BLOOD DERIVED MONOCYTIC CELLS REPOPULATE MICROGLIA DEPLETED MOUSE BRAINS AND MAINTAIN A MACROPHAGIC MORPHOLOGY

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In Alzheimer's disease (AD) microglia are found in close vicinity to beta-Amyloid (A beta) plaques, which are one of the pathological hallmarks of the disease. Recently, we have shown that almost complete ablation of resident microglia in mouse models of cerebral amyloidosis does not alter the formation or maintenance of A beta deposits (Grathwohl et al., Nature Neuroscience, 2009 Nov;12(11):1361-3). Numerous studies have indicated that in transgenic mouse models of cerebral amyloidosis blood-derived monocytic cells (BDMC) can enter the brain and migrate to areas of A beta deposition. However, the exact role of BDMC in AD pathogenesis and progression remains elusive. A novel method of repopulating the brain with BDMC in the absence of resident microglial cells was developed. Thereby, CD11b-HSVTK (TK mice) are exposed to the toxic thymidine analog Ganciclovir (GCV) for two weeks to ablate microglia. Upon discontinuation of GCV treatment, infiltrating BDMC rapidly repopulate the brain. Following complete repopulation BDMC distribute evenly throughout the brain and maintain a ramified morphology different from resident microglial cells. When TK mice were bred to APPPS1 transgenic mice a similar brain invasion of BDMC was observed in response to microglia ablation. Surprisingly, infiltrating BDMC did not migrate towards newly formed or existing A beta plaques in APPPS1/TK mice. We provide a new experimental approach to investigate the effect of BDMC in brain function and neurodegenerative disease. Our data suggest that without further activation BDMC reveal a limited role in cerebral amyloidosis of APPPS1 transgenic mice.