



Research Project Proposal

Project Nº 19
Title: Role of lncRNAs in cancer epigenetics
Department/ Laboratory. Department of Gene Therapy and Regulation of Gene Expression. Laboratory of Regulation of Gene Expression
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Summary: <p>The postgenomic era has revealed that mammalian cells encode thousands of mysterious long RNA molecules that lack protein-coding capacity. Although thousands of these long noncoding RNAs (lncRNAs) exist, only few of them have been functionally characterized. The few that have show powerful biological roles as regulators of gene expression, often through epigenetic mechanisms. Significantly, their expression patterns suggest that some lncRNAs are involved in cellular pathways critical in cancer, like the p53 pathway. Our laboratory has identified several lncRNAs transcriptionally regulated by p53 that are required for the proper p53 tumor suppressor response. We hypothesize that these p53-regulated lncRNAs play a critical role in cancer by affecting the epigenetic landscape of cells. In this project the student will investigate the mechanisms of epigenetic regulation by p53-regulated lncRNAs. To do that, he/she will apply techniques for RNA imaging (RNA-FISH) together with the techniques to detect RNA association with chromatin (ChIRP and ChART) followed by DNA deep sequencing. Additionally, he/she will perform in vivo and in vitro studies to determine the role of the lncRNAs in the development of tumors. Together, these experiments will be able to determine the genomic loci recognized by the RNA, and will gain insight into the mechanisms involved in cancer progression, creating new opportunities for therapeutic intervention.</p>
References: <ol style="list-style-type: none">1. Sánchez Y, Segura V, Marín-Béjar O, Athie A, Marchese FP, González J, Bujanda L, Guo S, Matheu A and Huarte M (2014). Genome-wide analysis of the human p53 transcriptional network unveils a lncRNA tumor suppressor signature. <u>Nature Communications</u>, 5:5812.



2. Marin-Bejar O, Marchese FP, Athie A, Sanchez Y, Gonzalez J, Segura V, Huang L, Moreno I, Navarro A, Monzo M, Garcia-Foncillas J, Rinn JL, Guo S, **Huarte M** (2013). Pint lincRNA connects the p53 pathway with epigenetic silencing by the Polycomb repressive complex 2. Genome Biol 14, R104.

3. **Huarte, M***, Guttman, M., Feldser, D., Garber, M., Khalil, A.M., Zuk, O., Amit, I., Regev, A., Lander, E.S., Jacks, T., Rinn, J.L*. (2010). A large intergenic noncoding RNA induced by p53 mediates global gene repression in the p53 response. Cell 142, 409-419.

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POSSIBILITY OF PhD

YES*

* (PhD grant required)