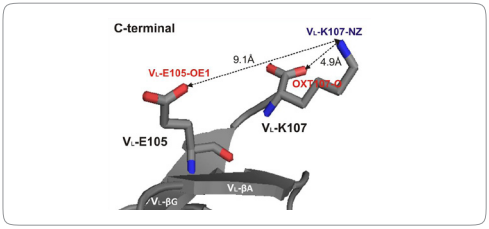


Fig. 1 C-terminus detail of ScFv showing the main interaction between VL-E105 and VLK107. Mutants: VL-el-R108G, VL-el-R108, VL-el-R108T109

UAB Research Park

Contact
Maite Ibern · UAB Technology Transfer Office
Maite.Ibern@uab.cat · T. +34 935 868 922