C. Amelie Pajip Megaptche

Dr. med.

The impact of CD44vl0 on leukemia homing into the skin

Fach: Chirurgie

Doktorvater: Prof. Dr. med. Markus W. Büchler

CD44-directed therapeutic approaches have most intensely been explored in hematological malignancies. Using a CD44v10 expressing thymoma, my findings suggest that depending on the type of leukemia, a blockade of CD44v can be preferable. Distinct to CD44s, a blockade of CD44v10 hardly interfered with the crosstalk between HSC and BM-Str, particularly not affecting HSC quiescence.

In concern of a concomitant cytotoxic drug therapy, apoptosis resistance of niche embedded HSC was distorted in the presence of EL4 and, less efficiently, EL4-v10, due to the less tight crosstalk between EL4-v10 with the BM-Str. But, the protective effect of the BM-Str was much weaker for EL4-v10 than EL4. This implies that in combination with cytotoxic drugs, the application of a CD44vspecific antibody could bring about an additional therapeutic advantage.

Particularly for cutaneous leukemia / lymphoma that frequently express CD44v10, a CD44v10 blockade has the additional advantage that CD44v10 binds OPN such that effector leukocytes are more efficiently recruited into the tumor, a process that can be significantly strengthened by a local inflammation, which, in addition, supports TIL activation. Due to the more restricted expression of CD44v10, side effects will also become mitigated.

For further improvement, I suggest as one option bi-specific antibody. The well described bi-specific antibodies, that link immune cells to the tumor cell as anti-CD3 in combination with anti-CD44v10 are one possibility. Alternatively, one could occupy with both antibody arms leukemia markers, where besides CD44v10 for the second specificity preferentially an antibody should be selected recognizing a functionally relevant leukemia antigen to drive the leukemic cell more efficiently into apoptosis.