Hypoxia induces rapid changes to histone methylation reprogramming chromatin for the cellular response

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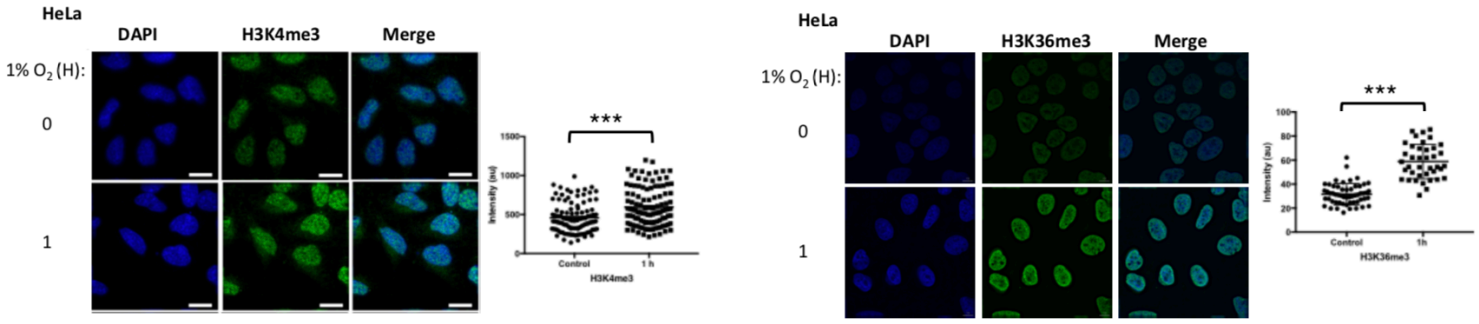

Figure 1: Immunofluorescence analysis histone methylation in HeLa cells exposed to 1% O_2 for 1 hour

In this paper, the authors try to understand if hypoxia affects directly histone demethylases, or if affects hypoxia inducible factors (HIF). The methylation of histones of HeLa cells under hypoxia was studied through immunoblot analysis, which revealed strong and fast alterations in methylation on histone H3. Furthermore, no changes in the histone methylation were observed, when in the presence of a ROS scavenger and also high levels of H_2O_2. It was also observed through immunoblot that during short periods of hypoxia conditions, both H3K36me3 and H3K4me3 would increase values. After the depletion of HIF 1B, it was observed that the methylation marks would increase, which the authors attribute to an inhibition of JmjC histone demethylases.

Using ChIP-seq, the authors demonstrated that the genes related to cell division and oxidative phosphorylation presented reduced H3K36me3 peaks, which suggests that these genes are related to acute response to low concentrations of oxygen. When analysing H3K4me3 peaks, it was discovered that HIF target genes and cell type conserved hypoxia induced genes were upregulated.

In normoxia and hypoxia, through the depletion of KDM5A, the authors observed a reduction of the proliferation and colony formation, as well as an increase in autophagy and apoptosis levels, which indicates that KDM5A is directly involved in the regulation of histone methylation.

Our suggestion is that the authors should further explain the pathways through which hypoxia induces the methylation of the histones in specific genes, and how these protect the cell from low oxygen stress.

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