LUISA MADDALONI 14/10/2022 PROVA ESTRATTA

21_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI, SECONDO LA NORMATIVA CONCORSUALE AI SENSI DEL D.P.C.M. DEL 21 APRILE 2021, PER N. 1 POSTO COLLABORATORE PROFESSIONALE DI RICERCA SANITARIA, CATEGORIA D, PER LA UOC NEUROLOGIA 8 – NEURONCOLOGIA MOLECOLARE

PROVA I

1. Richiesta di analisi molecolare per la ricerca delle mutazioni nel promotore del gene TERT: materiale biologico necessario, estrazione acidi nucleici, tecnica di analisi utilizzata.

2. Che differenza c'è tra hardware e software?

   a) L'hardware si riferisce al computer come macchina, il software si riferisce ai programmi
   b) Hardware e software designano rispettivamente computer difficili e facili da usare
   c) L'hardware è il corpo principale del computer, il software è costituito dai dischetti
   d) L'hardware è costituito dal sistema operativo, il software da tutti gli altri programmi

2. Leggere e tradurre

nature cancer

ARTICLES

https://doi.org/10.1038/s43018-020-00159-4

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Pathway-based classification of glioblastoma uncovers a mitochondrial subtype with therapeutic vulnerabilities

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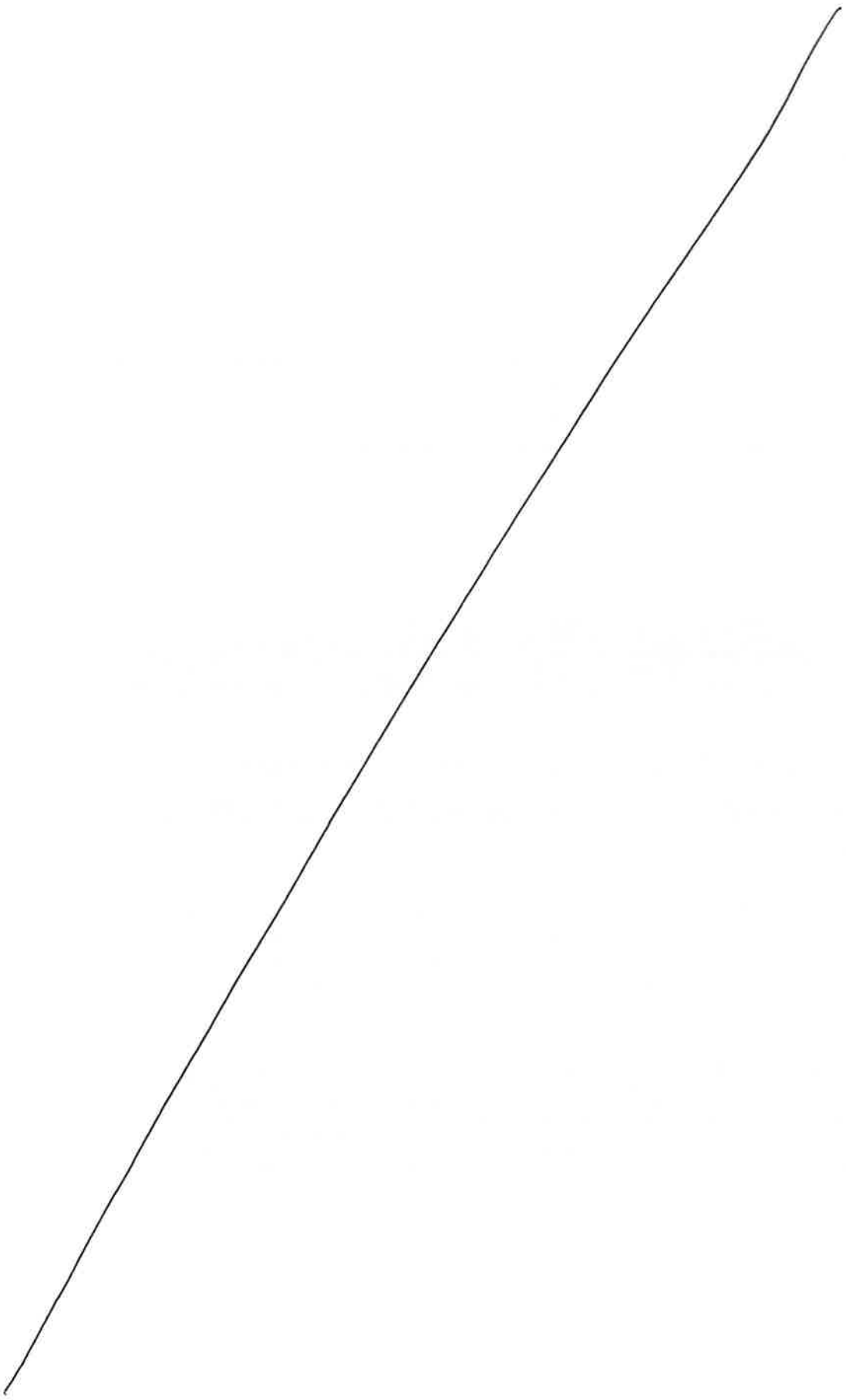
The transcriptomic classification of glioblastoma (GBM) has failed to predict survival and therapeutic vulnerabilities. A computational approach for unbiased identification of core biological traits of single cells and bulk tumors uncovered four tumor cell states and GBM subtypes distributed along neurodevelopmental and metabolic axes, classified as proliferative/progenitor, neuronal, mitochondrial and glycolytic/pluripotent. Each subtype was enriched with biologically coherent multiomic features. Mitochondrial GBM was associated with the most favorable clinical outcome. It relied exclusively on oxidative phosphorylation for energy production, whereas the glycolytic/pluripotent subtype was sustained by aerobic glycolysis and amino acid and lipid metabolism. Deletion of the glucose-proton symporter *SLC45A1* was the truncal alteration most significantly associated with mitochondrial GBM, and the reintroduction of SLC45A1 in mitochondrial glioma cells induced acidification and loss of fitness. Mitochondrial, but not glycolytic/pluripotent, GBM exhibited marked vulnerability to inhibitors of oxidative phosphorylation. The pathway-based classification of GBM informs survival and enables precision targeting of cancer metabolism.



LUISA MADDALONI 14/10/2022 PROVA NON ESTRATTA

21_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI, SECONDO LA NORMATIVA CONCORSUALE AI SENSI DEL D.P.C.M. DEL 21 APRILE 2021, PER N. 1 POSTO COLLABORATORE PROFESSIONALE DI RICERCA SANITARIA, CATEGORIA D, PER LA UOC NEUROLOGIA 8 – NEURONCOLOGIA MOLECOLARE

PROVA 2

1. Tecniche di sequenziamento note

2. Quale di questi programmi è un foglio di calcolo:

   a) Word
   b) Abobe Photoshop
   c) Excel
   d) Powerpoint

2. Leggere e tradurre

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Clinical Experience of Cerebrospinal Fluid–Based Liquid Biopsy Demonstrates Superiority of Cell-Free DNA over Cell Pellet Genomic DNA for Molecular Profiling

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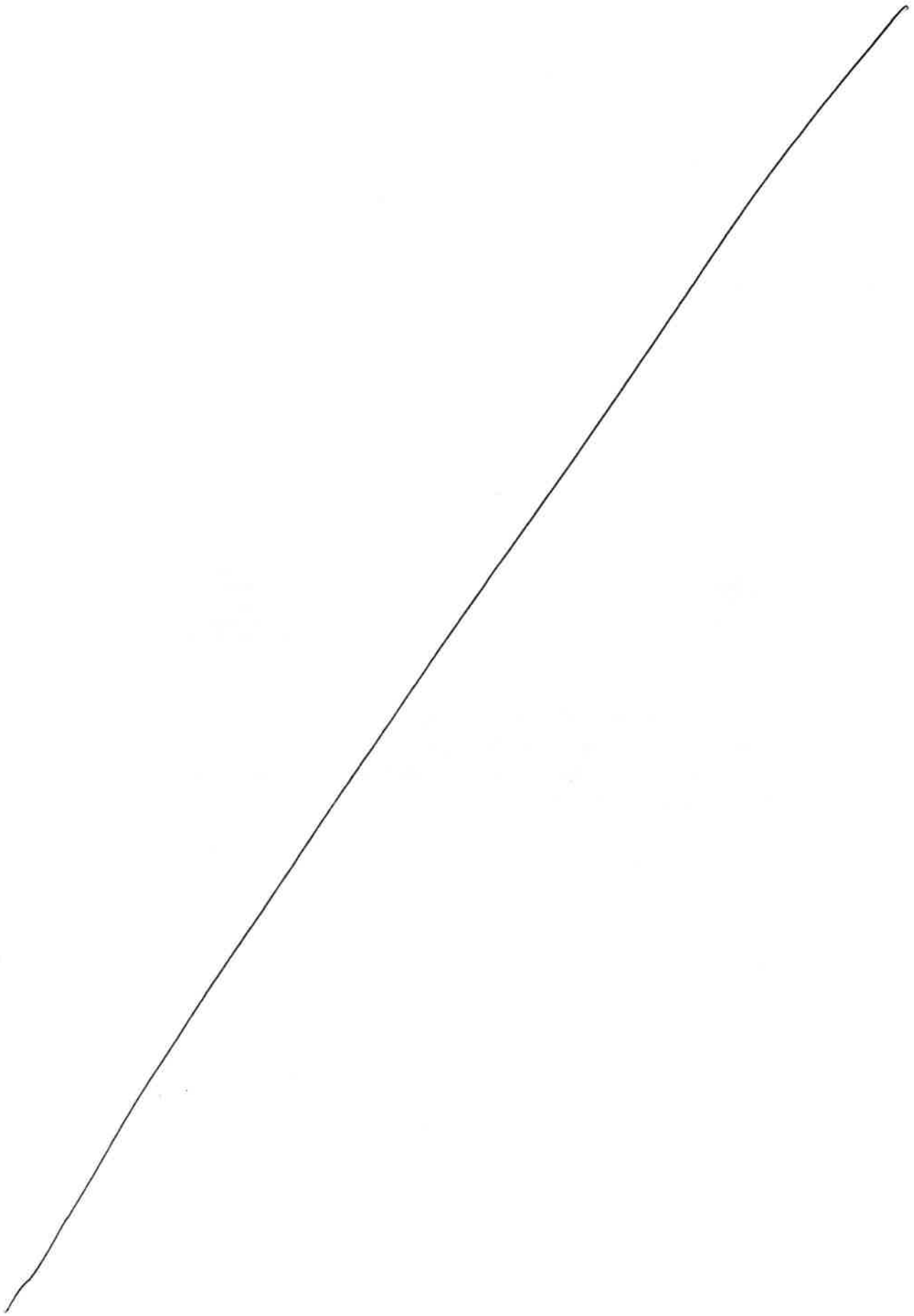
Cell-free DNA (cfDNA) from cerebrospinal fluid (CSF) offers unique opportunities for genomic profiling of tumors involving the central nervous system but remains uncommonly used in clinical practice. We describe our clinical experience using cfDNA from CSF for routine molecular testing using Memorial Sloan Kettering Integrated Mutation Profiling of Actionable Cancer Targets (targeting 468 cancer-related genes). In all, 148 cfDNA samples were assessed, comparing results of cfDNA versus genomic DNA (gDNA; gDNA from cell pellets) derived from the same CSF sample and the primary tumor. Of these, 71.6% (106/148) were successfully sequenced. Somatic alterations (mutations and fusions) were observed in 70.8% (75/106) of the samples; 97.3% (73/75) comprised variants confirming central nervous system involvement by a previously diagnosed tumor, 14.7% (11/75) had additional variants consistent with a therapy-related resistance mechanism, and 2.7% (2/75) had variants that independently diagnosed a new primary. Among samples with paired cfDNA and gDNA sequencing results, cfDNA was more frequently positive for at least one mutation [43.6% (55/126) versus 19.8% (25/126)] and harbored 1.6× more mutations (6.94 versus 4.65; $P = 0.005$), with higher mean variant allele fractions (41.1% versus 13.0%; $P < 0.0001$). Among mutation-positive cfDNAs, the corresponding gDNA was frequently negative (44.6%; 25/55) or failed sequencing (17.8%; 9/55). Routine molecular profiling of cfDNA is superior to gDNA from CSF, facilitating the capture of mutations at high variant allele frequency, even in the context of a negative cytology. (*J Mol Diagn 2021, 23: 742–752; https://doi.org/10.1016/j.jmoldx.2021.03.001*)



LUISA HADDOCCHI 24/10/2022 PROVA NON ESTRATTA

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PROVA 3

1. Quale/i materiale/i si potrebbe utilizzare per condurre un esame "diagnostico" in assenza di tessuto tumorale?

2. Quale di questi sono sistemi operativi:

   a) Windows e Linux
   b) Word ed Excel
   c) Windows e PowerPoint
   d) Word e PowerPoint

2. Leggere e tradurre

RESEARCH

CANCER GENOMICS

A noncoding single-nucleotide polymorphism at 8q24 drives *IDH1*-mutant glioma formation

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Establishing causal links between inherited polymorphisms and cancer risk is challenging. Here, we focus on the single-nucleotide polymorphism rs55705857, which confers a sixfold greater risk of isocitrate dehydrogenase (*IDH*)–mutant low-grade glioma (LGG). We reveal that rs55705857 itself is the causal variant and is associated with molecular pathways that drive LGG. Mechanistically, we show that rs55705857 resides within a brain-specific enhancer, where the risk allele disrupts OCT2/4 binding, allowing increased interaction with the *Myc* promoter and increased *Myc* expression. Mutating the orthologous mouse rs55705857 locus accelerated tumor development in an $Idh1^{R132H}$-driven LGG mouse model from 472 to 172 days and increased penetrance from 30% to 75%. Our work reveals mechanisms of the heritable predisposition to lethal glioma in ~40% of LGG patients.