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# Regulation of microRNA expression by chromatin remodelling complexes in Non-Small Cell Lung Cancer (NSCLC)

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**Background**: Non-Small-Cell Lung Cancer (NSCLC) causes more deaths worldwide than other types of tumours. In cell lines derived from this type of cancer, SMARCA4, the catalytic subunit of the SWI/SNF chromatin-remodelling complex, is mutated and its inactivation in lung cancer impairs cell differentiation. A previous study showed that the phenotype produced after silencing SMARCA4 in zebra fish resembled the phenotype obtained when blocking the production of microRNAs –small non-coding RNA molecules with key roles in gene expression and whose levels are also altered in cancer–. Our goal is to develop a cellular model of NSCLC in order to study changes in microRNA expression depending on the presence or absence of a functional SWI/SNF complex.

**Methods**: SMARCA4 expression was restored in NSCLC cell lines that lack of this protein. In addition, a small interference RNA was designed against the remaining catalytic subunit of the complex that is present in these cell lines: SMARCA2. With these two approaches we can work with cells that have a functional SWI/SNF complex or with an impaired SWI/SNF remodelling activity. With microRNA-Seq and ChIP-Seq, we are studying the changes of microRNA expression derived from the direct remodelling activity of the SWI/SNF complex.

**Results**: SMARCA4 expression was measured at the mRNA and protein level and the tumour suppressor effect of this protein was significantly observed. A similar result was obtained when silencing SMARCA2 due to the process called synthetic lethality. With these models we have obtained changes in several microRNAs after performing the microRNA-Seq experiment, but further validation is needed. Moreover, the ChIP-Seq will provide us information about the target sequences of the SWI/SNF complex and whether these sequences match with the regulatory regions of the validated microRNAs.

**Conclusions**: Our preliminary data suggests that the functionality of the SWI/SNF complex can be linked with the expression of some oncogenic or tumour suppressor microRNAs.

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