**Background**

A low level of endogenous replicative DNA damage may impact gene expression programs and cell biology features relevant to cancer progression. This can be visualized by the comparison of DNA ligase I (LigI) defective 46BR.1G1 fibroblasts, deriving from a patient who died at 19 for lymphoma, and 7A3 cells, a 46BR.1G1 clone that stably expresses the ectopic wild-type LigI cDNA. LigI deficiency impairs maturation of newly synthesized DNA and increases the number of DSBs and γH2AX foci, two features associated with genome instability commonly found also in pre-neoplastic lesions.

**LINC1 IncRNA expression profile is modulated in response to DNA damage**

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**Aim**

In order to decipher the strategy used to cope with replicative DNA damage, we have compared gene expression profiles in 46BR.1G1 and 7A3 cells. Among the differentially expressed genes, we identified a group of long noncoding RNAs (lncRNAs) which show significant transcriptional alteration in 46BR.1G1 cells, and appear to be relevant for cancer progression. We focused on LINC1 (IncRNA in nonhomologous end joining (NHEJ) pathway 1) which is known to be involved in DNA repair.

**Results**

**LINC1 IncRNA is overexpressed in 46BR.1G1 cells**

Aligned BAM files from RNA-seq were subjected to annotation according to the lncRNAs comprehensive annotation provided by GENCODE (n=13,870; release 18) and to gene quantification by the TopHat-Cufflinks protocol. A threshold of multiple testing corrected q-value < 0.05 was applied to define differentially expressed genes.

**LINP1 downregulation induces an increase of DDR markers in 46BR.1G1 cells**

**LINP1 downregulation affects 46BR.1G1 proliferation**

**LINP1 is mainly cytoplasmic however a fraction is chromatin bound in agreement with its role in DNA repair**

GAPDH transcript is mainly found in the cytoplasm while SRSF1-Int2 is only detectable in nucleoplasmic and chromatin-rich fractions, as expected by the fact that introns are removed co-transcriptionally. LINP1 is mostly in the cytoplasm, however, the fraction associated with chromatin, although drastically lower than SFRS1-Int2, is higher than that observed for GAPDH.

Subcellular and subnuclear distribution of GAPDH, SRSF1-Int2 and LINP1 transcripts were analysed by real-time RT-PCR.

**These results indicate a functional role of LINP1 expression in maintaining a sublethal level of DNA damage in 46BR.1G1 cells compatible with cell survival and proliferation.**