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The receptor for hyaluronic acid mediated motility (RHAMM/CD168) is a leukemia associated antigen eliciting both humoral and cellular immune responses in patients with acute myeloid leukemia (AML)

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To improve the clinical outcome of AML patients, immune therapies targeting leukemia associated antigens (LAAs) might be an approach additionally to chemotherapy and transplantation of hematopoietic stem cells. Ideal LAAs should be preferentially expressed in leukemic blasts, but neither on stem cells of normal hematopoiesis.

RHAMM/CD168 was defined as a LAA using the approach of serological screening of expression libraries (SEREX), eliciting IgG responses in 42% of patients with AML, but not in healthy volunteers (HV) or patients with autoimmune diseases. mRNA for RHAMM was demonstrated by qRT-PCR to be expressed in leukemic blasts of more than 80% of the AML patients, but not in PBMN or CD34+ stem cells of healthy volunteers. Among normal tissues, only testis, placenta and thymus showed significant mRNA expression for the antigen, therefore sharing the expression profile of some other SEREX antigens.

Immunostaining of cytospins and western blots of naive AML blasts and AML cell lines (e.g. K562) confirmed the RHAMM expression on the protein level in 70% of the patients.

To define T cell epitopes of RHAMM, 10 peptides were synthesized following the SYFPEITHY and PAProC algorithms and subjected to ELISPOT assays for interferon gamma and granzyme B. CD8+ T cells taken from the peripheral blood of AML patients and presensitized with peptide R3 or R5 were specifically reactive in the assays against T2 cells pulsed with R3/R5 or COS7 cells co-transfected with HLA-A*0201 and RHAMM. The successful co-transfection was confirmed by flow cytometry and immunocytology. Cross-reactivity was excluded. These results were confirmed using a Cr-51 release assay.

In an AML patient having received blast-derived dendritic cells, a higher frequency of RHAMM-directed T cells was observed after four vaccinations when compared to the status before vaccination. We are going to initiate a phase-I vaccination trial using peptide R3 on a carrier molecule as specific AML vaccine. There is evidence that RHAMM is also expressed in other leukemia types (CML, CLL) which might encourage futher clinical trials.