

Bioinformatics and Evolutionary Genomics of Cancer

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Activities 2007. The scientific activity of our lab focuses on genome analysis in the context of cancer development. Taking advantage of the increasing amount of available biological data we aim at obtaining a more integrated view of cancer genetics. Currently, we study cancer-specific traits involving both coding and non-coding regions of the human genome. We pursue three main lines of investigation:

- **Quantification of the hyper-mutability of cancer genome by ultradeep sequencing of non-coding regions.**

We are analysing non-coding regions of the human genome under strong purifying selection that has preserved them 100% identical across mammalian evolution and within human population. We have collected evidence that these remain unchanged also in cancer genome. We now plan to use their hypomutability as 'internal control' for measuring the mutation rate of cancer genome.

- **Evolution and systems biology of cancer genes.**

The high functional heterogeneity of cancer genes suggests the presence of common properties not directly dependent on their molecular function. We started to analyze ~600 genes mutated in cancer not focusing on each gene separately, but seeking for the presence of 'systems-level' properties. We have found that these genes tend to avoid duplications and code for central hubs of the protein-protein interaction network. We plan to use the detected properties to identify novel portions of the human network putatively involved in cancer.

- **In-depth evolutionary analysis of cancer gene families.**

In collaboration with experimental groups, we aim at characterizing the evolution of cancer-related genes to gain information on their functional roles. In the past year, we traced the metazoan origin of PRDM genes, a family of transcriptional regulators involved in human tumorigenesis. We also detected their expansion in vertebrates and further duplication in primates. We



experimentally showed that fast-evolving paralogs are poorly expressed and acquire tissue-specificity. Our findings allowed a novel interpretation of the role of PRDMs during cancerogenesis.