

BRAINART: MUSICA, MOVIMENTO E PATOLOGIE DEMENTIGENE

I BIOMARCATORI COME STRUMENTO DI DIAGNOSI, PROGNOSE E CONTROLLO DELLE PATOLOGIE NEURODEGENERATIVE

Presentazione del progetto:

Study of the effects
of adapted Tango and multidimensional intervention
in pREvention of dementia in agiNG:
developing healthY life style programs

STRENGTH project

Francesco Piacenza

Responsabile Unità Operativa Biomedica, IRCCS INRCA

Clinical Trial > Rejuvenation Res. 2014 Apr;17(2):235-8. doi: 10.1089/rej.2013.1516.

Epub 2014 Apr 11.

Effect of cognitive training on the expression of brain-derived neurotrophic factor in lymphocytes of mild cognitive impairment patients

Tiziana Casoli¹, Cinzia Giuli, Marta Ballei, Belinda Giorgetti, Moreno Solazzi, Patrizia Fattoretti

Affiliations + expand

PMID: 24127698 DOI: 10.1089/rej.2013.1516

I soggetti con MCI sottoposti a training cognitivo (10 sedute) hanno manifestato un abbassamento del livello di espressione genica del gene BDNF rispetto al baseline

J Alzheimers Dis. 2017; 57(1): 37-43.

PMCID: PMC5345639

Published online 2017 Mar 4. Prepublished online 2017 Feb 7. doi: 10.3233/JAD-161168

PMID: 28222525

Effect of a Comprehensive Intervention on Plasma BDNF in Patients with Alzheimer's Disease

Marta Ballei^{a,1,*}, Cinzia Giuli^{b,1}, Patrizia Fattoretti^a, Paolo Fabbietti^c, Roberta Papa^d, Demetrio Postacchini^b, and Fiorenzo Conti^{a,e}

Soggetti con «early AD» sottoposti a training cognitivo (10 sedute) hanno manifestato un abbassamento del livello di espressione genica del gene BDNF rispetto al baseline. Tale risultato non si è mantenuto dopo 24 mesi.

> J Trace Elem Med Biol. 2019 Sep;55:58-63. doi: 10.1016/j.jtemb.2019.06.001. Epub 2019 Jun 5.

Acetylcholinesterase inhibitors in Alzheimer's disease influence Zinc and Copper homeostasis

R Giacconi¹, C Giuli², T Casoli³, M Ballei³, L Costarelli⁴, M Provinciali⁵, A Basso⁵, F Piacenza⁵, D Postacchini², R Galeazzi⁴, P Fattoretti³, L Nisi⁵, P Fabbietti⁶, R Papa⁷, M Malavolta⁵

Affiliations + expand

PMID: 31345366 DOI: 10.1016/j.jtemb.2019.06.001

Zinco, rame e il rapporto Cu/Zn sono sensibili indicatori della risposta alla terapia con inibitori dell'Acetilcolinesterasi in pazienti con Alzheimer

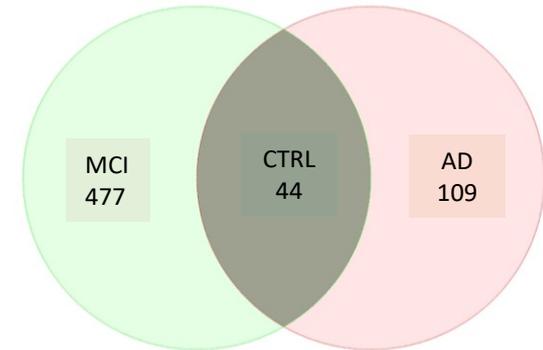
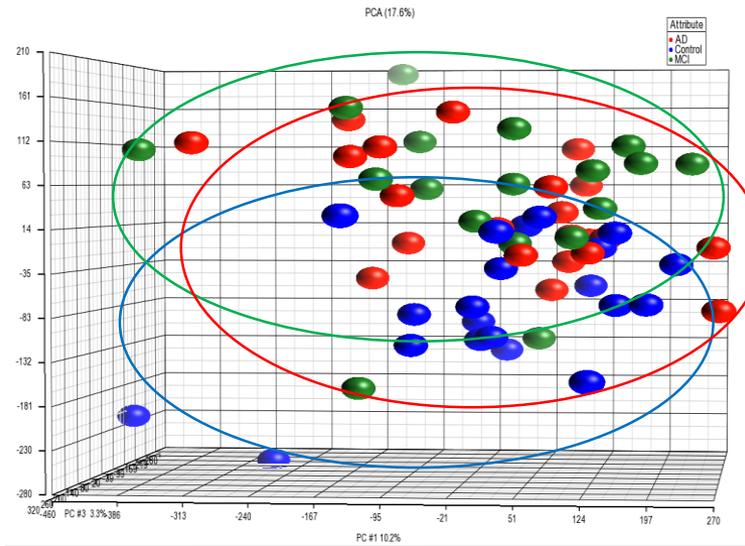
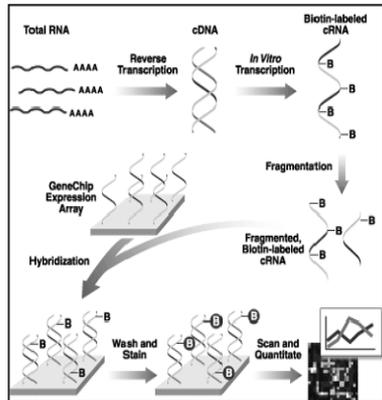
> Int J Mol Sci. 2020 Jul 20;21(14):5110. doi: 10.3390/ijms21145110.

Effect of a Cognitive Training Program on the Platelet APP Ratio in Patients with Alzheimer's Disease

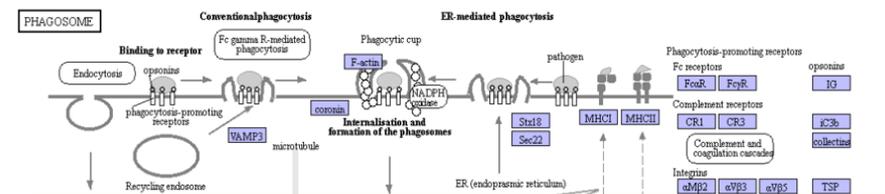
Tiziana Casoli¹, Cinzia Giuli², Marta Ballei¹, Paolo Fabbietti³, Fiorenzo Conti^{1,4}

Il «platelet amyloid precursor protein (APP) ratio (APPr), (il rapporto tra le due isoforme di APP) ha dimostrato essere un affidabile biomcatore periferico per studiare i meccanismi di plasticità sinaptica. L' APPr ha mostrato molteplici associazioni con endpoint clinici di misura della capacità cognitiva

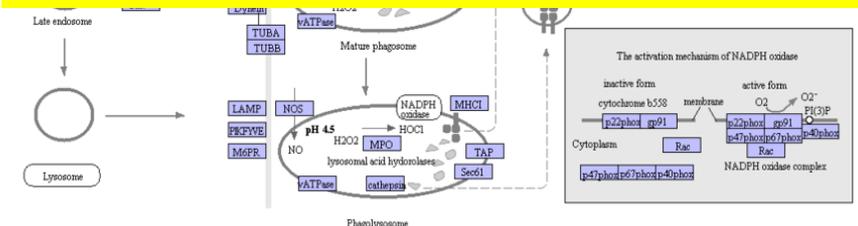
Progetto My Mind: Risultati sull'espressione genica



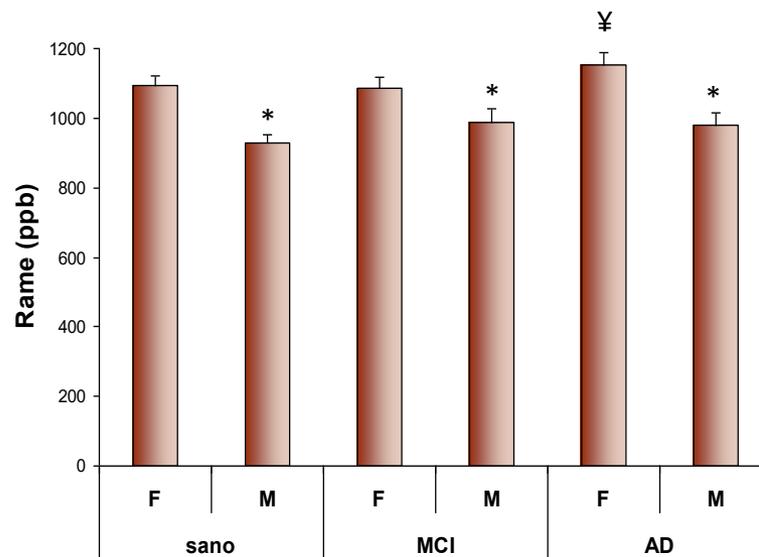
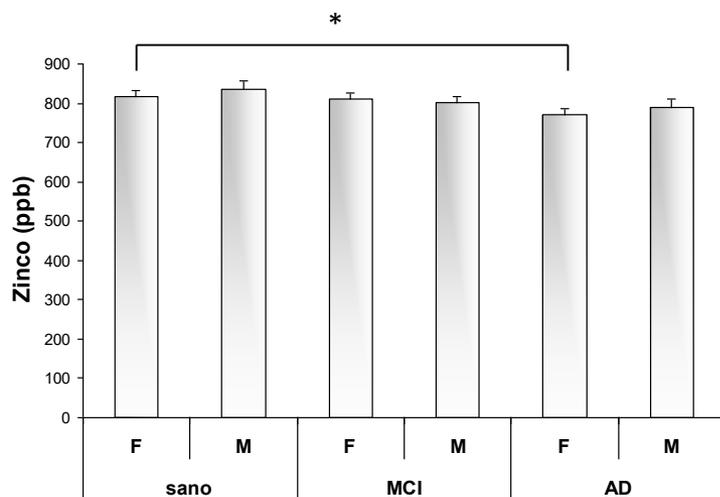
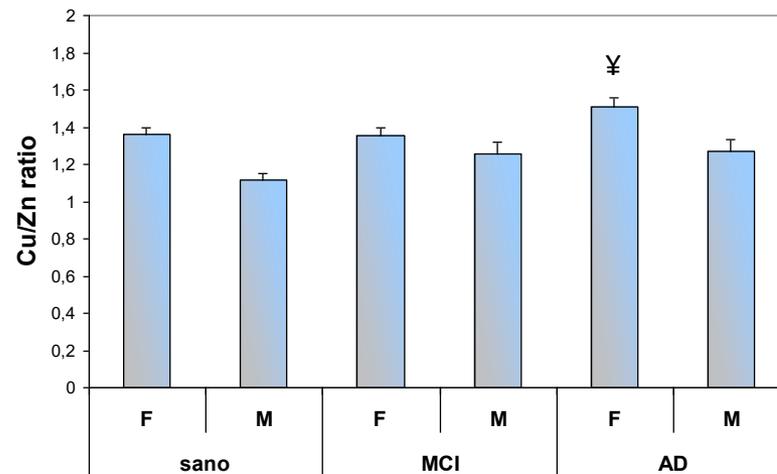
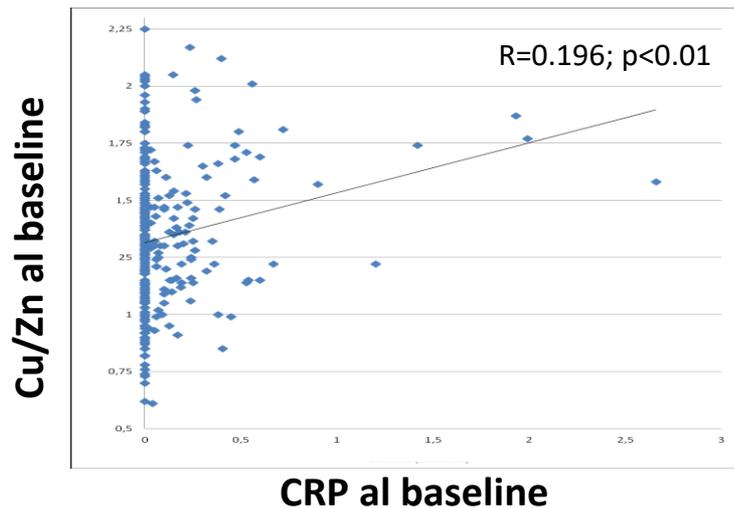
Gene Symbol	p-value (AD vs. CTRL)	Fold Change (AD vs. CTRL)	p-value (MCI vs. CTRL)	Fold Change (MCI vs. CTRL)
SLC22A25	3.45E-06	2.78649	0.0721901	1.45756
SHQ1	1.67E-05	2.6587	0.0263375	1.63216
TMX3	2.06E-05	2.46554	0.00050238	2.09965
HNRNPR	2.60E-05	2.3914	0.0017839	1.90727
RBM28	2.72E-05	2.38461	9.07E-06	2.61612
CLEC7A	1.21E-05	2.33937	0.000290516	2.02974
HERC3	8.29E-07	2.2928	1.30E-07	2.5521
UBE2G2	1.40E-05	2.26977	0.00144017	1.81709
GLYATL1	1.54E-07	2.17078	9.21E-05	1.75664
SRBD1	2.03E-05	2.1213	0.00103947	1.78333
PRDM10	2.15E-05	-2.12626	4.96E-05	-2.09671
LST1	7.02E-06	-2.14938	0.00904437	-1.54023
CENPK	5.09E-07	-2.16298	0.186992	-1.20642
LRRC71	8.09E-06	-2.1691	4.03E-07	-2.55112
PORCN	3.48E-05	-2.18557	0.149578	-1.30021
DLC1	7.56E-05	-2.20625	0.194077	-1.24346
PTMS	3.73E-05	-2.22802	0.000582064	-1.96423
ABCG5	4.31E-06	-2.24124	0.0724364	-1.34995
RBBP8NL	3.48E-06	-2.24591	0.000723329	-1.78875
TEX14	1.35E-05	-2.57502	0.000465961	-2.1442



Le cellule monocitarie dei soggetti Alzheimer sono caratterizzate da una alterata modulazione dell'espressione dei geni coinvolti nei processi di fagocitosi e di chemotassi.



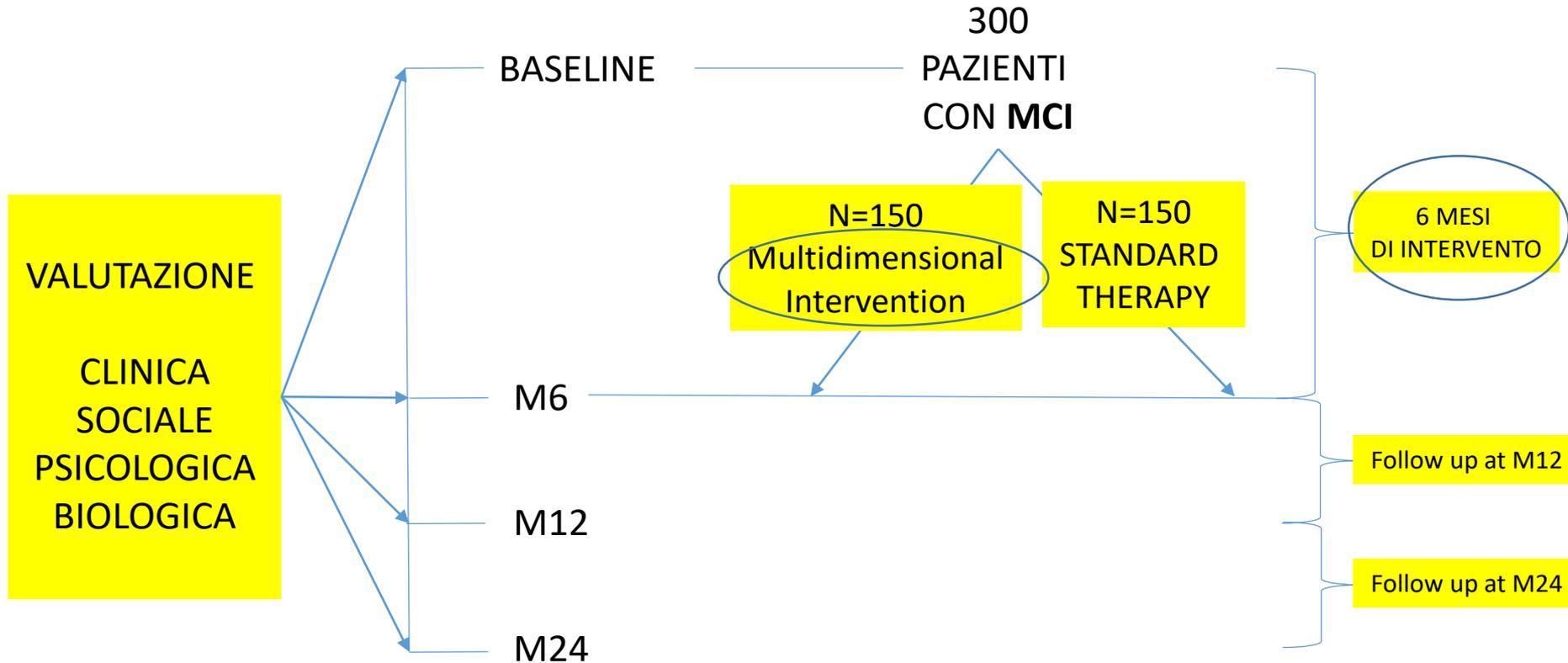
Rapporto Cu/Zn come parametro infiammatorio nei soggetti sani, MCI e AD



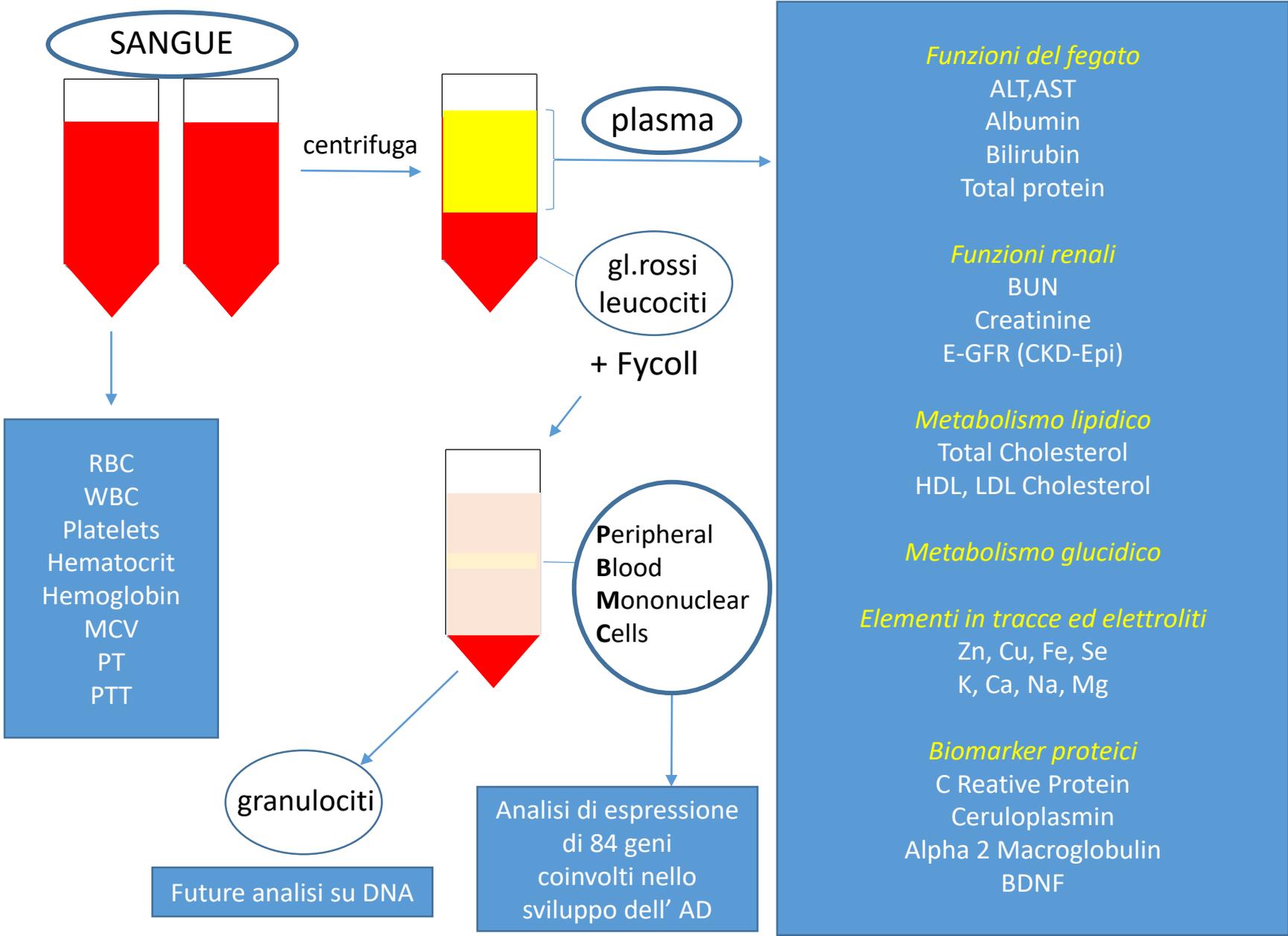
¥ rispetto a tutti i gruppi

* p<0.05 quando paragonato alle Femmine di ogni classe di soggetti

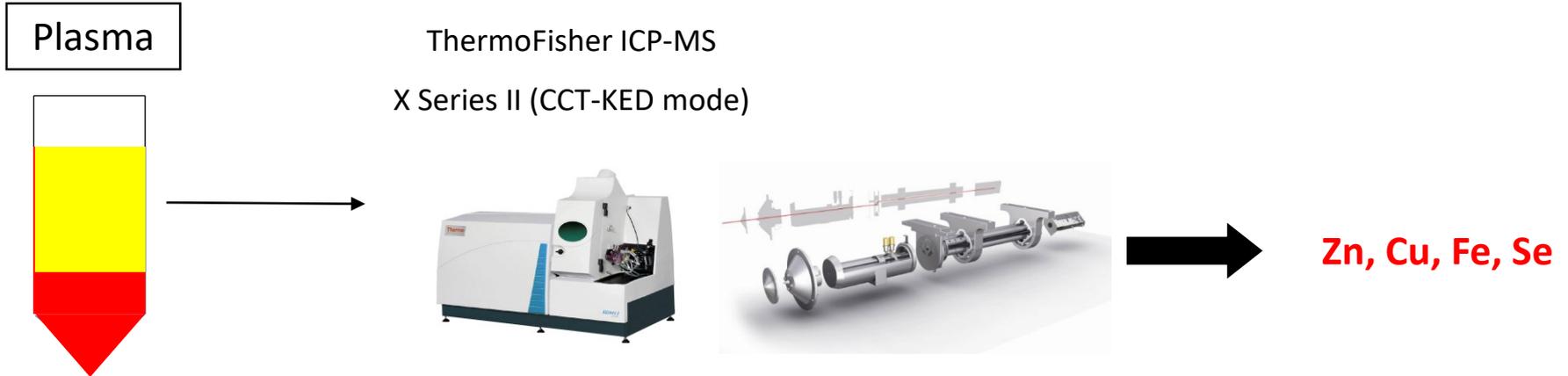
PROGETTO STRENGTH: DISEGNO DELLO STUDIO



VALUTAZIONE BIOLOGICA



MISURA DEI METALLI IN TRACCE



Ageing Research Reviews
Volume 11, Issue 2, April 2012, Pages 297-319

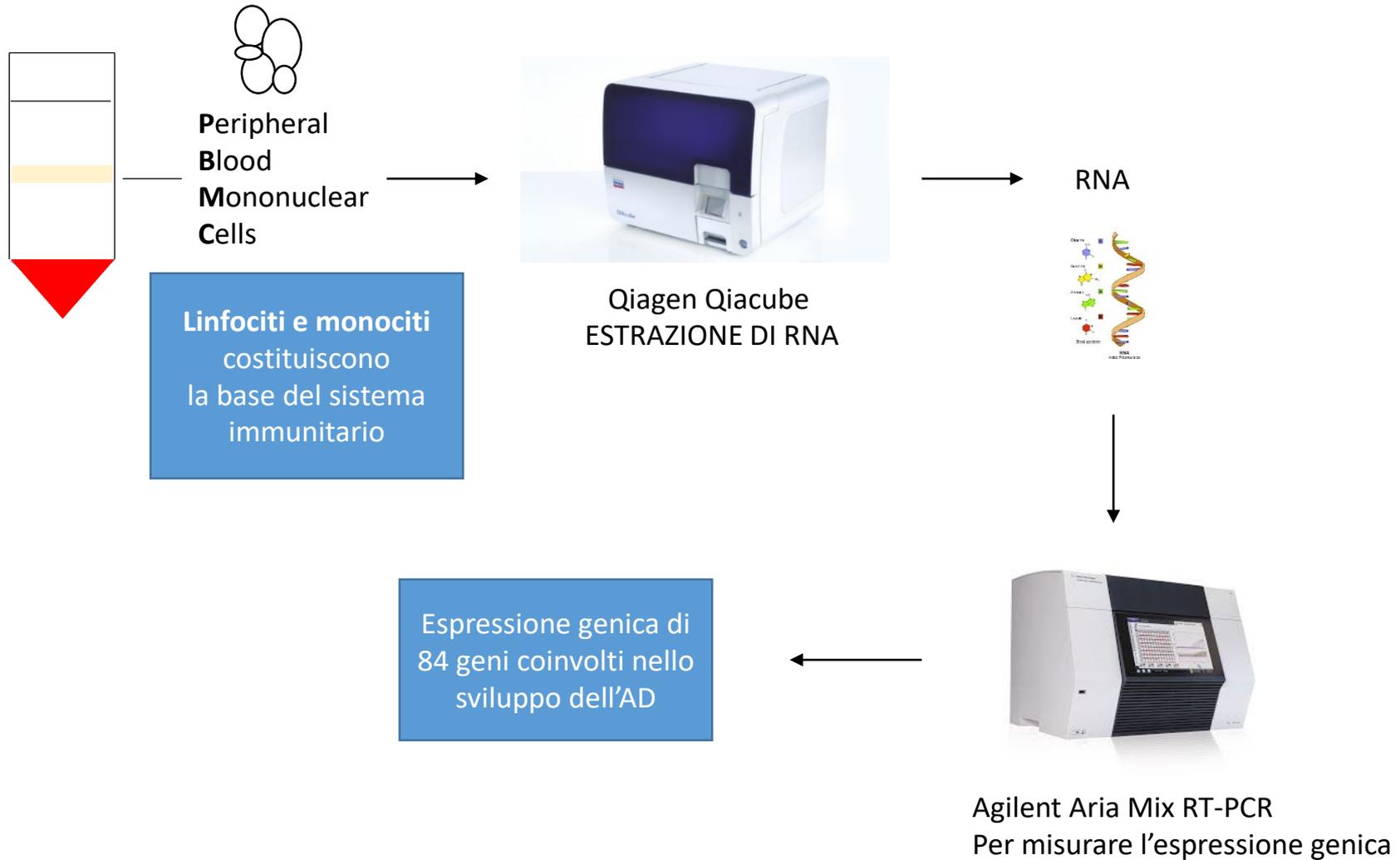


Review
Micronutrient (Zn, Cu, Fe)-gene interactions in ageing and inflammatory age-related diseases: Implications for treatments

Eugenio Mocchegiani , Laura Costarelli, Robertina Giacconi, Francesco Piacenza, Andrea Basso, Marco Malavolta

Zn, Cu, Fe, Se
SONO METALLI IN TRACCE
ESSENZIALI
PER LA STRUTTURA DELLE
MOLECOLE E PER ESSERE
COFATTORI ENZIMATICI DI
Più DI 300 ENZIMI

Misura di Espressione dell'mRNA



Beta-Amyloid Generation, Oligomerization, Clearance & Degradation

Secretases

ADAM9, APH1A, **BACE1**, BACE2, CTSB, NCSTN, PSE

> PLoS One. 2013 Apr 17;8(4):e61246. doi: 10.1371/journal.pone.0061246. Print 2013.

Mild oxidative stress induces redistribution of BACE1 in non-apoptotic conditions and promotes the amyloidogenic processing of Alzheimer's disease amyloid precursor protein

Jiang-Li Tan ¹, Qiao-Xin Li, Giuseppe D C Anthony Robert White, Genevieve Evin

Cytoskeleton Regulation

APOE, MAP2, MAPT, R

Synaptic Formation

ACHE, APBA1 (MINT F, CHAT.

Lipid Metabolism

ABCA1, APOA1, APO

Apoptosis

APL A, MAPT, MIF, C, NAE1, PRKCA, PRKCE, PRKCF, PRKCG, PRKCH, PRKI, PRKID, PRKIL, PRKIP, PRKIQ, PRKIS, PRKIT, PRKIZ, PRKJ, PRKL, PRKM, PRKN, PRKO, PRKP, PRKQ, PRKR, PRKS, PRKT, PRKV, PRKW, PRKX, PRKY, PRKZ, PSEN1, PSEN2, SNCA.

Cell Cycle

APBB1, APBB2, CDK1, CDK5, CDKL1, EP300, ERN1, IL1 A, NAE1, PRKCA.

Cell Signaling Molecules

WNT Signaling

GSK > Int J Mol Sci. 2020 Jul 20;21(14):5110. doi: 10.3390/ijms21145110.

Notc
ADA
G-P

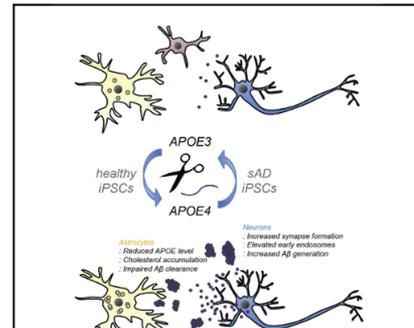
Effect of a Cognitive Training Program on the Platelet APP Ratio in Patients with Alzheimer's Disease

Tiziana Casoli ¹, Cinzia Giuli ², Marta Baietti ¹, Paolo Fabbietti ³, Fiorenzo Conti ^{1 4}

Neuron

APOE4 Causes Widespread Molecular and Cellular Alterations Associated with Alzheimer's Disease Phenotypes in Human iPSC-Derived Brain Cell Types

Graphical Abstract



Authors

Yuan-Ta Lin, Jinsoo Seo, Fan Gao, ..., Tak Ko, Bruce A. Yankner, Li-Huei Tsai

Correspondence

lhtsai@mit.edu

In Brief

By generating and characterizing isogenic APOE3- or APOE4-carrying human brain cell types, Lin et al. show that the APOE4 variant can lead to extensive gene expression alterations, and multiple cellular phenotypes potentially related to AD pathogenesis, in neurons, astrocytes, and microglia.

> Rejuvenation Res. 2020 Oct;23(5):411-419. doi: 10.1089/rej.2020.2307. Epub 2020 Apr 21.

Is Blood Brain-Derived Neurotrophic Factor a Useful Biomarker to Monitor Mild Cognitive Impairment Patients?

Marta Baietti ¹, Cinzia Giuli ², Tiziana Casoli ¹, Paolo Fabbietti ³, Fiorenzo Conti ^{1 4}

Cell Signaling

APBB2, PRKCA, PRKCB, PRKCD, PRKCE, PRKCF, PRKCG, PRKCH, PRKI, PRKID, PRKIL, PRKIP, PRKIQ, PRKIS, PRKIT, PRKIZ, PRKJ, PRKL, PRKM, PRKN, PRKO, PRKP, PRKQ, PRKR, PRKS, PRKT, PRKV, PRKW, PRKX, PRKY, PRKZ, PSEN1, PSEN2.

Signaling Molecules

DNB2, IDE, IL1A, INSR, NAE1, PLAU (UPA).

Cellular Regulation

APBB2 EP300 ERN1

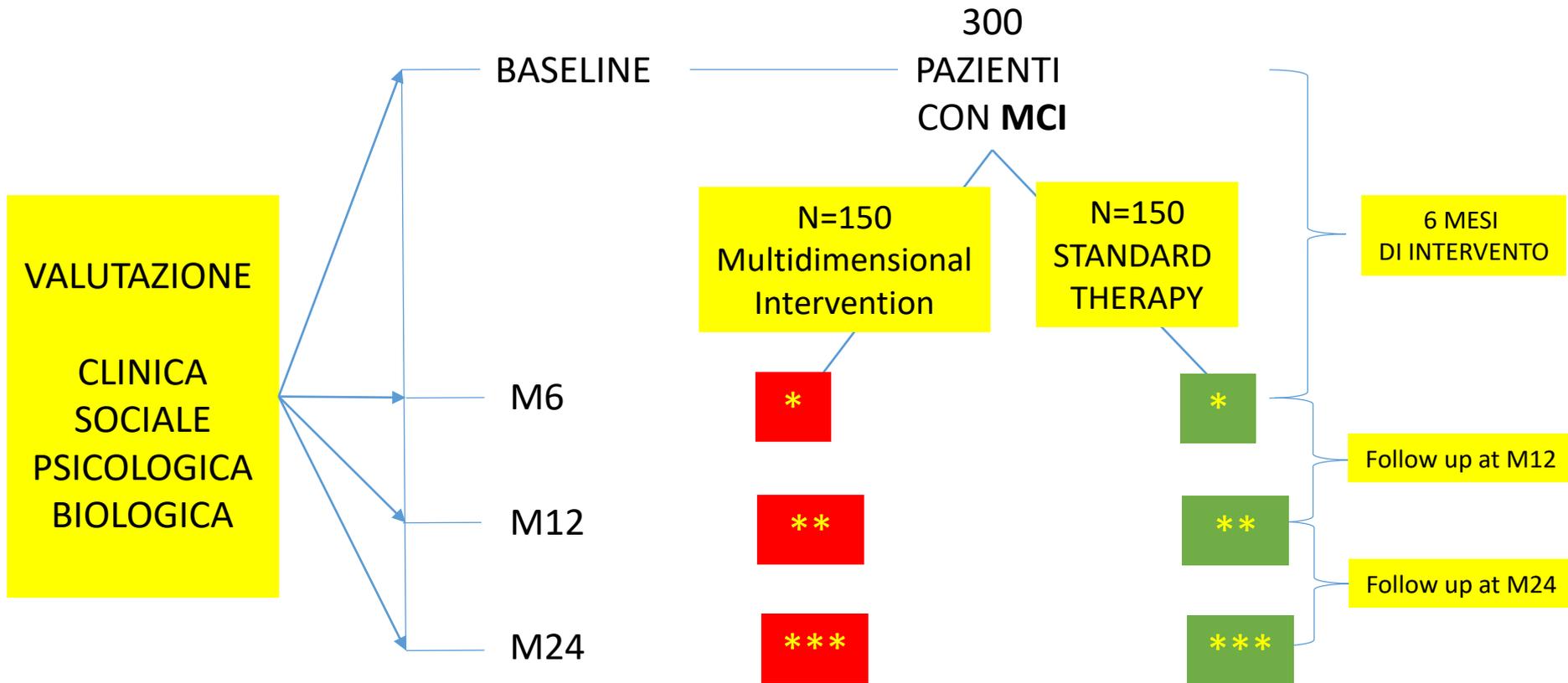
Randomized Controlled Trial > J Alzheimers Dis. 2018;63(4):1405-1414. doi: 10.3233/JAD-171117.

Oxidative Stress in Elderly with Different Cognitive Status: My Mind Project

Patrizia Fattorelli ¹, Marco Malavolta ², Paolo Fabbietti ³, Roberta Papa ⁴, Robertina Giacconi ², Laura Costarelli ⁵, Roberta Galeazzi ⁵, Cristina Paoloni ⁶, Demetrio Postacchini ⁶, Fabrizia Lattanzio ⁷, Cinzia Giuli ⁶

Proteases

ADAM10, APLP2, APP, CAPN1, CTSC, CTSD, CTSG, CTS L, SERPINA3, UQCRC2.



Lo studio dei biomarcatori

- può far luce sui **meccanismi** di azione/di non azione di una terapia rispetto a quella Standard
- Trovati i meccanismi è possibile indirizzare la ricerca verso lo **sviluppo di farmaci personalizzati**
- Può far luce sul perché alcuni pazienti **rispondono** alla terapia, altri no
- Può far luce sui meccanismi per i quali l'effetto della terapia **si mantiene/non si mantiene** nel tempo