Dipartimento di Matematica e Informatica

Università degli Studi di Perugia

Seminari di Divulgazione Scientifica

Aula A3 "Antonella Fiacca"
Dipartimento di Matematica e Informatica
Università degli Studi di Perugia

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Ore 13.00

"STUDI DI GENOMICA FUNZIONALE NELLA LEUCEMIA ACUTA MIELOIDE CON MUTAZIONE DI NUCLEOFOSMINA (NPM1)"

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http://www.dmi.unipg.it/Seminaridmi

ABSTRACT: Acute myeloid leukemia (AML) is a molecularly heterogenic and extremely aggressive cancer with a dismal prognosis. In the past years, no particular advances have been made for the treatment of this disease; therefore, the need to develop new more efficient treatment strategies is a crucial point.

Hypothesis-driven traditional approaches to find out novel tailored therapies can be of great value, as demonstrated by our previous data in the setting of a specific AML genetic entity, AML with nucleophosmin (NPM1) mutation, discovered in our Institute (Falini et al. NEJM 2005; Martelli et al. Blood 2015; Falini et al. NEJM 2015) e that continues to be extensively studied in our laboratory, supported by an ERC-advanced grant to B. Falini. However, the complexity of the intracellular pathways interactions in leukemic cells requires the use of wide screening-based approaches with application of novel technologies and bioinformatics tools to speed up the identification of new therapeutic targets specific for the disease.

Our aim is to focus on NPM1-mutated AML and which are their specific vulnerabilities. A combined analysis on the genes considered essential for this kind of leukemia and drugs considered active (or inactive) specifically for this genetic subtype will lead to novel hypotheses (ERC-funded project to Prof. MP Martelli). This strategy will allow the design of a therapy tailored on this specific subtype of leukemia using NGS techniques, in particular RNA-Seq for differential expression analysis.

To analyze in our laboratory the huge amount of data that we are producing, we developed our custom pipeline (https://github.com/giuliospinozzi/creo_pipelines). The application can be used by command line or by using a graphical interface and allows to choose between different methods of alignment, quantification and differential expression analysis. In particular, it makes quality control, pre-processing, alignment, transcript quantification and differential expression analysis. Given the input files and the working directory, the pipeline is completely automated and moreover it is possible to perform an optional meta-analysis on the results (Gene Ontology and KEGG Pathway enrichment analyses). Finally, the results obtained and saved in the appropriate folders can be viewed in an interactive Shiny App (Chang et al., 2018), from which you can also download a report with all the results. The advantage of show the results in this form is that, once the Shiny App is launched, it is intuitive and easy to use even for those who are not familiar with computer science.