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Doctoral school in Complex Systems in Medicine and Life Sciences

Ph.D programme in complexity in post-genomic biology

XXVI Cycle 2009-2011

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1. **Reviewer:** *Prof. Jean Baptiste Demoulin*
2. **Reviewer:** *Prof. Stefano Volinia*

Title: Network motifs combining microRNAs and Transcription factors in the human regulatory network.

In the last years, much interest has been attracted by the study of local connections between transcriptional and post-transcriptional (miRNA mediated) regulatory interactions. Among various possible ways to integrate together TF-mediated and miRNA-mediated interactions, Feed-Forward Loops (FFLs) play a prominent role, allowing a fine tuning of the expression level of target genes, and, in the case of incoherent FFLs, a careful control of fluctuations in the level of target proteins. During my PhD I focused my attention to study network motifs, particularly FFLs and self loops mediated by intronic microRNAs. Employing independent databases with computational prediction and experimental validated data, we identified several mixed network motifs. We then studied their statistical and functional properties.

We found that these network motifs are statistically overrepresented in the global regulatory network, with a wide implications in cell cycle and cancer diseases.