

39_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI PER N. 1 POSTO DI RICERCATORE SANITARIO DA ASSEGNARE ALLA SC NEUROLOGIA 7 – EPILETTOLOGIA CLINICA E SPERIMENTALE

PROVA I

1. Descrivere brevemente il trattamento di un campione cerebrale derivante da chirurgia dell'epilessia ai fini dell'esecuzione di analisi istologiche e immunohistochimiche

2. Cos'è il pacchetto Office?
 - a. un prodotto software di produttività aziendale composto da un insieme di programmi specifici
 - b. un programma specifico di gestione contabilità
 - c. un programma di grafica

3. Leggere e tradurre il testo seguente

ARTICLE

doi:10.1038/nature.21029

Neurotoxic reactive astrocytes are induced by activated microglia

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Reactive astrocytes are strongly induced by central nervous system (CNS) injury and disease, but their role is poorly understood. Here we show that a subtype of reactive astrocytes, which we termed A1, is induced by classically activated neuroinflammatory microglia. We show that activated microglia induce A1 astrocytes by secreting IL-1 α , TNF and C1q, and that these cytokines together are necessary and sufficient to induce A1 astrocytes. A1 astrocytes lose the ability to promote neuronal survival, outgrowth, synaptogenesis and phagocytosis, and induce the death of neurons and oligodendrocytes. Death of axotomized CNS neurons *in vivo* is prevented when the formation of A1 astrocytes is blocked. Finally, we show that A1 astrocytes are abundant in various human neurodegenerative diseases including Alzheimer's, Huntington's and Parkinson's disease, amyotrophic lateral sclerosis and multiple sclerosis. Taken together these findings help to explain why CNS neurons die after axotomy, strongly suggest that A1 astrocytes contribute to the death of neurons and oligodendrocytes in neurodegenerative disorders, and provide opportunities for the development of new treatments for these diseases.



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PROVA 2

1. Descrivere brevemente le principali eziologie che si riscontrano in chirurgia dell'epilessia e quali marcatori utilizzare per la loro caratterizzazione istopatologica
2. In Access cosa è una "Query"?
 - a. uno strumento idoneo all'interrogazione ed alla manipolazione dei dati
 - b. una tabella di visualizzazione di attributi di un elemento geografico
 - c. una tabella di visualizzazione di attributi di un elemento grafico
3. Leggere e tradurre il testo seguente

DOI: 10.1111/epl.18325

RESEARCH ARTICLE

Epilepsia

Cytomegalic parvalbumin neurons in fetal cases of hemimegalencephaly

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Abstract

Objective: Mutations in genes of the mTOR pathway have been identified as a major cause of hemimegalencephaly (HMG), focal cortical dysplasia type II, and tuberous sclerosis, cortical malformations associated with epilepsy. These conditions are characterized at the cellular level by increased size of pyramidal neurons that grow with dysmorphic features and in some cases by the presence of giant balloon cells. Our previous research in tuberous sclerosis has shown that parvalbumin (Pvalb) and calbindin immunoreactive cells in cortical and subcortical tuberal lesions show cytomegalic features, suggesting the involvement of GABAergic cells in mTOR-related pathologies. In the present report, we propose to deepen our understanding of the role of interneurons in mTOR-related cortical malformations by analyzing the maturation of Pvalb neurons in fetal samples of HMG.

Methods: We performed immunohistochemical staining of cortical samples from individuals with HMG from 21 gestational weeks to 10 postnatal months. The study focused on Pvalb cells, and pS6 counterstaining was performed to assess the activation of the mTOR pathway. To investigate the pathomechanisms behind the cytomegalic features, we examined mTOR pathway gene expression in Pvalb interneurons and cortical projection neurons using a single-cell transcriptomic atlas of the human neocortex.



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PROVA 3

1. Descrivere brevemente la preparazione di un campione di tessuto cerebrale ai fini dell'esecuzione di un esperimento di spettrometria di massa MALDI imaging
2. Con il termine "Data Base" si intende:
 - a. una collezione di dati, inerenti una specifica attività, opportunamente strutturati e accessibili tramite un software di gestione
 - b. un linguaggio di programmazione
 - c. un insieme di dati distribuiti sulla rete e accessibili solo tramite un browser
3. Leggere e tradurre il testo seguente



Molecular subtypes of epilepsy associated with post-surgical seizure recurrence

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* These authors contributed equally to this work.

Approximately 50% of individuals who undergo resective epilepsy surgery experience seizure recurrence. The heterogeneous post-operative outcomes are not fully explained by clinical, imaging and electrophysiological variables. We hypothesized that molecular features may be useful in understanding surgical response, and that individuals with epilepsy can be classified into molecular subtypes that are associated with seizure freedom or recurrence after surgical resection. Pre-operative blood samples, brain tissue and post-operative seizure outcomes were collected from a cohort of 40 individuals with temporal lobe epilepsy, 23 of whom experienced post-operative seizure recurrence. Messenger RNA and microRNA extracted from the blood and tissue samples were sequenced. The messenger RNA and microRNA expression levels from the blood and brain were each subjected to a novel clustering approach combined with multiple logistic regression to separate individuals into genetic clusters that identify novel subtypes associated with post-operative seizure outcomes. We then compared the microRNAs and messenger RNAs from patient blood and brain tissue that were significantly associated with each subtype to identify signatures that are similarly over- or under-represented for an outcome and more likely to represent endophenotypes with common molecular aetiology. These target microRNAs and messenger RNAs were further characterized by pathway analysis to assess their functional role in epilepsy. Using blood-derived microRNA and messenger RNA expression levels, we identified two subtypes of epilepsy that were significantly associated with seizure recurrence (clusters A1 and B4) (adjusted $P < 0.20$). A total of 551 microRNAs and 2486 messenger RNAs were associated with clusters A1 and B4, respectively (adjusted $P < 0.05$). Clustering of brain-tissue messenger RNA expression levels revealed an additional subtype (C2) associated with seizure recurrence that had high overlap of dysregulated messenger RNA transcripts with cluster B4. Clusters A1, B4 and C2 also shared significant overlap of subjects, which altogether suggests a coordinated mechanism by which microRNA and messenger RNA transcripts may be related to seizure recurrence. Epileptic subtypes A1, B4 and C2 reveal both known and novel microRNA and messenger RNA targets in seizure recurrence. Furthermore, targets identified in A1 and B4 are quantifiable in pre-operative blood samples and could potentially serve as biomarkers for surgical resection outcomes.



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