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POSTER ABSTRACTS

651.MULTIPLE MYELOMA AND PLASMA CELL DYSCRASIAS: BASIC AND TRANSLATIONAL

Integrative Analysis of Proteomics and Transcriptomics Reveals the Etrb As Novel Single Target and New Combinatorial Targets for Multiple Myeloma

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Abstract Background: Despite the recent introduction of next-generation immunotherapeutic agents, multiple myeloma (MM) remains an incurable disease. Increasing the number of targeted antigens may result in a more effective therapy by preventing antigen escape, clonal evolution and/or disease progression. Moreover, combinatorial approaches (in which activation depends on the presence of 2 antigens) may result in more efficient and specific treatments that limit toxicity on normal tissues. In this work, we adapted an algorithm that integrates proteomic and transcriptomic results of myeloma cells to identify new antigens and possible antigen combinations.
Methods: We performed cell surface proteomics on six myeloma cell lines based on biotin labeling, protein recovery using NeutrAvidin agarose beads and mass spectrometry. These results were combined with gene expression studies comparing myeloma cells with normal plasma cells and B cells and an annotated tissue distribution of identified proteins. The expression of retained proteins was further studied by flow cytometry on normal and malignant plasma cells, hematopoietic stem cells (HSC) and immune effector cells (T and NK cells).
Results: Our algorithm identified 209 surface proteins that are overexpressed in myeloma cells from which 52 proteins could be selected for combinatorial pairing. This list could be further reduced to 23 proteins based on tissue distribution and pairing rules. Flow cytometry analysis of primary samples confirmed the expression of FCRL5, BCMA and ICAM2 in all samples and IL6R, ETRB, SLCO5A1 and PRL3 in more than 60%. Based on single cell RNA-sequencing studies, ETRB is mainly expressed on myeloma cells in the bone marrow and its expression has prognostic value. By analysing the expression on HSC, T and NK cells, different pairs could be proposed that can target myeloma cells and avoid toxicity on other organs.
Conclusions: Our approach validated the expression and distribution of known and new antigens that can be integrated in single-antigen or combinatorial-antigen targeting strategies for novel immunotherapies.

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