Methods: Peripheral and tonsillar T cell and B cell from healthy controls were purified. The biotinylation of Abatacept was used to study its binding on T and B cells by flow cytometry and confocal microscopy. A well-established co-culture model between CpG-stimulated B cells and anti-CD3/anti-CD28 stimulated T cells was set up in which Abatacept or anti-IgG control was added to evaluate any change in B cell regulatory functions. Activation markers (e.g. CD25, CD69, CD40, CD152) and regulation markers (e.g. FoxP3, TGF-β) were assessed by flow cytometry. Similar analysis were also performed on rheumatoid arthritis patients before and three months after Abatacept therapy. All patients gave their informed consent.

Results: Abatacept increases the inhibition of T cell proliferation by B cells compared to IgG control in the co-culture model (p<0.03). Interestingly, alone, Abatacept does not modify T cell proliferation. This can be explained by the increase in IL-10 and TGF-β producing B cells and the CD152 expression. Abatacept is able to bind B cells at day 0 of co-culture and T cells at day 4.5 of co-culture. Abatacept has a direct effect on B cells by increasing the CD25 (p<0.03) and CD152 (p<0.02) expression (p<0.02) reflecting a higher activation level. Nevertheless, Abatacept had no direct effect on B cell proliferation. In RA patients, the treatment with Abatacept resulted in an increased regulation of T cell proliferation and this effect is related to a higher percentage of IL-10 secreting B cells 3 months after the therapy (p<0.03).

Conclusions: In our in vitro and in vivo models, Abatacept has a direct effect on B cells leading to an increase capability of regulation of T cell proliferation which directly linked to higher production of IL-10 and TGF-β.

REFERENCES:

Disclosure of Interest: None declared