



SELECTED OPPORTUNITY IN ONCOLOGY

**Novel melanoma antigens
(BIO08305, BIO15077)**

Product factsheet

Clinical stage
Clinical trial ongoing

▶ **Product/Technology:**

- ◆ Novel class of tumor specific immunogenic antigens for vaccination : Meloe-derived antigens, such as MELOE-1 derived peptides presented in the class I (HLA-A2) and class II (DP, DQ and DR) contexts

▶ **Application:**

- ◆ Melanoma immunotherapy

▶ **Rational / POC:**

- ◆ Correlation between the presence of MELOE-1 specific CTL and prevention of relapse after lymph node surgery in HLA-A2 metastatic melanoma patients treated through adoptive transfer of TIL - Tumour Infiltrating Lymphocytes- (retrospective study).
- ◆ MELOE-1 derived long peptides : Tumor specific antigens, over-expressed in all melanoma cell lines, shown to be Immunogenic in animal by vaccination.
- ◆ Increased cross-presentation of class I epitopes to CD8-specific T cell clones :
 - after in vitro stimulation of PBMC from healthy donors with aSLP and
 - in vivo following aSLP vaccination of HLA*A0201/HLA-DRB0101 transgenic mice.
- ◆ Vaccination with aSLP inhibit the growth of transplanted tumors in mice.
- ◆ Ongoing phase I/II clinical trial MELSORT : Adoptive transfer of Melan-A and MELOE-1 specific CD8 T lymphocytes sorted with HLA-peptide multimers to metastatic melanoma patients (7 included/17).
<https://clinicaltrials.gov/ct2/show/NCT02424916>

▶ **Patent and publication:**

- ◆ WO2010026165 : NOVEL MELANOMA ANTIGEN PEPTIDE AND USES THEREOF
- ◆ PCT/EP2019/059421 : NEW VACCINAL STRATEGY
- ◆ Rabu C. et al. Oncoimmunology 2019 : Cancer Vaccines: Designing Artificial Synthetic Long Peptides to Improve Presentation of Class I and Class II T Cell Epitopes by Dendritic Cells
- ◆ Godet Y. et al., J Exp Med. 2008, 205 (11), 2673-82
Rogel, Cancer Immunol Immunother 2011 60 (3), 327-37
- ◆ Godet Y. et al Eur. J. Immunol. 2010. 40: 1786-94
Bobinet M. et al. PLoS One. 2013; 8(9): e75421

Proof of concept

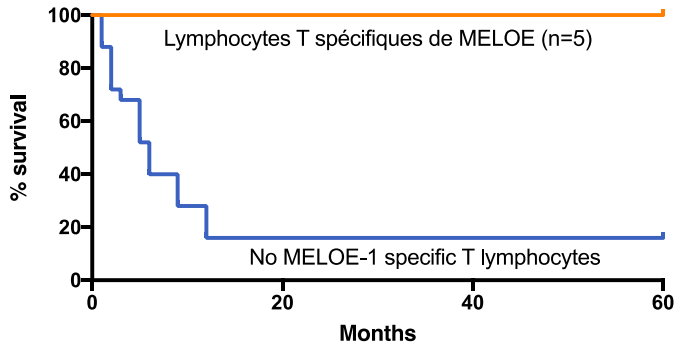


Figure 1 : Overall survival of melanoma patients who received adoptive transfer of TIL containing or not MELOE-1 specific T cells (Godet et al., 2008)

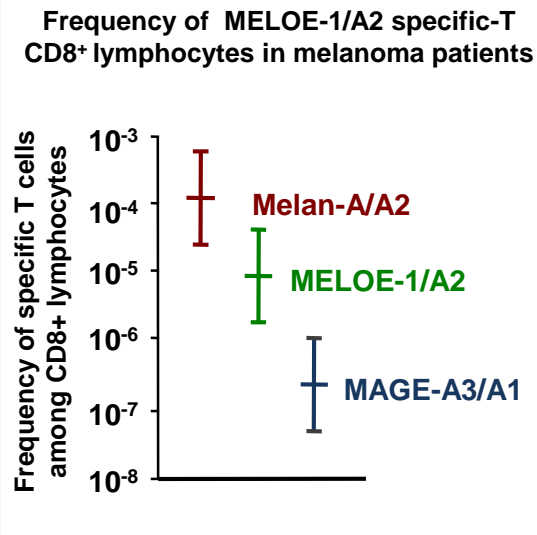
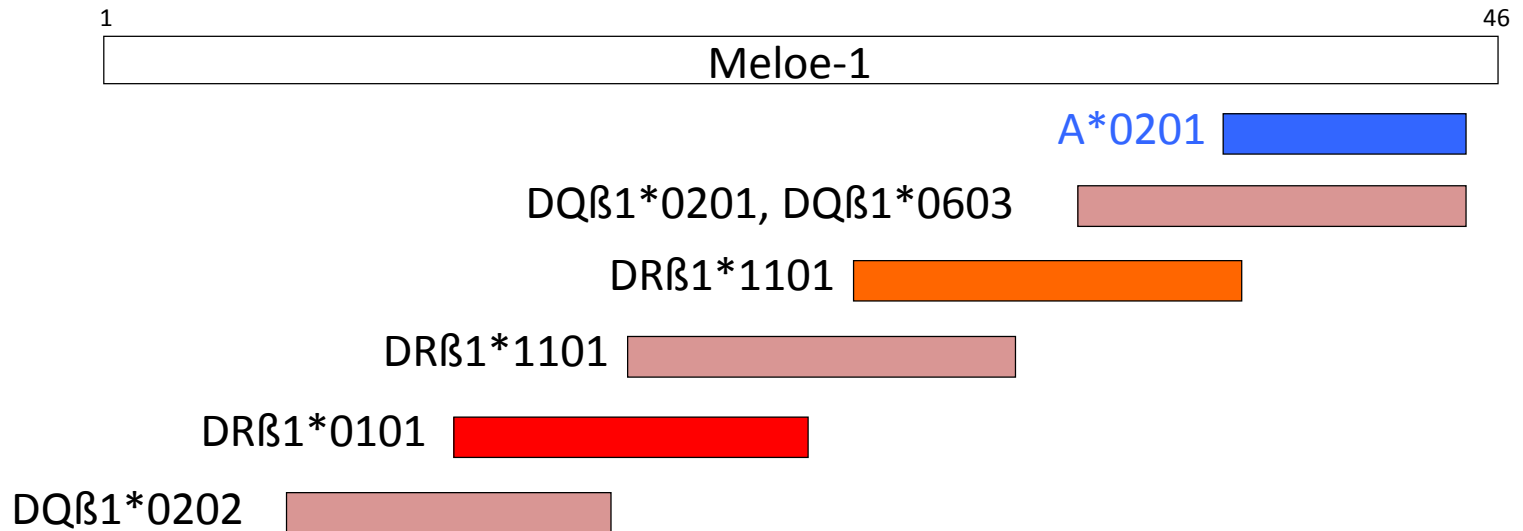


Figure 2 : Frequency of MELOE-1/A2 specific T lymphocytes in melanoma patients, compared to that of Melan-A and MAGE-A3 specific T lymphocytes (Godet et al., 2010)

NOVEL MELANOMA ANTIGENS AND SYNTHETIC LONG PEPTIDES SLP (BIO08305, BIO15077)

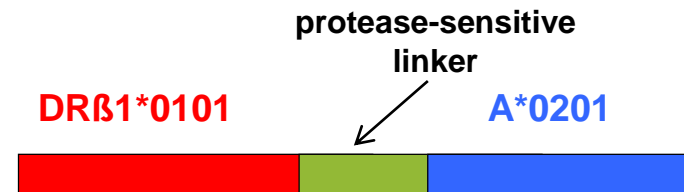
Products

Meloe-derived epitopes for melanoma immunotherapy



Meloe gene : derived from a lncRNA, multiple short ORF, no splicing, translated in melanomas through the specific activation of IRES sequences

SLP Synthetic Long Peptide (new strategy)

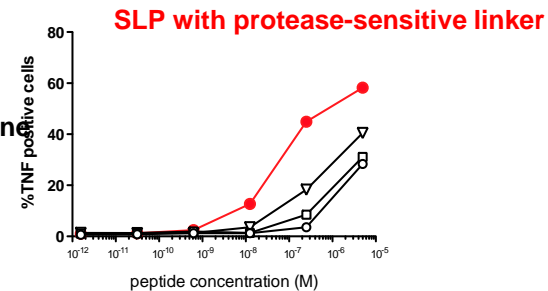
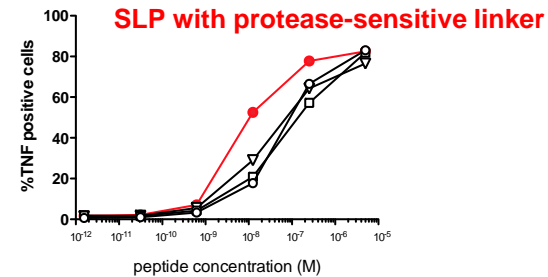
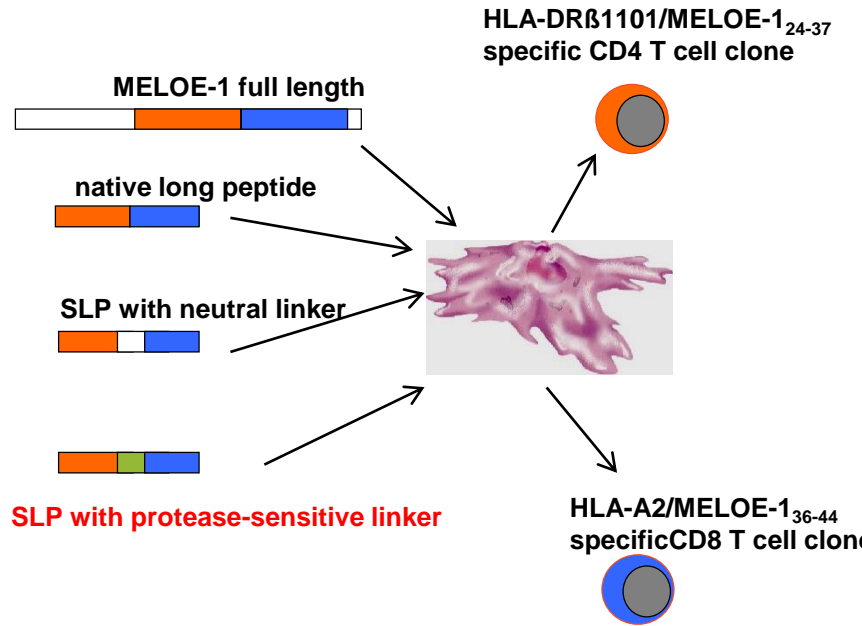


SYNTHETIC LONG PEPTIDES SLP TO IMPROVE PRESENTATION OF CLASS I AND CLASS II T CELL EPITOPES (BIO08305, BIO15077)

Proof of concept

In vitro immunogenicity of DR1101/A2 restricted MELOE-1 derived SLP

DR1101/A2 restricted SLP from MELOE-1



CD4 and CD8 MELOE-1 specific T cell clones were activated with DC loaded either with full length MELOE-1 polypeptide or SLP associating the immunodominant HLA-A2 epitope with the DR1 epitope with or without an optimized protease-sensitive linker.

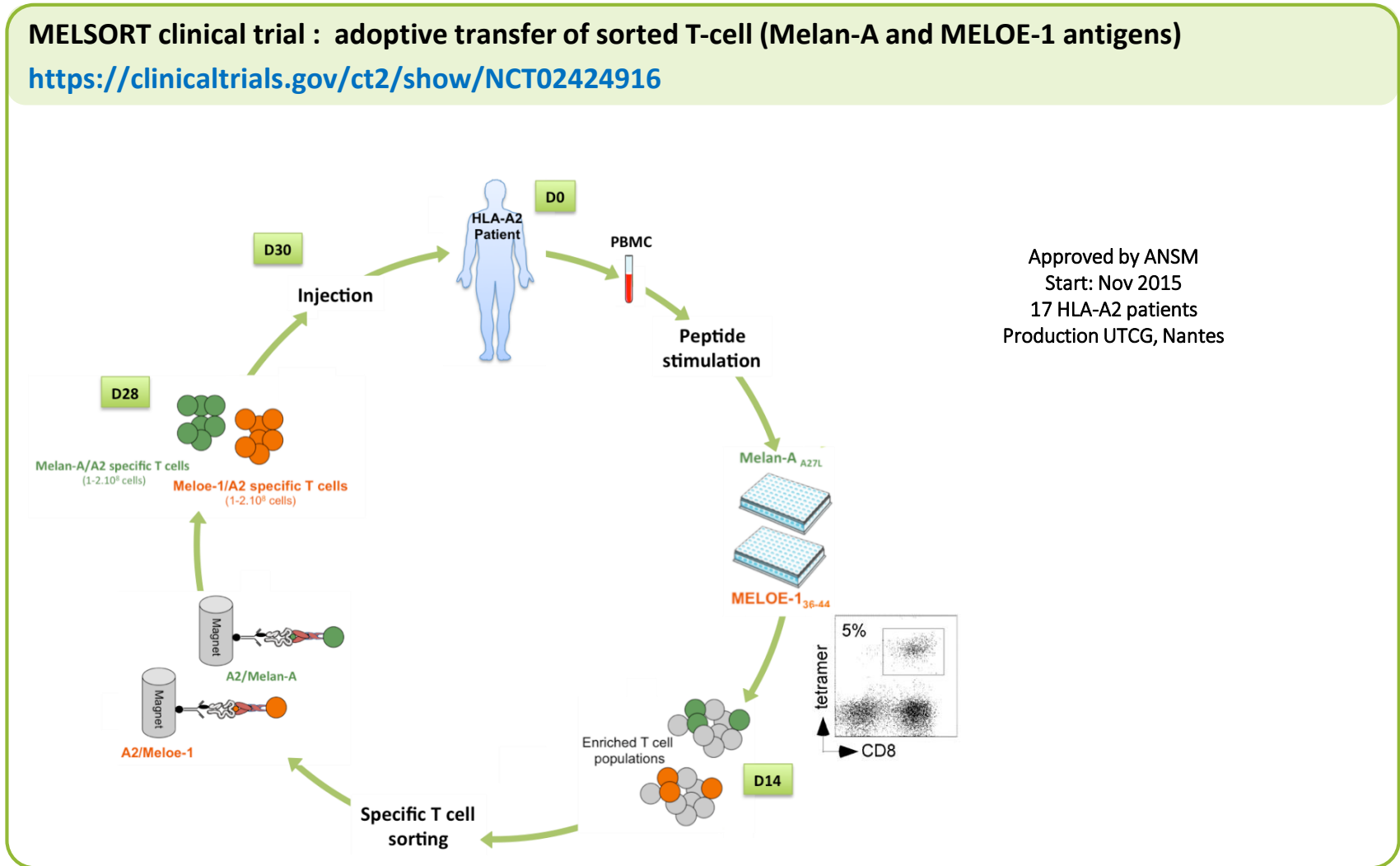
The use of the linker clearly improved the cross-presentation of the HLA-A2 peptide and the presentation of the class II epitope.

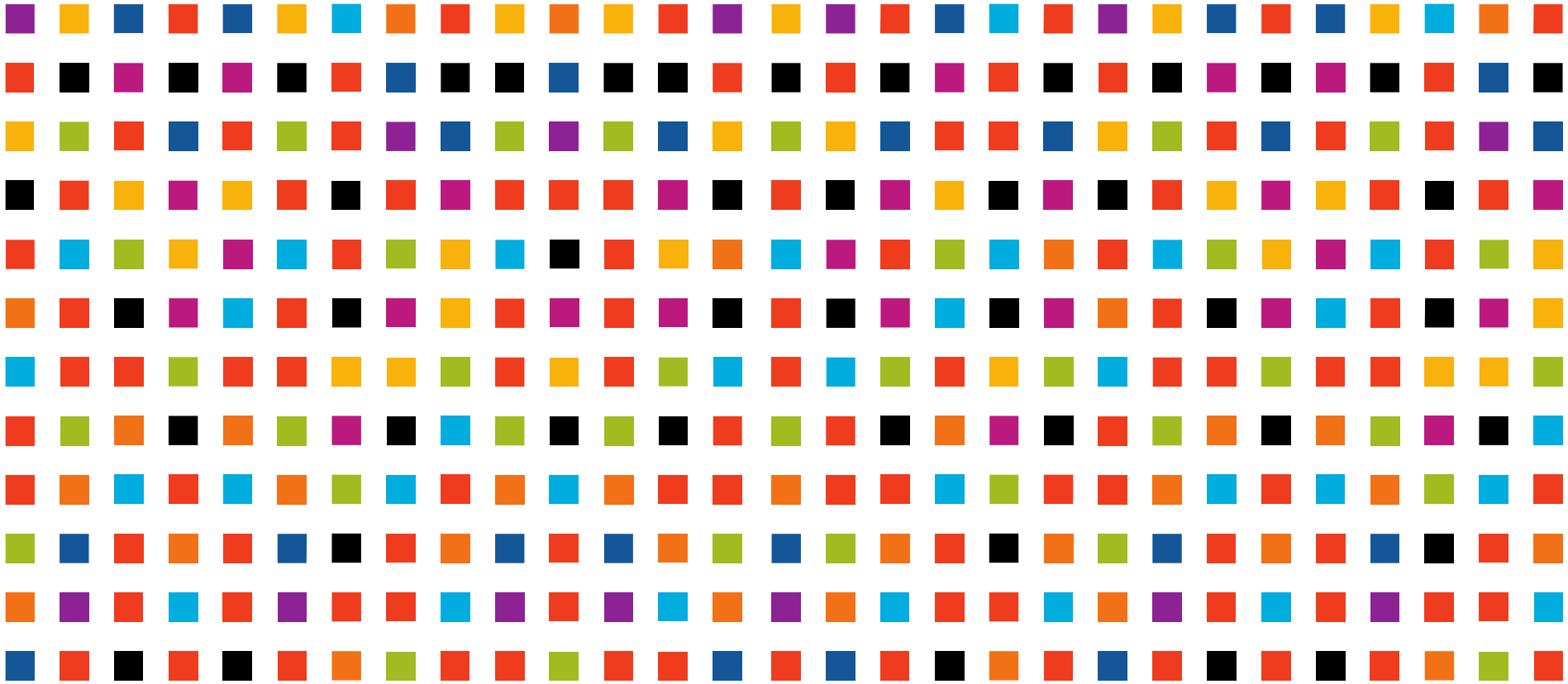
Clinical trial

MELSORT clinical trial : adoptive transfer of sorted T-cell (Melan-A and MELOE-1 antigens)

<https://clinicaltrials.gov/ct2/show/NCT02424916>

Approved by ANSM
Start: Nov 2015
17 HLA-A2 patients
Production UCG, Nantes





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