Dokumenttyp: journal article

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Titel des Beitrags: Anti-CD20 B-cell depletion enhances monocyte reactivity in neuroimmunological disorders.

Abstract: Clinical trials evaluating anti-CD20-mediated B-cell depletion in multiple sclerosis (MS) and neuromyelitis optica (NMO) generated encouraging results. Our recent studies in the MS model experimental autoimmune encephalomyelitis (EAE) attributed clinical benefit to extinction of activated B-cells, but cautioned that depletion of naïve B-cells may be undesirable. We elucidated the regulatory role of un-activated B-cells in EAE and investigated whether anti-CD20 may collaterally diminish regulatory B-cell properties in treatment of neuroimmunological disorders. Myelin oligodendrocyte glycoprotein (MOG) peptide-immunized C57Bl/6 mice were depleted of B-cells. Functional consequences for regulatory T-cells (Treg) and cytokine production of CD11b+ antigen presenting cells (APC) were assessed. Peripheral blood mononuclear cells from 22 patients receiving anti-CD20 and 23 untreated neuroimmunological patients were evaluated for frequencies of B-cells, T-cells and monocytes; monocyctic reactivity was determined by TNF-production and expression of signalling lymphocytic activation molecule (SLAM). We observed that EAE-exacerbation upon depletion of un-activated B-cells closely correlated with an enhanced production of pro-inflammatory TNF by CD11b+ APC. Paralleling this
pre-clinical finding, anti-CD20 treatment of human neuroimmunological disorders increased the relative frequency of monocytes and accentuated pro-inflammatory monocyte function; when reactivated ex vivo, a higher frequency of monocytes from B-cell depleted patients produced TNF and expressed the activation marker SLAM. These data suggest that in neuroimmunological disorders, pro-inflammatory APC activity is controlled by a subset of B-cells which is eliminated concomitantly upon anti-CD20 treatment. While this observation does not conflict with the general concept of B-cell depletion in human autoimmunity, it implies that its safety and effectiveness may further advance by selectively targeting pathogenic B-cell function.

Zeitschriftentitel / Abkürzung: J Neuroinflammation

Jahr: 2011

Band: 8

Seiten: 146

Sprache: eng


TUM Einrichtung: Neurologische Klinik und Poliklinik; r Medizinische Statistik und Epidemiologie; III. Medizinische Klinik und Poliklinik

Occurences:
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > III. Medizinische Klinik und Poliklinik (Hämatologie / Onkologie) > 2011
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Neurologische Klinik und Poliklinik > 2011
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Institut für Medizinische Statistik und Epidemiologie > 2011

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