Evaluation of new immunotherapeutic targets for multiple myeloma

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Introduction

- Multiple myeloma (MM) is an incurable hematologic cancer characterized by uncontrolled proliferation and accumulation of monoclonal plasmocytes in the bone marrow.
- Within the last decade, chimeric antigen receptor (CAR) immunotherapy has become a promising treatment option for MM and B-cell maturation antigen (BCMA) is the main antigen of the currently avaible CAR-T treatment.

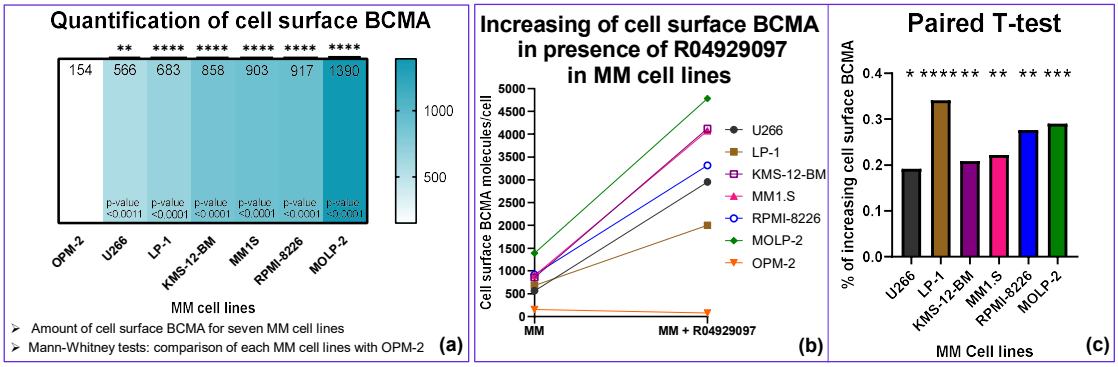
Objective

This project aims to validate the presence of different surface antigens on MM cells; BCMA, Fc receptor-like 5 (FRCL5), and a novel tumor-specific antigen endothelin receptor B (ETRB).

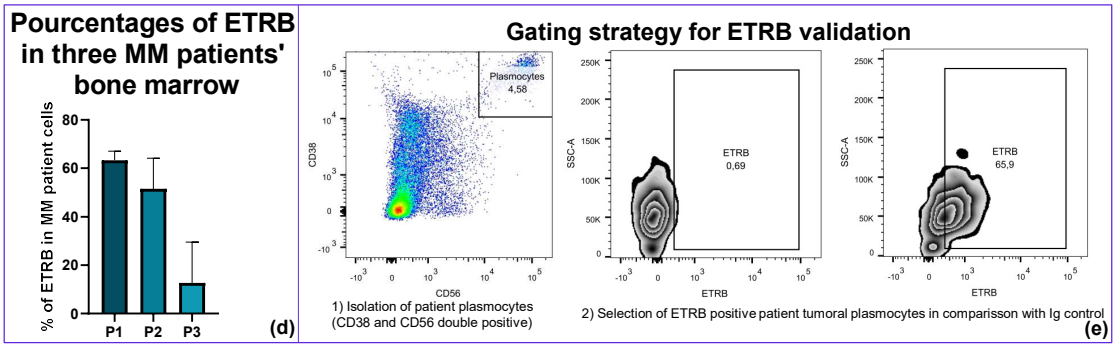
Methods and Results

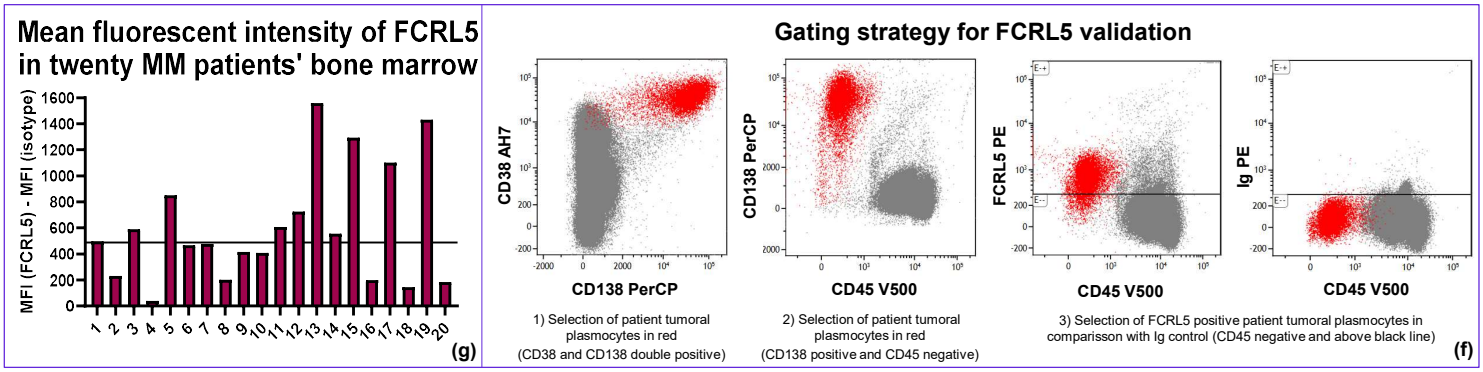
1) BCMA was quantified in seven MM cell lines using the BD Quantibrite™Beads-PE kit **(a)**. The MM cell line OPM-2 was used as a negative control (154). MOLP-2 expresses the highest cell surface BCMA (1390), followed by RPMI-8226 (917), MM1.S (903), KMS-12-BM (858), LP-1 (683) and U266 (566).

2) As a positive control, MM cell lines were incubated with a γ-secretase inhibitor (R04929097), which prevents natural cleavage of cell surface BCMA **(b)**. It resulted in a higher cell surface BCMA expression in tested cell lines **(c)**.



3) A proteomic analysis was performed on six different MM cell lines to uncover a new tumoral target (ETRB). ETRB was successfully validated on three MM patients' bone marrow samples **(d)** using flow cytometry and rendomomab49 **(e)**. Lastly, the presence of FCRL5 was also validated **(f)** on twenty MM patient's bone marrow samples with almost 100% expression frequency **(g)**.





Conclusion

In conclusion, this data validates that BCMA, ETRB and FCRL5 are localized to the tumoral plasmocytes' cell surface. Thus, these antigens constitute the development of new CAR-T immunotherapies.

Acknowledgments and contact

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