C-1. Pericentromeric tandem repeat DNA transcription in mesenchymal stem cells from multiple myeloma patients

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Satellite DNA repeats are tandem arrays located in the centromeric and pericentromeric regions of chromosomes. Tandem repeats (TR) remain silent under normal conditions, but appear to be extensively transcribed in tumor biopsy samples (Ting et al., 2011). In our laboratory, transcription of the pericentromeric TR (human satellite 3, HS3) in solid tumor’s microenvironment fibroblasts was shown. The study was aimed on the investigation of HS3 transcripts in mesenchymal stem cells (MSCs) obtained from multiple myeloma (MM) patients with different percentage of plasmatic cells (PC). MSCs are an important cell type forming bone marrow microenvironment that can display genomic alterations in MM which is liquid tumor and has no known cause to date. MSCs were obtained from bone marrow aspirates of 5 patients with MM and one healthy donor. Median age of MM patients was 59 years, ranging from 49 to 71 years. Two patients had high degree of bone marrow infiltration (from 14 % to 47 % PC in biopsy) and 3 patients had low (under 5 % PC). The fluorescence in situ hybridization for HS3 was performed on slides with fixed cells. In MSCs, the amount of HS3 transcripts correlated with the severity of the disease. All signals were localized in nucleus and not in cytoplasm and disappeared after RNase treatment. MSCs from patients with high percentage of plasma cells displayed higher HS3 transcriptional activity than ones with low infiltration. Two of three patients with single tumor cells were negative for HS3 while the third one had no treatment and exhibited MSCs positive for this satellite. MSCs from healthy donors displayed no HS3 transcriptional activity. HS3 transcription in MSCs from MM correlated with cancer-associated phenotype that included smooth muscle actin and SA-β-gal expression. In conclusion, HS3 transcription in bone marrow microenvironment is associated with the progression of MM and can indicate a poorer prognosis.

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D-1. Nuclear function of vinculin in mouse primary oocytes

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Meiosis is a key process of sexual reproducing organisms and contributes to their genetic variability. The identification of new players affecting meiosis during gametogenesis could lead to revelation of new functions of chromosomal dynamics and to identification of some possible complications during meiosis that remain unexplained. It has been shown that inaccuracies during the meiotic phases result in the chromosomal aberrations and nondisjunctions, that underlie various human genetic disorders (Down’s syndrome, Klinefelter’s syndrome, Turner’s syndrome) or lead to infertility (up to 15 % of the human population). Our project focuses on the dynamics of chromosomes during gametogenesis in the eukaryotic model M. musculus, especially on the role of vinculin (VCL) in the nucleus of mouse meiocytes. VCL is known as a cytoplasmic actin-binding protein associated with cell-cell and cell-matrix junctions. However, we observed a localization of VCL to the nuclei of primary spermatocytes in prophase I. The depletion of VCL in the primary spermatocytes has an effect of reduced fertility, premature desynapsis of homologous chromosomes in the diplotene stage and VCL also showed to be important for the exit from diplotene stage of meiosis I. My part of the project is to study VCL in primary oocytes. My aim is to answer the questions: what is the localization of VCL in prophase I oocytes? Is the involvement of VCL in prophase I oocytes similar as we observe in spermatocytes? What is the effect of VCL depletion on the progression of meiosis I in oogenesis? Are there any chromosomal aberrations? What is the fertility of these VCL-deficient females? Main methods I am using to answer these questions are: crossing mice to generate a conditional VCL knockout in mouse oocytes using the Cre lox-P system; isolation of embryonic ovaries in 15-18 dpc; phenotyping the mature ovaries of adult mice. So far, we confirmed a reduced fertility of VCL cKO females, specifically a significantly lower number of pups. Thus, we plan an in vitro fertilization assay to specify the fertility phenotype. Next, we observed a co-localization of VCL with the synaptonemal complex so we want to study the assembly and disassembly process of synaptonemal complex after depletion of VCL in primary oocytes.

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D-2. Structural reorganization of nuclei of wheat antipodal cells during programmed cell death

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The endosperm is an important part of definitive seed. It is known that endosperm cannot nor-