

Understanding transcription factors through quantitative biology

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The original concept of cell differentiation as a unidirectional process of progressively restricted potential and increased specialization has been dramatically revised by the discovery of cellular reprogramming. The appropriate cocktail of transcription factors (TFs) allows the production of Induced Pluripotent Stem Cells (iPSCs) from almost any type of somatic cell, with extended self-renewal capabilities and broad differentiation potential. This concept has infused an unprecedented boost in the use of TFs not only in reprogramming to pluripotency but, in general, to drive cell fate decisions in vitro.

In our laboratory, we design and apply quantitative methods to dissect the role of transcription factors during reprogramming, conversion, and differentiation of human cells. We also study how rare genetic disorders alter the normal function of TFs (and proteins in general) with the final aim to predict the severity of rare genetic variants even before their onset in the general population.

I will describe two general approaches to these scopes: i) an approach of quantitative single-cell genomics to identify the subpopulations that arise during the reprogramming process to pluripotency and reconstruct their relationships. ii) a quantitative method to test in parallel hundreds of distinct rare variants of TP63, a TF that acts as the master regulator of skin development and whose mutation are associated with AEC syndrome, a monogenic disorder with severe skin defects.

Presenter: Dr CACCHIARELLI, Davide (Tigem and Università di Napoli Federico II)