Regenerative potential of M2-polarized anti-inflammatory macrophages in the context of inflammation-based neurodegeneration in a model of APPβ+ Alzheimer disease

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Abstract

Lately, there is accumulating evidence evidence for silent inflammation as a major contributor to Alzheimer Disease (AD), associated as one potential underlying pathomechanism. This includes innate immunity, specifically M1-polarised inflammatory macrophages which trespass the blood brain barrier. Using wild-type and amyloid precursor protein β protein transduced mice we compared the cognitive abilities of four different experimental groups (n=8). 1. Wild type mice (not transduced with APPβ), 2. APPβ+ animals treated with saline, 3. APPβ+ mice treated with radiated (7 gy) REMs (M2-polarized anti-inflammatory macrophages), and 4. APPβ+ mice treated with non-radiated REMs. REMs (radiated and non-radiated) were injected intravenously into APPβ+ animals at the age of 2 months. Cognitive capacity was tested using a water-maze and labyrinth test model, at the age of two months (young mice) and at 6 months (old mice) of age. We found a significant reduced capacity of learning and orientation capacities in all four groups when comparing young and old mice. There was a significant cognitive decline when comparing wild-type animals with APPβ+ animals treated with saline ($p<0.01$) or radiated REMs ($p<0.01$). Treatment with non-radiated REMs prevented the development of AD in all 8 animals tested whose cognitive functional scores did not differ significantly from wild-type animals. In a pilot observation n=7 Alzheimer patients were treated with autologous REM´s generated from patient's monocytes. Based on MMSE (MINI-Mental-State-Examination) n=4 patients had an improvement of the cognitive activity. Our results indicate that the anti-inflammatory properties of regenerative M2-polarized REM macrophages is able to prevent astrocyte and microglial activation in APPβ+ animals and underscores silent inflammatory-based neuronal damage as a major pathomechanism in this animal model. Additionally, first clinical results show that this cellular therapy has a positive effect on the cognitive activity of Alzheimer patients.

Biography:

Prof. Fändrich is acknowledged for his pioneer work on using M2-polarized anti-inflammatory macrophages in allogeneic and autologous settings for tolerance induction in kidney transplantation and age-related diseases including neurodegenerative diseases, respectively. Prof. Fändrich chairs the Dept. of Applied Cellular Medicine which was established in 2008 at the University UKSH, Campus Kiel, with the focus to translate basic acaedemic research in the field of cellular medicine into clinical application.

Speaker Publications:

1. "The neuropathology of alcohol-related braindamage. Alcohol Alcohol"; 2009, 44:136-140.
2. "Pharmacological treatment of alcohol dependence: Target symptoms and target mechanisms. Pharmacology and therapeutics"; 2006, 111:855-876.
3. "Acutealcohol intoxication potentiates neutrophil-mediated intestinal tissue damage after burn injury Shock"; 2008, 29:377.

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