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► **To cite this version:**

Elodie Picarda, Ignacio Aneon, Carole Guillonneau. Alloantigenic recognition properties of CD8+ regulatory T cells. 6th european workshop on immune-mediated inflammatory diseases, Nice, France. BioMed Central, 9 (Suppl 2), pp.P29, 2011. <inserm-00643968>

**HAL Id: inserm-00643968**

**<http://www.hal.inserm.fr/inserm-00643968>**

Submitted on 23 Nov 2011

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POSTER PRESENTATION

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# Alloantigenic recognition properties of CD8<sup>+</sup> regulatory T cells

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From 6th European Workshop on Immune-Mediated Inflammatory Diseases  
Nice, France. 23-25 November 2011

## Background

We recently reported that in a rat major histocompatibility complex (MHC) mismatched heart allograft model, treatment with CD40Ig, a chimeric molecule that blocks CD40L, leads to indefinite allograft survival mediated by CD8<sup>+</sup>CD45RC<sup>low</sup> Tregs [1]. Although essential, the exact role of TCR/MHC/peptide interaction in Treg activity is still unknown. We therefore characterize the allogeneic peptide(s) recognized and the TCR usage of the CD8<sup>+</sup>CD45RC<sup>low</sup> Tregs.

## Material and methods

Allogeneic peptide(s) were derived from polymorphic regions of donor MHC molecules [2,3]. Sixty-two overlapping peptides of sixteen amino acids (aa) were tested in a coculture of Tregs with syngeneic pDCs (ratio 4:1). Moreover, the repertoire of the TCR of the CD8<sup>+</sup> Tregs was studied by flow cytometry analysis and sequencing the CDR3 region.

## Results

After six days of culture, two peptides in particular led to the activation of Tregs, as shown by the upregulation of the CD25 molecule (from 25.89% to 29.27% of CD25 expression). These activator peptides were characterized by prominent amino acids (aa) at rather central position, which could result in a large TCR repertoire diversity of the specific Tregs. We showed previously that CD8<sup>+</sup>CD45RC<sup>low</sup> Tregs expressed a specific altered V 11 repertoire, with the same CDR3 length in all animals (9 aa). This upregulation was confirmed at the protein level, since 19.9±3.7% of Tregs from a CD40Ig-treated animal expressed the V 11 chain compared to 6.1±2.3% in naïve ones. Sequencing of 160 clones of V 11 TCRs from six long-surviving animals suggested a preferential use of a

aa long CDR3 and a particular J region (J 1.6). Interestingly, conserved sequences were frequently found but no common clonotype was shared between animals, suggesting the private nature of the repertoire.

## Conclusion

This study demonstrated that CD8<sup>+</sup>CD45RC<sup>low</sup> Tregs recognize two potential allogeneic epitopes leading to a private TCR repertoire.

Published: 23 November 2011

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doi:10.1186/1479-5876-9-S2-P29

Cite this article as: Picarda et al: Alloantigenic recognition properties of CD8<sup>+</sup> regulatory T cells. *Journal of Translational Medicine* 2011 **9**(Suppl 2):P29.