



DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

## Life & Chemical Sciences Seminars

# MYCN: Always booming still with a lot to say

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### **Abstract**

MYCN encode for a bHLH-LZ transcription factor (N-Myc) involved in many biological aspects like cell proliferation and growth. Indeed, N-Myc controls transcription of an impressive plethora of genes involved in many multiple cellular processes and, furthermore, MYCN gene amplification is a critical marker of poor prognosis in neuroblastoma patients. P53 (TP53 gene) is a homotetrameric transcription factor that works as the essential supervisor of the genome integrity. TP53 gene is altered in a very high percentage of adult tumors but remarkably it is nearly not mutated in childhood tumors like Neuroblastoma. In this study, we tested the hypothesis that MYCN amplification alters p53 transcriptional activity in neuroblastoma. Interestingly, we found that MYCN directly binds to the tetrameric form of p53 at its C-terminal domain, and this interaction is independent of N-Myc/MAX heterodimer. Recent findings have shown that N-Myc regulatory activity extends to non-coding RNA genes suggesting potentially novel roles for this oncoprotein in neuroblastoma. In this research, among the several lncRNAs that N-Myc can stimulate, we singled out RP1X, a long non-coding RNA, that in addition to be selectively highly expressed in high MYCN cells only, is also strongly and almost uniquely transcribed in neuroblastoma among all types of cancer. Dissection of the mechanism revealed that MYCN stimulates transcription of lncNB1 which induce an increase of E2F1 translation through a direct interaction with a 60S ribosomal protein.

### **Biosketch**

I am a Post-doctoral fellow (AIRC/FIRC 2016-2018) at the department of Pharmacy and Biotechnology-FaBiT under the supervision of Prof. Giovanni Perini. I received Bachelor and Master's degree in Cellular and Molecular Biology at the University of Palermo. After Master's degree graduation (October 2011), I was enrolled in the PhD program (January 2012) in Cellular and Molecular biology under the supervision of Prof. Giovanni Perini in the laboratory of functional genomics and epigenetics, FaBiT-University of Bologna, Italy. Here, I focused on cancer biology and particularly on the molecular mechanisms underlying the arising and progression of neuroblastoma, a childhood solid tumour. More specifically I investigated the role of the N-Myc oncoprotein whose altered expression represents an important marker of prognosis in most neuroblastomas. During the three years PhD training my studies focused on three distinct projects. First, the isolation and characterization of a novel long non-coding RNA lncUSMycN, that works as a critical regulator of MYCN expression in neuroblastoma cancer. Second, the characterization of the N-Myc/LSD1 and N-Myc/WDR5 protein complexes in modifying the epigenetic signature of critical neuroblastoma prognostic genes. After receiving PhD in Molecular and Cellular Biology (April 2015), I spent the last three years focusing my attention particularly on: 1) the cross-talk between p53 and N-Myc pathways in neuroblastoma; 2) the role of a novel MYCN associated Long non-coding RNA.

*Commissione Ricerca e Attività Correlate*