# Improving immunotherapy for melanoma: models, biomarkers and regulatory T cells
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## Stellingen behorende bij het proefschrift getiteld
## Improving Immunotherapy for Melanoma: Models, Biomarkers and Regulatory T cells

1. Using gene expression profiles determining CD8 T cell infiltration and activity as a predictive tool could be a starting point to stratify patients into sub-groups with different likelihood of responses, especially in trials evaluating combination approaches to immune checkpoint blockade. – this thesis

2. The competitive advantage of regulatory T cells due to their metabolism could also become their Achilles' heel, which provides new avenues for specific therapeutic targeting, which already shows promising early results. – this thesis

3. Recent advances have allowed the use of *in vitro/ex vivo* platforms for pre-clinical research, consequently reducing the need for animal experiments. However, such models are limited in the number of cell types and their dynamic interactions that can be simultaneously examined. – this thesis

4. The lower IFN-γ response of MeVa2.1.dOVA might result in the difference in sensitivity of the MeVa2.1.dOVA and MeVa2.2.dOVA cell lines to OT-I CD8 T cell mediated killing. – this thesis

5. In the PEMDAC trial (with n=24 patients), entinostat dose reduction/interruption was essential due to toxicity in 31% of patients and treatment had to be discontinued due to toxicity in 10% of patients, but overall, the adverse events were reportedly manageable. – this thesis and Ny L et al., *Nat Commun.* (2021)

6. Suppressive functions of regulatory T cells with FoxP3 deficiency could be restored by Rictor deletion, which in turn inhibited mTORC2. – Charbonnier LM et al., *Nat Immunol.* (2019)

7. Administration of sodium bicarbonate for one week to a small cohort (n=10) of patients with acute myeloid leukemia who relapsed after allogenic hematopoietic cell transplantation therapy, resulted in increased mitochondrial function in, and increased production of IFN-γ and TNF-α by CD8 T cells, due to neutralized acidity in the periphery. – Uhl FM et al., *Sci Transl Med.* (2020)

8. While some therapies can drive anti-tumor immune responses, this could also increase compensatory immunosuppressive mechanisms and become detrimental to tumor growth control. It is important to consider this possibility during the development of new immunotherapeutic strategies. – Sharma P et al., *Cancer Discov.* (2021)

9. Treatment with immunotherapy resulted in an unprecedented long term durable responses in patients with some cancer types. It is imperative that such "wonder drugs" are completely accessible to low-income societies as well.

10. Globally mandated standard practices for sample storage are essential to prevent wastage of precious research work.

11. A mind filled with pre-conceived data is a scientist's biggest enemy.

12. Gender equality in the workforce cannot be fully achieved until each individual, and especially women, have overcome their unconscious gender-bias.