38_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI PER N. 2 POSTI DI RICERCATORE SANITARIO, DA ASSEGNARE ALLA SC NEUROLOGIA 5 – NEUROPATOLOGIA E SSD SERVIZIO DI MEDICINA DI LABORATORIO – SMEL 122 CON PUNTO PRELIEVI

PROVA I

1. Il candidato descriva i test a disposizione per fare diagnosi di FTD/AD

2. Il termine "Open Source" indica:
   a) un software i cui autori ne permettono e favoriscono il libero studio e l'apporto di modifiche da parte di altri programmatori
   b) un software che può essere modificato da chiunque a patto di corrispondere all'autore una offerta libera
   c) un software protetto da diritti d'autore che non può essere modificato da nessuno tranne da chi ne detiene i diritti

3. Leggere e tradurre il testo seguente

Mechanisms underlying TDP-43 pathology and neurodegeneration: An updated Mini-Review

Benjamin I. Nilaver and Henryk F. Urbanski *

Division of Neuroscience, Oregon National Primate Research Center, Beaverton, OR, United States

TAR DNA binding protein 43 kDa (TDP-43) plays an important role in several essential cell functions. However, TDP-43 dysfunction has been implicated in the development of various brain diseases including amyotrophic lateral sclerosis (ALS), frontotemporal lobar degeneration (FTLD), and limbic predominant age-related TDP-43 encephalopathy (LATE). Recent investigations into the individual components of TDP-43 pathology show how broader TDP-43 dysfunction may precede these disease end states, and therefore could help to explain why TDP-43 dysfunction continues to be implicated in a rapidly expanding category of neurodegenerative diseases. The literature reviewed in this article suggests that dysregulation of TDP- 43 initiated by some environmental and/or genetic insults can lead to a snowballing dysfunction across the cell, involving impaired gene expression, mRNA stability, as well as the function and coordination of those pathways directly regulated by TDP-43. Furthermore, the hallmarks of TDP-43 pathology, such as hyperphosphorylation and insoluble cytoplasmic accumulation of the protein may actually be artifacts of an upstream impairment in TDP-43's normal function. Overall, the present article summarizes current knowledge regarding TDP-43's normal and pathological cell functions and sheds light on possible mechanisms that underlie its causal role in neurodegeneration.

Annalisa Lombardo

PROVA NON ESTRATTA

03/06/2025 Aula Lombardo

38_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI PER N. 2 POSTI DI RICERCATORE SANITARIO, DA ASSEGNARE ALLA SC NEUROLOGIA 5 – NEUROPATOLOGIA E SSD SERVIZIO DI MEDICINA DI LABORATORIO – SMEL 122 CON PUNTO PRELIEVI

PROVA 2

1. Il candidato descriva i test ultrasensibili per la rilevazione di proteine misfolded in tessuti periferici di pazienti con malattie neurodegenerative

2. In Excel cosa è una "funzione"?
   a) un algoritmo di calcolo precostituito che ci permette di elaborare un calcolo complesso sui dati contenuti nelle celle
   b) un comando che ci permette di stampare
   c) un comando che ci permette di creare un grafico

3. Leggere e tradurre il testo seguente

Seed amplification assay for the detection of pathologic alpha-synuclein aggregates in cerebrospinal fluid

Luis Concha-Marambio[1], **Sandra Pritzkow**[2], **Mohammad Shahnawaz**[2], **Carly M. Farris**[1], **Claudio Soto**[1,2]
[1]R&D Unit, Amprion Inc., San Diego, CA, USA.
[2]Mitchell Center for Alzheimer's Disease and Related Brain Disorders, University of Texas McGovern Medical School, Houston, TX, USA.

Abstract

Misfolded alpha-synuclein (αSyn) aggregates are a hallmark event in Parkinson's disease (PD) and other synucleinopathies. Recently, αSyn seed amplification assays (αSyn-SAAs) have shown promise as a test for biochemical diagnosis of synucleinopathies. αSyn-SAAs use the intrinsic self-replicative nature of misfolded αSyn aggregates (seeds) to multiply them in vitro. In these assays, αSyn seeds circulating in biological fluids are amplified by a cyclical process that includes aggregate fragmentation into smaller self-propagating seeds, followed by elongation at the expense of recombinant αSyn (rec-αSyn). Amplification of the seeds allows detection by fluorescent dyes specific for amyloids, such as thioflavin T. Several αSyn-SAA reports have been published in the past under the names 'protein misfolding cyclic amplification' (αSyn-PMCA) and 'real-time quaking-induced conversion'. Here, we describe a protocol for αSyn-SAA, originally reported as αSyn-PMCA, which allows detection of αSyn aggregates in cerebrospinal fluid samples from patients affected by PD, dementia with Lewy bodies or multiple-system atrophy (MSA). Moreover, this αSyn-SAA can differentiate αSyn aggregates from patients with PD versus those from patients with MSA, even in retrospective samples from patients with pure autonomic failure who later developed PD or MSA. We also describe modifications to the original protocol introduced to develop an optimized version of the assay. The optimized version shortens the assay length, decreases the amount of rec-αSyn required and reduces the number of inconclusive results. The protocol has a hands-on time of ~2 h per 96-well plate and can be performed by personnel trained to perform basic experiments with specimens of human origin

ANNALISA LOMBARDO

PROVA NON ESTRATTA

03/06/2025

Annalisa Lombardo

38_CONCORSO PUBBLICO, PER TITOLI ED ESAMI, PER LA COPERTURA A TEMPO DETERMINATO, DELLA DURATA DI CINQUE ANNI PER N. 2 POSTI DI RICERCATORE SANITARIO, DA ASSEGNARE ALLA SC NEUROLOGIA 5 – NEUROPATOLOGIA E SSD SERVIZIO DI MEDICINA DI LABORATORIO – SMEL 122 CON PUNTO PRELIEVI

PROVA 3

1. Il candidato descriva le metodologie utili per la diagnosi pre- e post-mortem delle malattie da prioni

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

Mechanisms and pathology of protein misfolding and aggregation

Nikolaos Louros [1,2], Joost Schymkowitz[1,2] & Frederic Rousseau [1,2]

Abstract

Despite advances in machine learning-based protein structure prediction, we are still far from fully understanding how proteins fold into their native conformation. The conventional notion that polypeptides fold spontaneously to their biologically active states has gradually been replaced by our understanding that cellular protein folding often requires context-dependent guidance from molecular chaperones in order to avoid misfolding. Misfolded proteins can aggregate into larger structures, such as amyloid fibrils, which perpetuate the misfolding process, creating a self-reinforcing cascade. A surge in amyloid fibril structures has deepened our comprehension of how a single polypeptide sequence can exhibit multiple amyloid conformations, known as polymorphism. The assembly of these polymorphs is not a random process but is influenced by the specific
conditions and tissues in which they originate. This observation suggests that, similar to the folding of native proteins, the kinetics of pathological amyloid assembly are modulated by interactions specific to cells and tissues. Here, we review the current understanding of how intrinsic protein conformational propensities are modulated by physiological and pathological interactions in the cell to shape protein misfolding and aggregation pathology.

ANNALISA LOMBARDO

PROVA ESTRATTA

03/06/2025