



Consiglio Nazionale delle Ricerche
Istituto di Genetica Molecolare
Luigi Luca Cavalli-Sforza



12th ARTURO FALASCHI LECTURE

June 3rd, 2024

10:30 a.m.

**Istituto di Genetica Molecolare CNR
Aula Arturo Falaschi**

Prof. Ernesto Guccione

**Director Mount Sinai Center for OncoGenomics
and Innovative Therapeutics (COGIT)
Icahn School of Medicine at Mount Sinai**

***“Precision Medicine:
new tools and (some) new ideas”***

In science having good hypothesis-driven ideas is important, but sometimes it's fun to let your next experiment be driven by data in an unbiased manner.

For that to happen, you need innovative yet solid tools to explore the complexity of biology. In the lab we do a bit of all of the above and I'll discuss a few ongoing projects that are keeping us busy.

First, I will describe how we have taken advantage of murine organoid models of Hepatocellular Carcinoma (HCC) to screen for novel small molecules and identify a compound that selectively kills HCC with hyperactive WNT signaling. We call this molecule WNTinib (Rialdi et al Nature Cancer 2023), and we are currently completing the IND enabling studies to bring it to the clinic.

Second, I will talk about a project dissecting the complexity of epigenetic plasticity in Colorectal Cancer (CRC). While driver mutations have been widely studied for their cancer-enabling characteristics, such as sustaining proliferative signaling and evading cell death, we have only recently started to appreciate their role as gatekeepers of phenotypic plasticity and promoters of non-mutational epigenetic reprogramming. I will discuss our recent attempts at characterizing cell plasticity in solid tumors with the ultimate goal of identifying new therapeutic options (Mzoughi et al in revision).

Last, I will present our efforts to build a platform to optimize design and delivery of RNA therapeutics (with a specific focus on Splice-switching antisense Oligonucleotides - ASOs)(Tabaglio et al in revision).



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