תוכנית מנחים עמיתים

משרד החינוך
המינהל הפדגוגי
האגף למחוננים ולמצטיינים

מכון הנרייטה סאלד
המכון הארצי למחקר במדעי ההתנהגות

שימוש בתאי CAR-T מפציפיים ל-MOG להפחתת אקטיבציה של תאי T DR2 מפציפיים ל-MBP

Use of MOG Specific CAR-T Cells to Reduce MBP/DR2 T Cells Activation

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הפקולטה לביולוגיה, הטכניון, חיפה

Subject

Use of MOG Specific CAR-T Cells to Reduce autoreactive MBP/DR2 T Cells Activation.

Aim

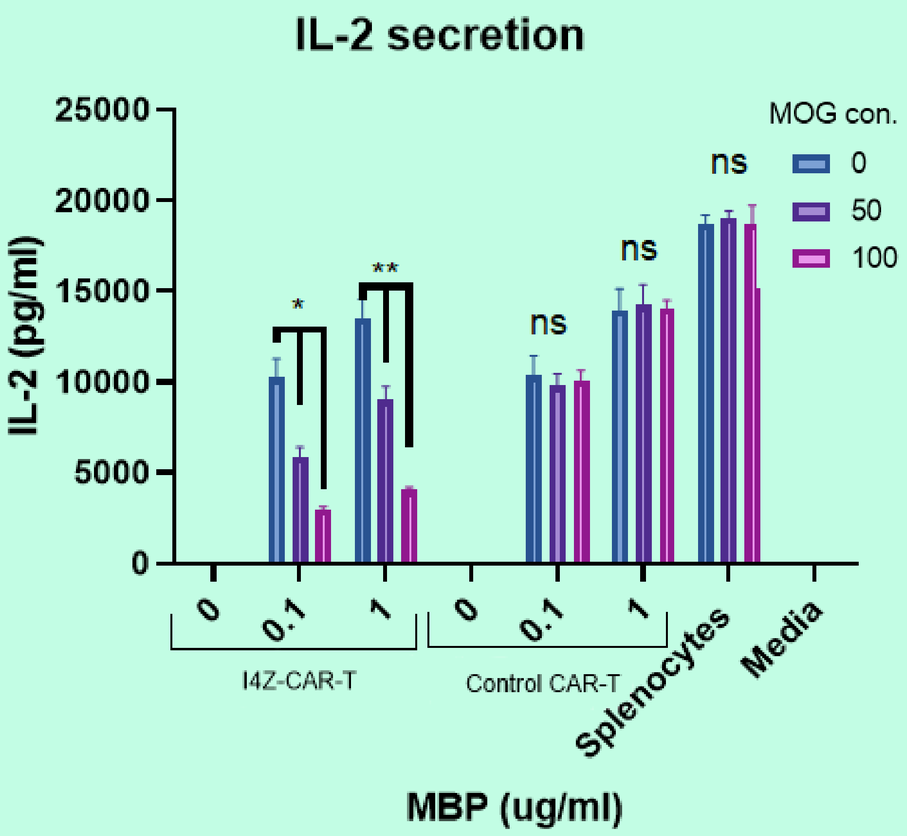
Reduce MBP/DR2 autoreactive T cell activation, by targeted elimination of myelin peptide presenting APCs, using MOG/DR2 specific CAR-T cells.

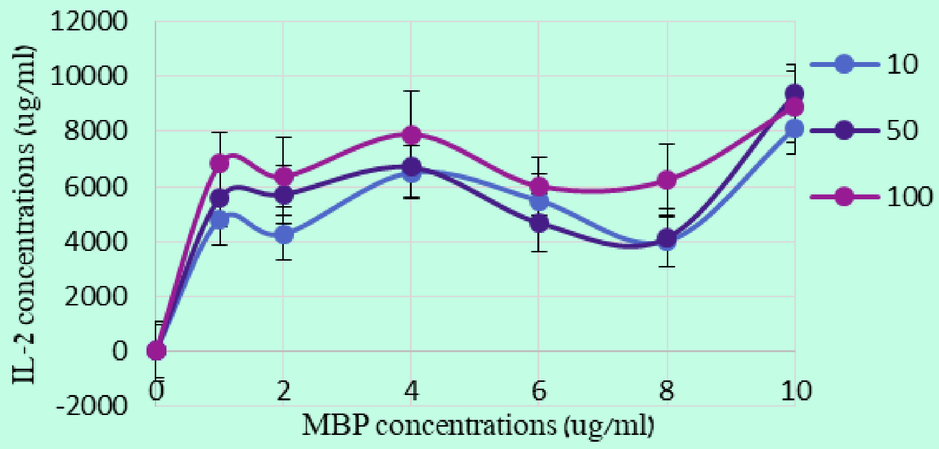
Abstract

Multiple sclerosis is a chronic-demyelinating disease of the central nervous system. MS is generated by myelin-specific auto-reactive T-cells that infiltrate the CNS and mediate an inflammatory response against the myelin sheath. As disease progresses, new myelin antigens are presented by APCs (epitope spreading), leading to subsequent activation of newly infiltrated T cells, targeting different myelin peptides like MOG and MBP.

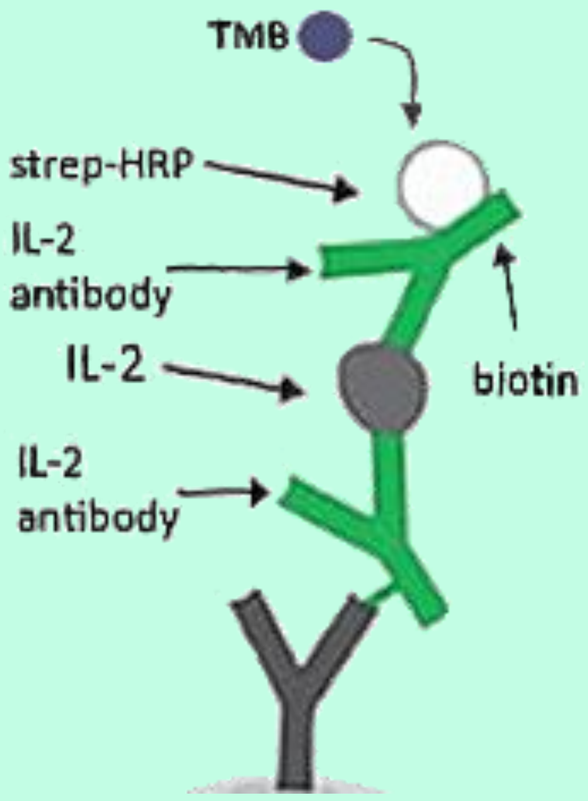
Methods

Using ELISA assay, we tested supernatant IL-2 concentration, secreted by activated MBP/DR2 autoreactive T cells, in the presence of MBP loaded APCs.





Autoreactive MBP/DR2 T cells and APCs were incubated with CARs either I4-Z or MUC1 and with different concentrations of MOG and MBP. IL-2 concentrations were measured using ELISA assay.



An ELISA

Autoreactive MBP/DR2 T cells and APCs were incubated for 48h with different concentrations of MBP and MOG peptides. IL-2 was secreted by activated autoreactive T cells and measured using ELISA assay.

Results

1. Autoreactive T cells exhibit high IL-2 secretion, in response to a wide range of MBP loading concentration.
2. I4Z MOG/DR2 targeting CAR-T cells reduced MBP/DR2 autoreactive T cells activation.

Discussion

We suggest to specifically inhibit the activation of myelin targeted autoreactive T cells, by reducing the presentation of myelin peptides on APCs, using MOG/DR2 directed CAR T cells. As showed, MOG/DR2 specific CARs reduced autoreactive T cells activation, suggesting a specific method to eliminate epitope spreading phenomenon during an autoimmune response. The usage of CARs to target specific myelin peptides should be furthered explored and treatment of other autoimmune diseases that are affected by the spreading of self-antigens with peptide-specific CAR T cells should be further studied.