treatment, suggesting oxidative stress-induced di-sulfide bonds are also impaired in these mutants. We conclude that the oxidation of B2 box in PML plays a key role in PML-NBs assembly and sumoylation. We also identified a specific C-terminal cysteine in PML that participates in the formation of intermolecular disulfide bonds, yet not essential for PML-NBs assembly. This oxidized PML might contribute to maintain a specific redox environment in cells.

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Z-1. Lysine methyltransferase SETDB1 and regulation of the three-dimensional organization of the genome during lung cancer progression

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SETDB1 histone H3 lysine 9 (H3K9) methyltransferase (KMT) is known to be involved in tumorigenesis; however, the exact mechanisms of this involvement remain mainly unknown. SETDB1 regulates chromosomal conformation (Jiang *et al.*, 2017); we recently found that SETDB1 interacts and could methylate members of the Cohesin complex. CTCF and Cohesin complex delimit Topologically Associated Domains (TADs) through direct binding at TAD boundaries. CTCF binding to chromatin is inhibited by H3K9 - and DNA-methylation. H3K9 trimethylation (H3K9me3) is a marker of metastasis in lung cancer patients, where SETDB1 gene is amplified. SETDB1 overexpression was associated with elevated cell growth and invasiveness of lung cancer cells (Rodriguez-Paredes *et al.*, 2014). On the other hand, SETDB1 could act as a metastasis suppressor strongly downregulated in highly metastatic lung cancer cells. Aim: Here, we address the role of SETDB1 in the regulation of 3D genome architecture and gene expression patterns in an epithelial lung cancer cell line with different expression levels of SETDB1 (normal, low or high). Results: We found that SETDB1 regulates the epithelial-mesenchymal transition that is a crucial in cancer progression and metastasis. We plan to perform CTCF, SETDB1 and H3K9me3 ChIP-Seq assays combined with Bis-Seq to study DNA methylation at the CTCF binding sites in our cellular models. We will next correlate Hi-C maps with the defined epigenetic landscape. Conclusions: We expect that SETDB1 interacts with the Cohesin complex and affects CTCF occupancy at TAD boundaries, impacting 3D genome architecture and gene expression during during cancer progression.

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Z-2. Investigating the nucleolar epigenetic code at ultrastructural level

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The nucleolus is a nuclear body where different important molecular processes occurs. Beyond ribosomal biogenesis, other relevant functions were recently assigned to this nuclear region, which are related to cell proliferation control and apoptosis, involvement in telomere formation, transfer RNA modifications and stress sensing. Morphologically it is organized in three main areas: roundish electron-light regions, known as Fibrillar Centers (FCs), surrounded by the Dense Fibrillar Component (DFC). These fibrillary structures lie inside the Granular Component (GC), which constitutes most of the nucleolus. Moreover patches of heterochromatin delimitate the nucleolar periphery, interspaced by euchromatin, with thin strands of condensed chromatin enter the nucleolar body. Some aspects of nucleolar morphology have been correlated to their corresponding molecular activity. It is established that rDNA is present within the FC, DFC, in the perinucleolar heterochromatin and in its intranucleolar strands, whereas ribosomal RNA was localized to DFC and GC. rRNA transcription occurs in the FC/DFC complex, while outside the nucleolus reside transcriptionally inactive rDNA repeats. However we still have little knowledge about the condensed regions of perinucleolar heterochromatin. In order to characterize the molecular activity of this area, we decided to investigate its epigenetics status. We hypothesized that, being a condensed region, it would show the classical markers of repression find in the other nuclear regions characterized by compact chromatin. Indeed we analysed at ultrastructural level the distribution of the histone markers H3K27me3 and H3K9me3, which are known to be involved in chromatin condensation and gene silencing. This study was carried out by immunocytochemistry of these histone marker distributions at electron microscopy. Moreover quantifications and statistics of the marker distributions using bioinformatics tools were carried out. We were able to highlight that not only in all compact regions of the nuclear and nucleolar heterochromatin these two repressive histone markers were present, but also that they were specifically confined to the heterochromatin. From our analysis no significant difference in their density or distributions were found between the nucleolar associated and nuclear heterochromatin. Considering these results, we hypothesize that the general mechanisms of chromatin condensation which involve H3K27me3 and H3K9me3 could be similar in different nuclear domains.