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Analysis of leukemic stem cell populations comparing *NPM1*^{wt} and *NPM1*^{mut} AML patients and potential therapeutic targets

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Abstract

This lecture will address immune therapeutic approaches for AML treatment strategies comparing expression patterns of *NPM1*^{mut} and *NPM1*^{wt} AML patients, in order to look for new target structures on the leukemic stem cell fraction. NPM1 mut patients have a much better overall survival, which might be due to molecular mechanisms which are not completely understood. We are interested in immunological gene expression differences between both patient groups, eventually explaining the better overall survival of the *NPM1*^{mut} patients. Immunotherapeutic treatment strategies are part of the personalized medicine, and offer great adjuvant therapy to improve the patients overall survival, and therefore are in our focus of interest.

Methods and Results: We enriched the LSC fraction of primary AML PBMCs, by FACS and MACS, comparing both methods in efficiency and feasibility. Notably, the enrichment was performed successfully, using *NPM1*^{mut} and *NPM1*^{wt} AML samples using FACS. The cell number and RNA quality was sufficient for further Microarray studies offering a lot of analysis possibilities. We showed that enriched CD34+CD38- cells in *NPM1*^{mut} AML samples harbor cytoplasmic nucleophosmin via immunocytochemical staining, indicating that these cells belong to the leukemic clone. The Microarray data analysis showed significant differences in gene expression patterns, comparing the *NPM1*^{mut} and the *NPM1*^{wt} group using class comparison analysis. To confirm our data we analyzed differential regulated pathways, indicating the importance of immunological factors, finding same genes differentially expressed as in the class comparison analysis. We identified two genes of interest and performed functional assays, confirming the biological importance of these factors.

Biography

Vanessa Schneider studied Biological Sciences at the University of Constance, which is in the excellence cluster of german universities. She accomplished her Masters work at Ulm University, in the field of leukemia research, investigating the patterns of leukemic stem cell biology. By now she is finishing the second year of Ph.D, supported by the International Graduate School in Molecular Medicine Ulm, which also belongs to the german excellence cluster. Her mentor, Prof. Dr. Jochen Greiner, has more than 15 years of research experience in the field of tumorimmunology and published over 60 articles in several international high impact journals.