UNIVERSITÀ DEGLI STUDI DI MILANO

SELEZIONE PUBBLICA, PER TITOLI ED ESAMI, PER IL RECLUTAMENTO DI N. 1 UNITÀ DI TECNOLOGO DI SECONDO LIVELLO - CATEGORIA D, POSIZIONE ECONOMICA D3 - PRESSO IL DIPARTIMENTO DI SCIENZE DELLA SALUTE, PER L'ATTUAZIONE DEL PROGETTO DAL TITOLO "D3 4 HEALTH - DIGITAL DRIVEN DIAGNOSTICS, PROGNOSTICS AND THERAPEUTICS FOR SUSTAINABLE HEALTH CARE"- PNRR - CODICE 22313

La Commissione giudicatrice della selezione, nominata con Determina Direttoriale n. 12002 del 18/07/2023, composta da:

Prof.ssa Rita Clara Paroni	Presidente
Prof.ssa Gabriella Roda	Componente
Dott.ssa Eleonora Casagni	Componente
Sig.ra Giuseppina Nisi	Segretaria

comunica i quesiti relativi alla prova orale:

PROVA 1

Cosa si intende per analisi semiquantitativa o analisi quantitativa in spettrometria di massa.

Lettura e traduzione – lingua inglese - tratto da Biomedicines 2021, 9, 1121

Spns2 Transporter Contributes to the Accumulation of S1P in Cystic Fibrosis Human Bronchial Epithelial Cells

The role of S1P in Cystic Fibrosis (CF) has been investigated since 2001, when it was first described that the CFTR channel regulates the inward transport of S1P. From then on, various studies have associated F508del CFTR, the most frequent mutation in CF patients, with altered S1P expression in tissue and plasma. We found that human bronchial epithelial immortalized and primary cells from CF patients express more S1P than the control cells, as evidenced by mass spectrometry analysis. S1P accumulation relies on two- to four-fold transcriptional up-regulation of SphK1 and simultaneous halving of SGPL1 in CF vs. control cells. The reduction of SGPL1 transcription protects S1P from irreversible degradation, but the excessive accumulation is partially prevented by the action of the two phosphatases that are up-regulated compared to control cells. For the first time in CF, we describe that Spns2, a non-ATP dependent transporter that normally extrudes S1P out of the cells, shows deficient transcriptional and protein expression, thus impairing S1P accrual dissipation. The in vitro data on CF human bronchial epithelia correlates with the impaired expression of Spns2 observed in CF human lung biopsies compared to healthy control.

PROVA 2

Descrivere brevemente quali sono i principali requisiti che deve avere uno spettrometro di massa per poter essere utilizzato in studi -omici untargetted

Lettura e traduzione – lingua inglese - tratto da Nature (2021) 11:10370

In-vitro and in-vivo metabolism of diferent aspirin formulations studied by a validated liquid chromatography tandem mass spectrometry method

Low-dose aspirin (ASA) is used to prevent cardiovascular events. The most commonly used formulation is enteric-coated ASA (EC-ASA) that may be absorbed more slowly and less efciently in some patients. To

uncover these “non-responders” patients, the availability of proper analytical methods is pivotal in order to study the pharmacodynamics, the pharmacokinetics and the metabolic fate of ASA. We validated a high-throughput, isocratic reversed-phase, negative MRM, LC–MS/MS method useful for measuring circulating ASA and salicylic acid (SA) in blood and plasma. ASA-d4 and SA-d4 were used as internal standards. The method was applied to evaluate: (a) the "in vitro" ASA degradation by esterases in whole blood and plasma, as a function of time and concentration; (b) the "in vivo" kinetics of ASA and SA after 7 days of oral administration of EC-ASA or plain-ASA (100 mg) in healthy volunteers (three men and three women, 37–63 years). Parameters of esterases activity were Vmax 6.5 ± 1.9 and Km 147.5 ± 64.4 in plasma, and Vmax 108.1 ± 20.8 and Km 803.2 ± 170.7 in whole blood. After oral administration of the two formulations, tmax varied between 3 and 6 h for EC-ASA and between 0.5 and 1.0 h for plain-ASA. Higher between-subjects variability was seen after EC-ASA, and one subject had a delayed absorption over eight hours. Plasma AUC was 725.5 (89.8–1222) for EC-ASA, and 823.1(624–1196) ng h/mL (median, 25–75% CI) for plain ASA. After the weekly treatment, serum levels of TxB2 were very low (< 10 ng/mL at 24 h from the drug intake) in all the studied subjects, regardless of the formulation or the tmax. This method proved to be suitable for studies on aspirin responsiveness.

PROVA 3

Quali sono i principali step per lo sviluppo e la validazione di un metodo analitico quantitativo in spettrometria di massa?

Lettura e traduzione – lingua inglese - tratto da Nature (2021) 11:10370

CA.ME.LI.A. An epidemiological study on the prevalence of cardiovascular, metabolic, liver and autoimmune diseases in Northern Italy

Background and Aims. CA.ME.LI.A (CA rdiovascular risks, ME tabolic syndrome, LI ver and A utoimmune disease) is a cross-sectional, epidemiological study performed 2009-2011 Abbiategrasso (Milan, Italy), to estimate the prevalence of cardiovascular risk factors, metabolic syndrome, liver and autoimmune diseases in the general adult population. This report focuses on the description and presentation of baseline characteristics of the population. Methods and Results. Citizens were randomly selected from the city electoral registers (n=30903), yielding a sample of 2554 subjects (M=1257, F=1297; age, 47±15 yrs; range 18-77 yrs). Men had higher prevalence of overweight or obesity (60.8% vs 41.6%; p5.0 mg/L) CRP were lower. Compared to normal weight men, risk-ratio (RR) of CRP elevation was 1.32 (ns) in overweight and 2.68 (p<0.0001) and 5.18 (p<0.0001). Metabolic syndrome was more frequent in men (32.7% vs. 14.5%; RR: 2.24, p<0.0001).
Interadventitia common carotid artery diameter was higher in men and increased with age and BMI.
Conclusions. The present study reports on the overall characteristics of a large population from Northern Italy. It aims to identify the associations among cardiovascular risk factors to prevent their development and progression, improve healthy lifestyle and identify subjects liable to pharmacological interventions.

Milano, 15 settembre 2023

La Commissione

Prof.ssa Rita Clara Paroni Presidente

Prof.ssa Gabriella Roda Componente

Dott.ssa Eleonora Casagni Componente

Sig.ra Giuseppina Nisi Segretaria