Targets for the treatment of drug resistant chronic lymphocytic leukemia
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Colour figures
Chapter 4. Figure 2. Co-culture of CLL cells with CD31-transfected fibroblasts does not result in an altered expression profile of apoptosis regulating genes. CLL samples were co-cultured for 3 days with 3T3, 3T31 or 3T40L cells (CD38low n=2; CD38high n=4 for 3T3 and 3T31 and n=3 for 3T40L). The relative expression level of indicated genes, as assessed by RT-MLPA, was related to the average expression in the CLL samples co-cultured with 3T3 cells. The resulting matrix was imported in the program MultiExperiment Viewer (www.tigr.org), and values were assigned green or red colors; green for values between 0 and 1 indicating downregulation and red for values >1 indicating upregulation. The CLL samples are ordered as indicated below the matrix. In the right hand column, the genes are ordered by functional category (HKG= house-keeping genes; β2M= β-2-microglobulin). A significant change in expression level was defined as a two-fold up- or downregulation of the average expression of a gene in samples co-cultured with 3T31 or 3T40L cells compared to samples co-cultured with 3T3 cells and a statistical significant difference with a p-value <.05 (two-sided students T-test for 5 paired samples). No significant differences were found after co-culture with 3T3 or 3T31 cells; genes with a significant differential expression level after co-culture with 3T40L are denoted with *. To exclude the possibility that variations in gene-expression occur at time-points earlier or later than 72 hours, of two CD38high CLL patients additional RNA was isolated after 24 and 120 hours of co-culture. Also at these time-points, no differences were found (data not shown).
Chapter 6. Supplemental figure 2. MEC1 is a p53 dysfunctional human pro-lymphocytic cell line
(A) May-Grunwald-Giemsa staining (500x) (B) Upper panel: fluorescent in situ hybridization (FISH) of MEC1 showing trisomy 7 (CEP7) and 1 x deletion of 17p (p53). Lower panel: western blot showing lack of p53 induction upon 5 Gy radiation. I-83, a p53-functional CLL cell-line, is used as control.
Chapter 7. Figure 2. Co-treatment of CLL cells with F-ara-A and CDDP induces upregulation of Noxa. (A) Cells of 3 p53 functional (pt no 11, 18, 22) and 3 p53 dysfunctional (pt no 2, 4, 5) CLL patients were treated with 10 μM CDDP, 10 μM F-ara-A or the combination in the presence of Q-VD-OPh. The mRNA expression level of 30 apoptosis regulating genes was assessed by RT-MLPA (as described in the Methods section). Gene expression upon treatment was related to gene expression in untreated cells. The resulting matrix was imported in the program MultiExperiment Viewer (www.tigr.org/software/tm4), and values were assigned green or red colors; green for values between 0 and 1 indicating downregulation and red for values >1 indicating upregulation. The CLL samples are ordered as indicated below the matrix. In the right hand column, the genes are ordered by functional category (HKG = house-keeping genes; β2M = β-2-microglobulin). Significant changes in expression are indicated with (*) for p53+ samples and (†) for p53- samples (p < .05, Kruskal Wallis test with post-hoc Dunns-test).