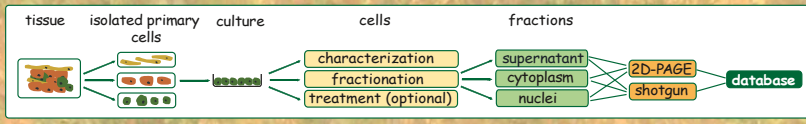


Extracellular matrix remodeling and stromal cell-derived tumor promotion in the bone marrow reflect the progression of MGUS to multiple myeloma.

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Cell characterisation I

After cultivation for 3-5 passages, cells were analysed by FACS in order to determine the identity and purity of the fibroblast population.

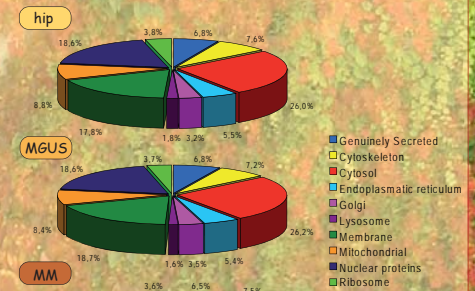


Background:

The pathogenesis of multiple myeloma (MM) is regarded as a multistep process, in which an asymptomatic stage of MGUS precedes virtually all cases of MM. Molecular events leading to transition from MGUS to MM are still poorly defined. Genetically, MGUS plasma cells resemble MM plasma cells in many features, and the clinically apparent step-wise progression of MGUS to MM is poorly reflected by genetic aberrations. We hypothesized that the bone marrow microenvironment is critically involved in the pathogenesis of monoclonal gammopathies. Therefore, we performed a comparative proteome profiling study and investigated the contribution of bone marrow fibroblast precursor cells to disease progression in MM.

Cell characterisation II

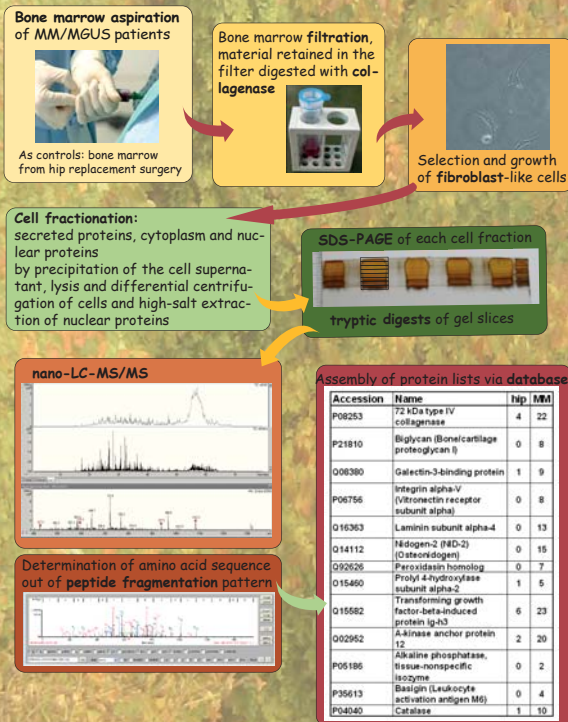
Out of a total of 1980 (hip), 2120 (MGUS) and 2250 (MM) distinct proteins identified in the respective cells, the distribution according to subcellular compartments was almost identical.



Conclusion:

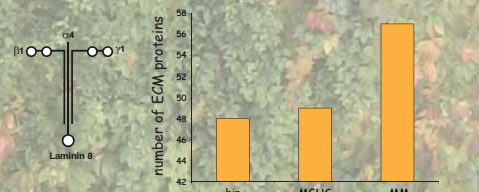
Our results indicate that ECM remodeling and stromal cell-derived tumor promotion in the bone marrow takes place already at the level of MGUS and becomes even more pronounced in MM. Thus, for the first time, marker proteins could be identified indicating a step-wise progression from MGUS to MM.

Applied Methods:

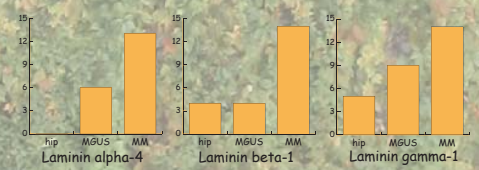


Results I:

The number of different ECM proteins identified in the secretome of the BM-fibroblasts is increased in MGUS- and MM-derived cells

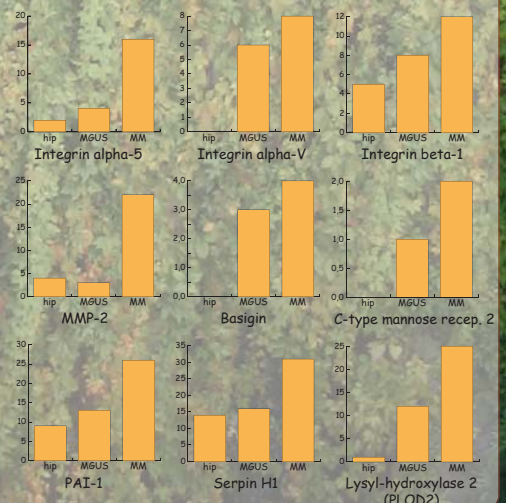


The relative amount (determined by the number of distinct peptides per protein as a semi-quantitative measure) of laminin-8 subunits is also increased.



Results II:

Several ECM proteins and ECM-modulating enzymes also show increased expression levels



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