



SELEZIONE PUBBLICA, PER TITOLI ED ESAMI, PER IL RECLUTAMENTO DI N. 1 UNITÀ DI TECNOLOGO DI PRIMO LIVELLO, CON RAPPORTO DI LAVORO SUBORDINATO A TEMPO DETERMINATO E PARZIALE AL 70%, DELLA DURATA DI 18 MESI, PRESSO IL DIPARTIMENTO DI ONCOLOGIA ED EMATO-ONCOLOGIA - BANDITA CON DETERMINA N. 4311/2020 del 9/04/2020 E PUBBLICATA SUL SITO INTERNET D'ATENEO IN DATA 9/04/2020 - CODICE 20848

La Commissione giudicatrice della selezione, nominata con determina n. 6394/2020 del 5/06/2020 e così composta:

Prof.ssa Licitra Lisa Francesca Linda - Presidente

Prof.ssa Guerrini Luisa Francesca - Componente

Prof. Bolli Niccolo' - Componente

Sig.ra Beretta Manuela Piera - Segretario

Comunica i quesiti relativi alla prova orale:

GRUPPO DI QUESITI N. 1

1 Il candidato parli di metodologia per l'analisi di varianti nucleotidiche in esperimenti di next-generation sequencing.

2 Il candidato parli di metodologia per l'analisi di "Copy number alterations" in esperimenti di next-generation sequencing.

Brano in inglese: Multiple myeloma is an incurable plasma cell malignancy with a complex and incompletely understood molecular pathogenesis. Here we use whole-exome sequencing, copy-number profiling and cytogenetics to analyse 84 myeloma samples. Most cases have a complex subclonal structure and show clusters of subclonal variants, including subclonal driver mutations. Serial sampling reveals diverse patterns of clonal evolution, including linear evolution, differential clonal response and branching evolution. Diverse processes contribute to the mutational repertoire, including kataegis and somatic hypermutation, and their relative contribution changes over time. We find heterogeneity of mutational spectrum across samples, with few recurrent genes. We identify new candidate genes, including truncations of SP140, LTB, ROBO1 and clustered missense mutations in EGR1. The myeloma genome is heterogeneous across the cohort, and exhibits diversity in clonal admixture and in dynamics of evolution, which may impact prognostic stratification, therapeutic approaches and assessment of disease response to treatment.

GRUPPO DI QUESITI N. 2

1 Il candidato parli di come pianificherebbe un esperimento per valutare l'evoluzione clonale nella progressione del mieloma multiplo smoldering.

2 Il candidato parli di quali tecniche alternative conosce all'isolamento del DNA dalle plasmacellule del midollo per l'identificazione delle mutazioni nel mieloma.

Brano in inglese: We analyzed whole genomes of unique paired samples from smoldering multiple myeloma (SMM) patients progressing to multiple myeloma (MM). We report that the genomic landscape, including mutational profile and structural rearrangements at the smoldering stage is very similar to MM. Paired sample analysis shows two different patterns of progression: a "static progression model", where the subclonal architecture is retained as the disease progressed to MM suggesting that progression solely reflects the time needed to accumulate a sufficient disease burden; and a "spontaneous evolution model", where a change in the subclonal composition is observed. We also observe that activation-induced cytidine deaminase plays a major role in shaping the mutational landscape of early subclinical phases, while progression is driven by APOBEC cytidine deaminases. These results provide a unique insight into



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myelomagenesis with potential implications for the definition of smoldering disease and timing of treatment initiation.

Milano, 30 giugno 2020

La Commissione

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