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ISTITUTO NAZIONALE PER L'ASSICURAZIONE
CONTRO GLI INFORTUNI SUL LAVORO

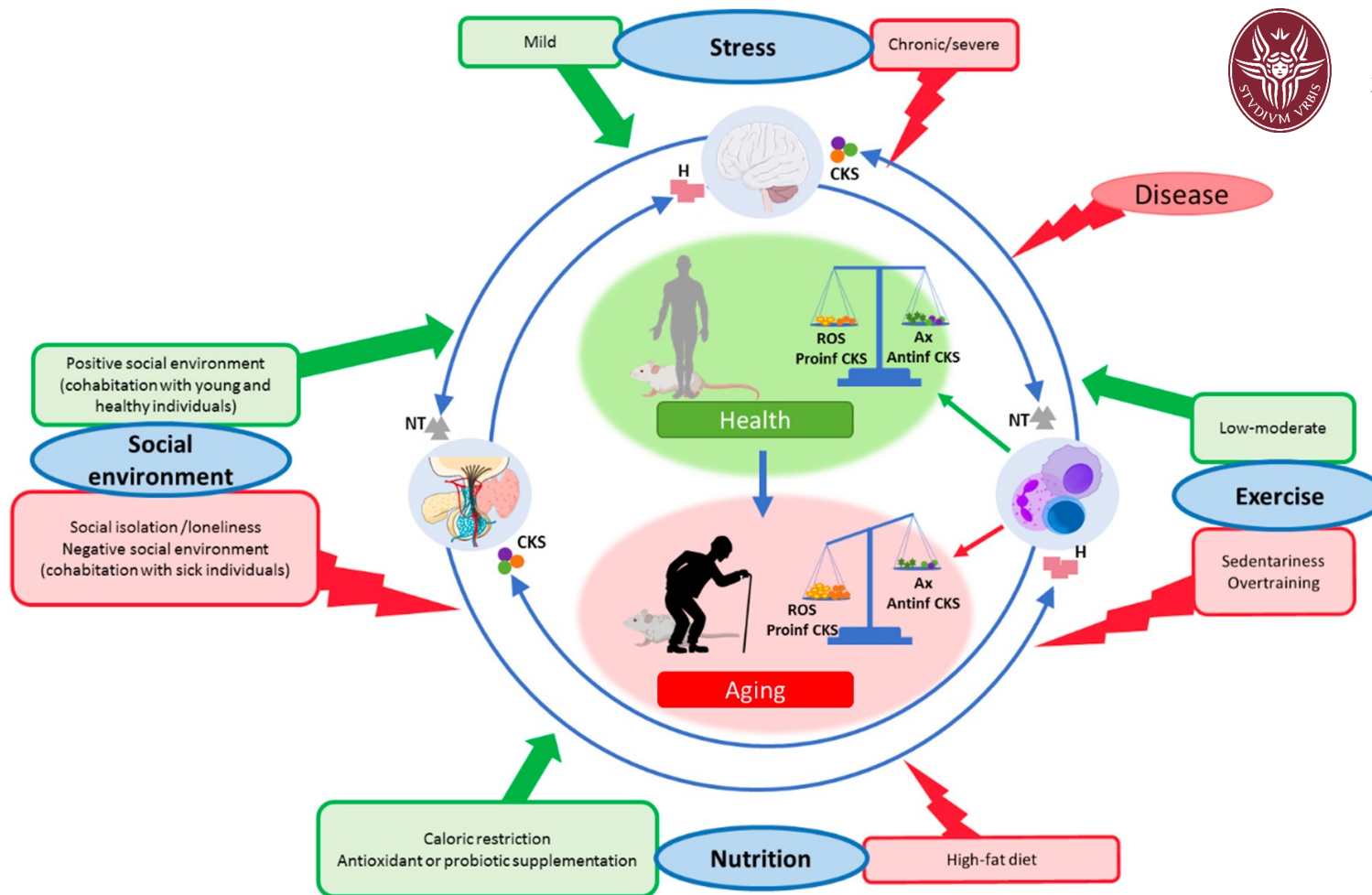


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ESPOSIZIONE AD ATMOSFERE IPERBARICHE: ANALISI DEL PROFILO INFIAMMATORIO

Gaeta 14.3.26

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Medico-chirurgiche
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Martínez de Toda, I.; Ceprián, N.; Díaz-Del Cerro, E.; De la Fuente, M. The Role of Immune Cells in Oxi-Inflamm-Aging. *Cells* 2021, 10, 2974.

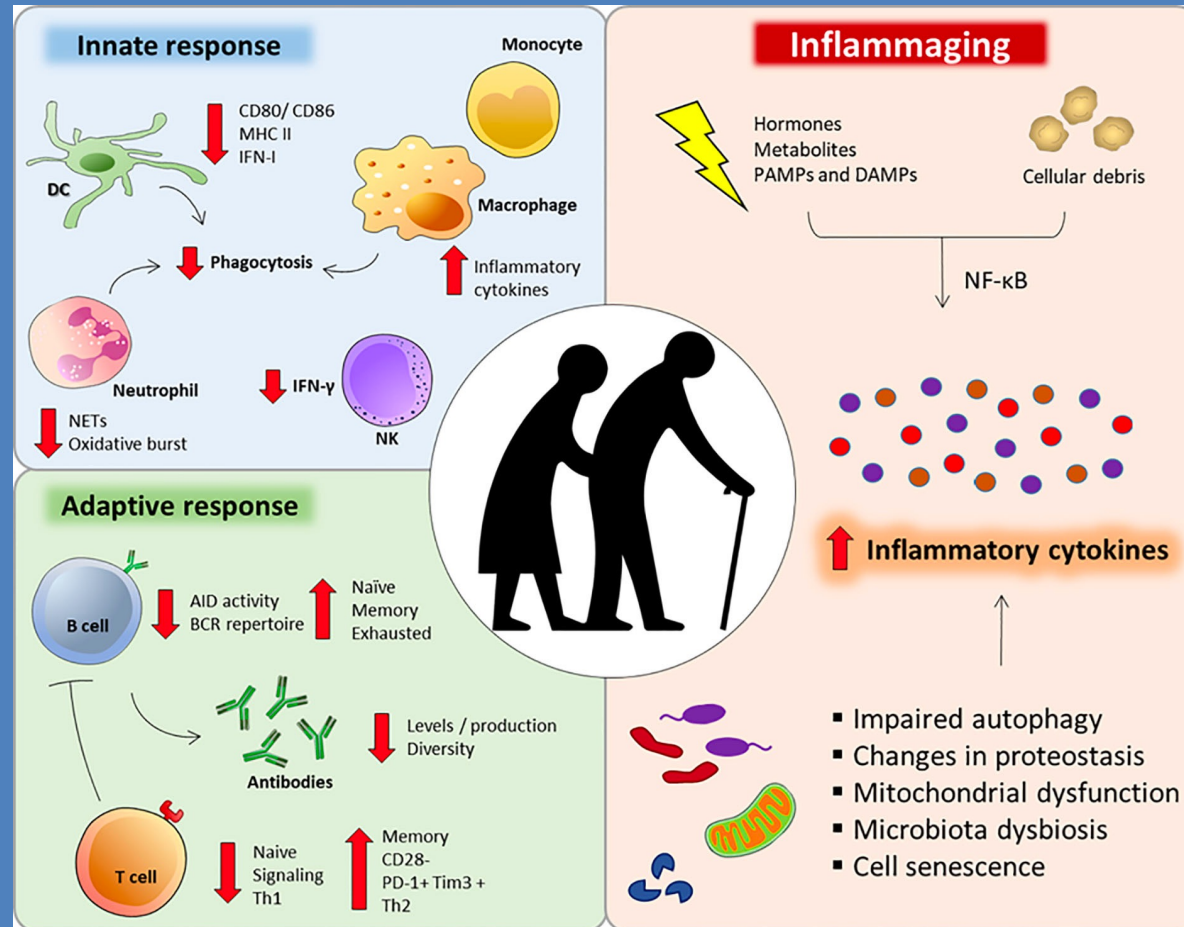


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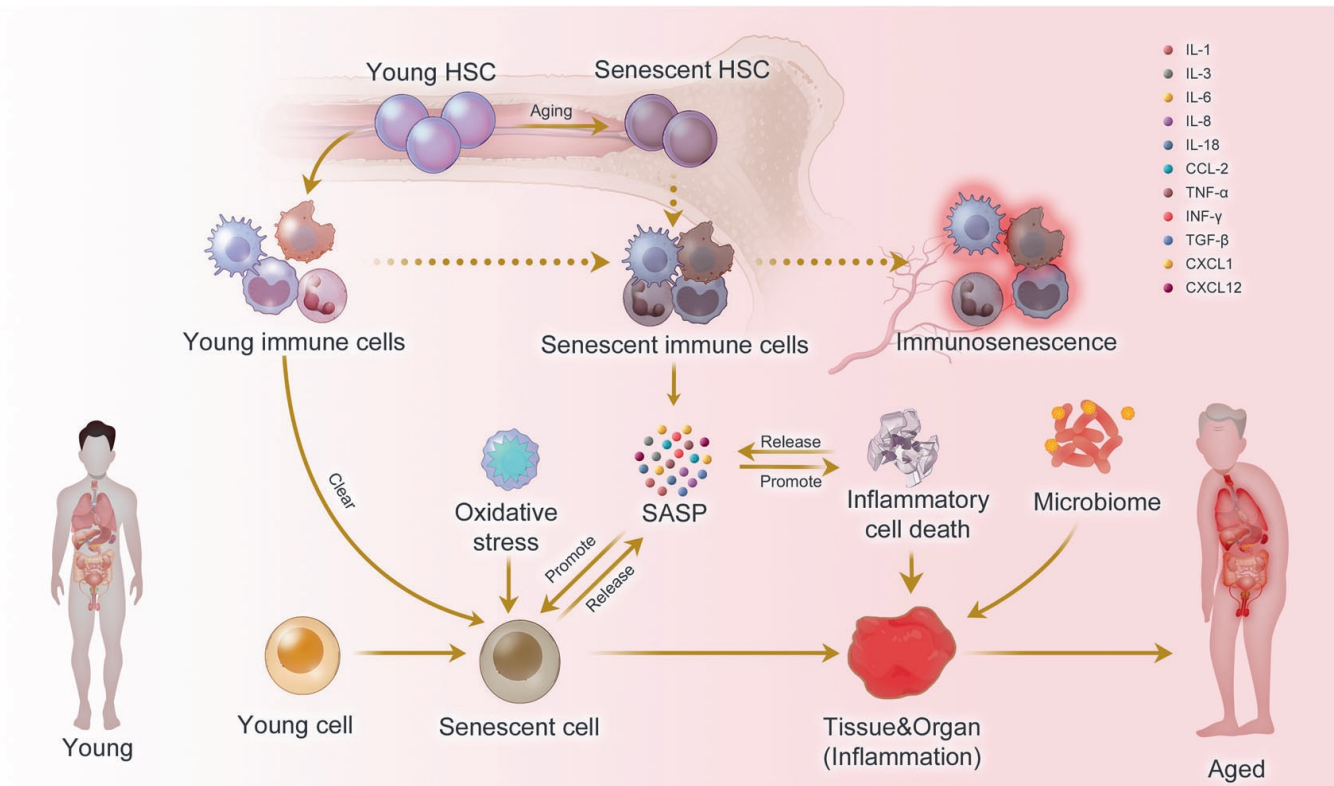


- **AGING:**
- Dysregulation of immunity and metabolism
- Immunosenescence
- Chronic low-grade inflammation
- Autophagy and mitophagy dysfunction
- Dysregulation of the ubiquitin-proteasome system
- Mitochondrial dysfunction
- Metainflammation
- Dysbiosis





Zia A. et al Curr Pharm Biotechnol. 2025
doi:10.2174/0113892010328697250210065420.



Inflammaging at the molecular, cellular, and organ levels. During the aging process, almost all cells in the body undergo senescence, a state characterized by a dysfunctional state and **senescence-associated secretory phenotype (SASP)**. While immune cells play a crucial role in recognizing and eliminating these senescent cells, they are also affected by SASP, leading to a phenomenon called **immunosenescence**. Immunosenescence can impair the immunity to respond to infections and diseases, making the organism more vulnerable to illnesses. Moreover, the accumulation of senescent cells can trigger inflammation in organs, leading to organ damage and an increased risk of age-related diseases. This process is exacerbated by positive feedback loops that drive the accumulation of inflammation and organ damage, leading to further inflammation and an even higher risk of aging-related diseases

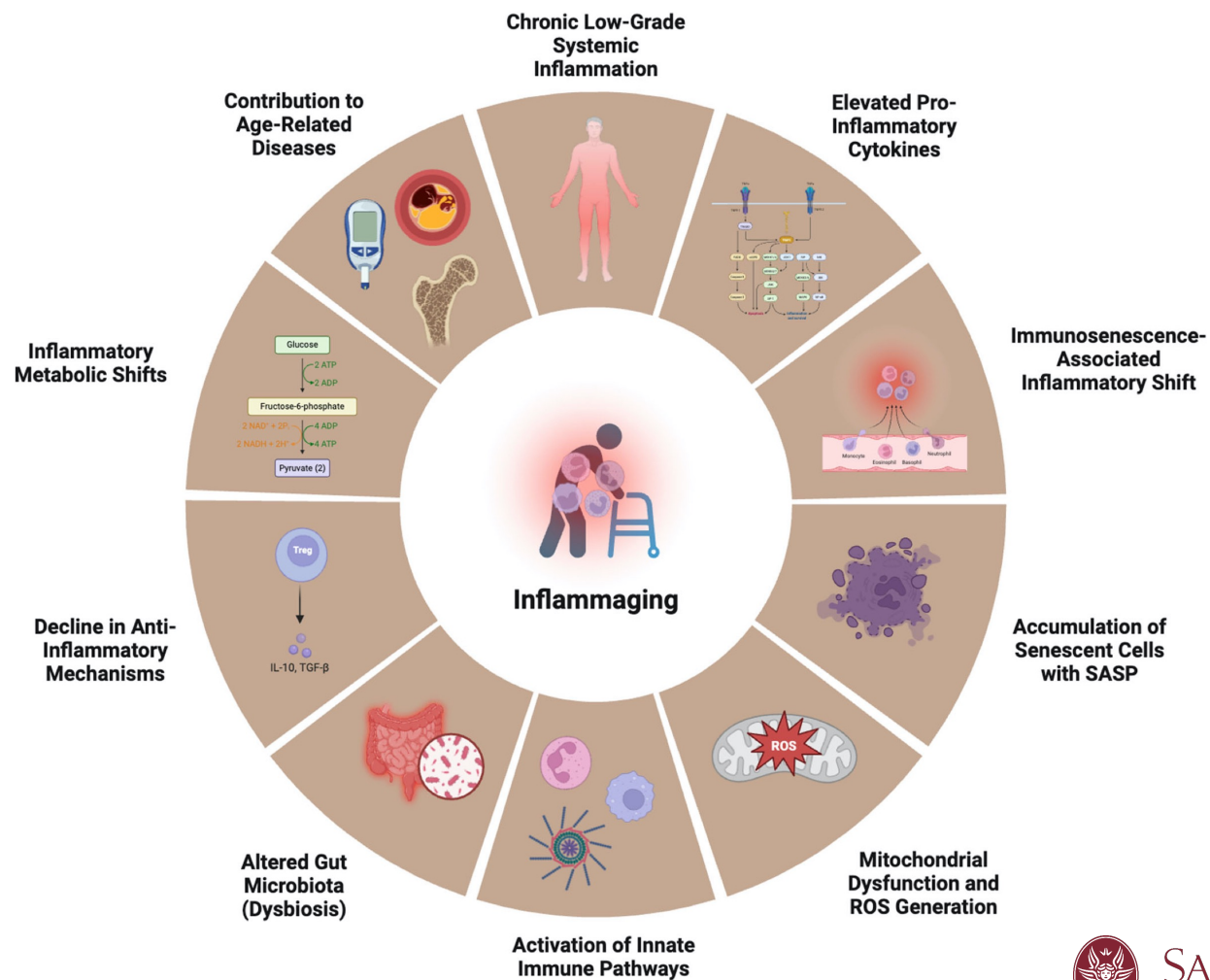
Li et al. Signal Transduction and Targeted Therapy (2023) 8:239

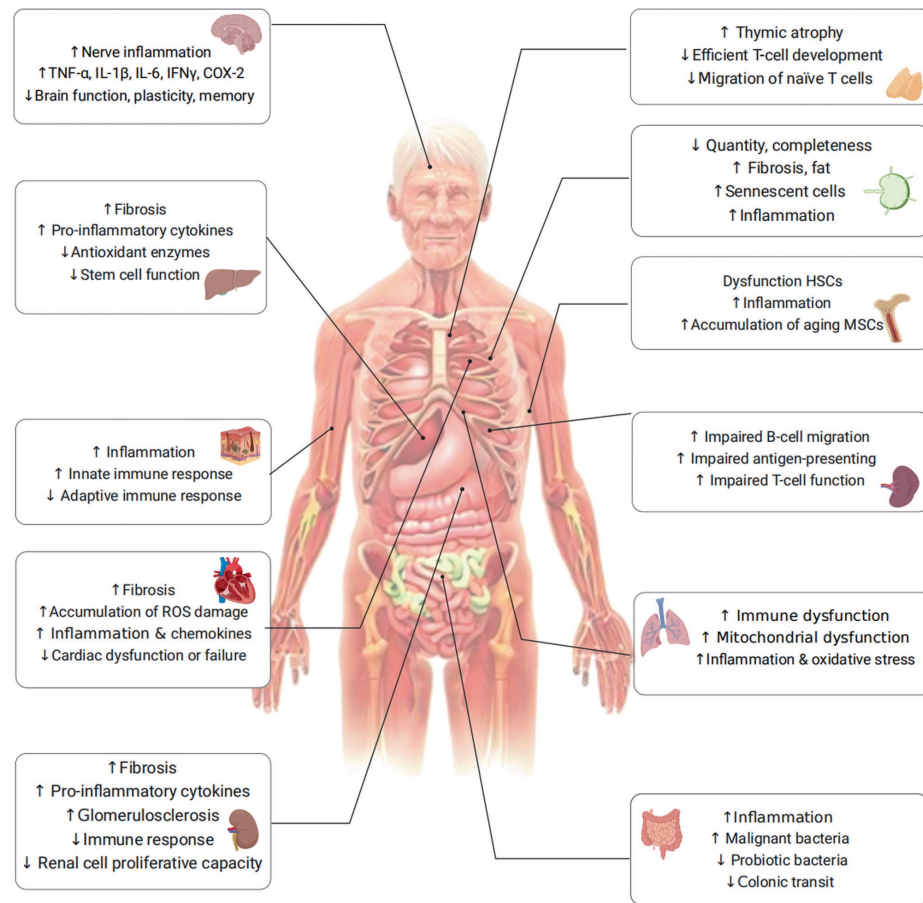
Hallmarks of inflammaging. Central to inflammaging is persistent chronic low-grade systemic inflammation, driven by elevated levels of pro-inflammatory cytokines and an immunosenescence-associated inflammatory shift—where aged immune cells acquire a pro-inflammatory phenotype. The accumulation of senescent cells secreting the **senescence-associated secretory phenotype (SASP)** further propagates inflammation.

Mitochondrial dysfunction and the generation of reactive oxygen species (ROS) activate innate immune pathways, while aging-associated changes in the gut microbiota (dysbiosis) promote systemic exposure to microbial products like lipopolysaccharide (LPS).

Simultaneously, there is a decline in anti-inflammatory mechanisms, such as the reduced secretion of IL-10 and TGF- β by regulatory T cells (Tregs).

Fetrayani, D et al. *Med. Sci.* **2025**, *13*, 100.

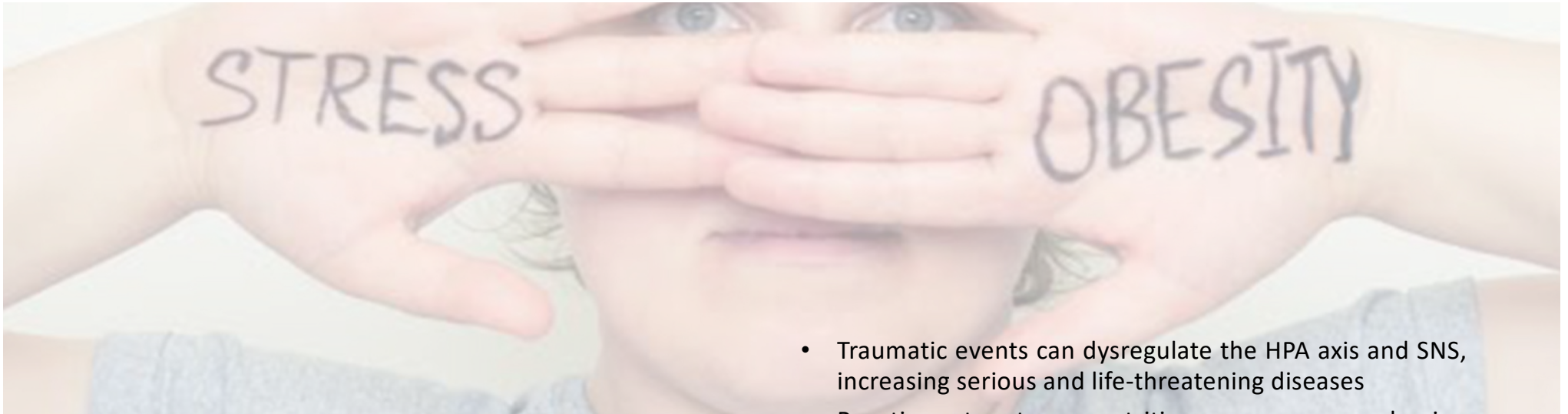




Aging manifests as a decline in organ function and an increased susceptibility to diseases. Functional changes in cells are shown in each organ.

Li et al. Signal Transduction and Targeted Therapy (2023) 8:239





J Neuroimmune Pharmacol (2013) 8:212–226
DOI 10.1007/s11481-012-9432-6

PERSPECTIVE

Stress and Obesity as Risk Factors in Cardiovascular Diseases: A Neuroimmune Perspective

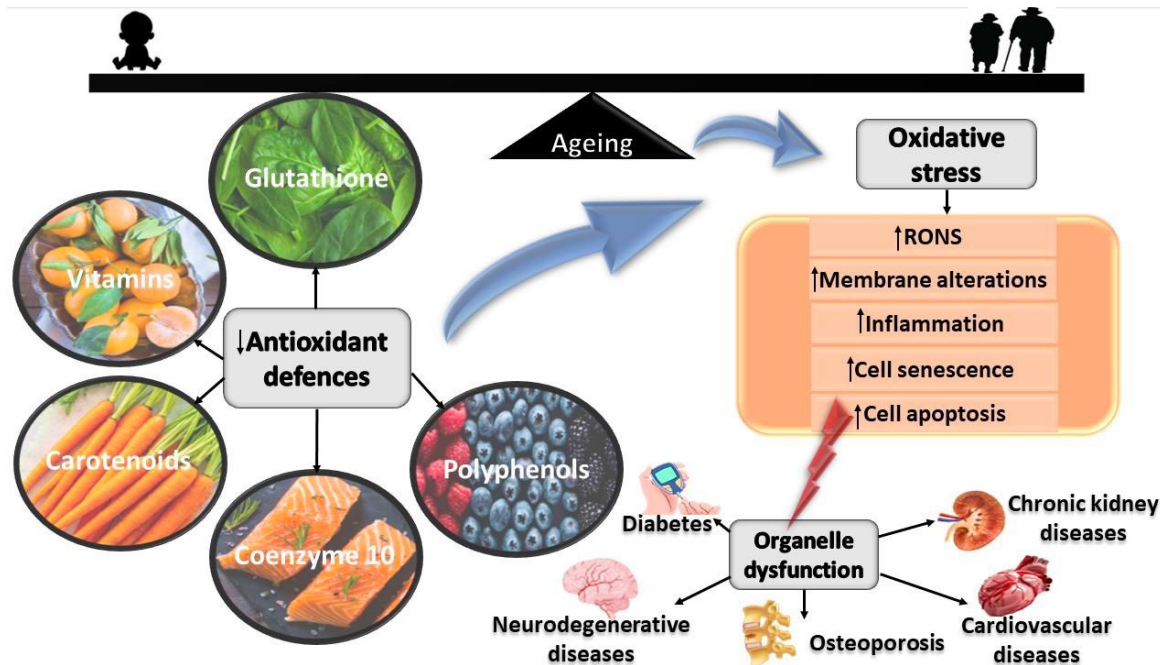
Flora Ippoliti · Nicoletta Canitano · Rita Businaro



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- Traumatic events can dysregulate the HPA axis and SNS, increasing serious and life-threatening diseases
- Reactions to stress: nutrition as a neuroendocrine reward response
- Long-term exposure to glucocorticoids stimulates the brain's reward system (Heber and Carpenter 2011), thus encouraging the pursuit of “comfort foods” (high in fat and sugar).
- People can choose calorie-rich foods to blunt their stress response or reduce anxiety. Calorie intake may also increase in response to elevated cortisol levels.
- Chronic stress triggers comfort food seeking, causing obesity, low-grade inflammation, energy dysregulation, and leptin and insulin resistance.

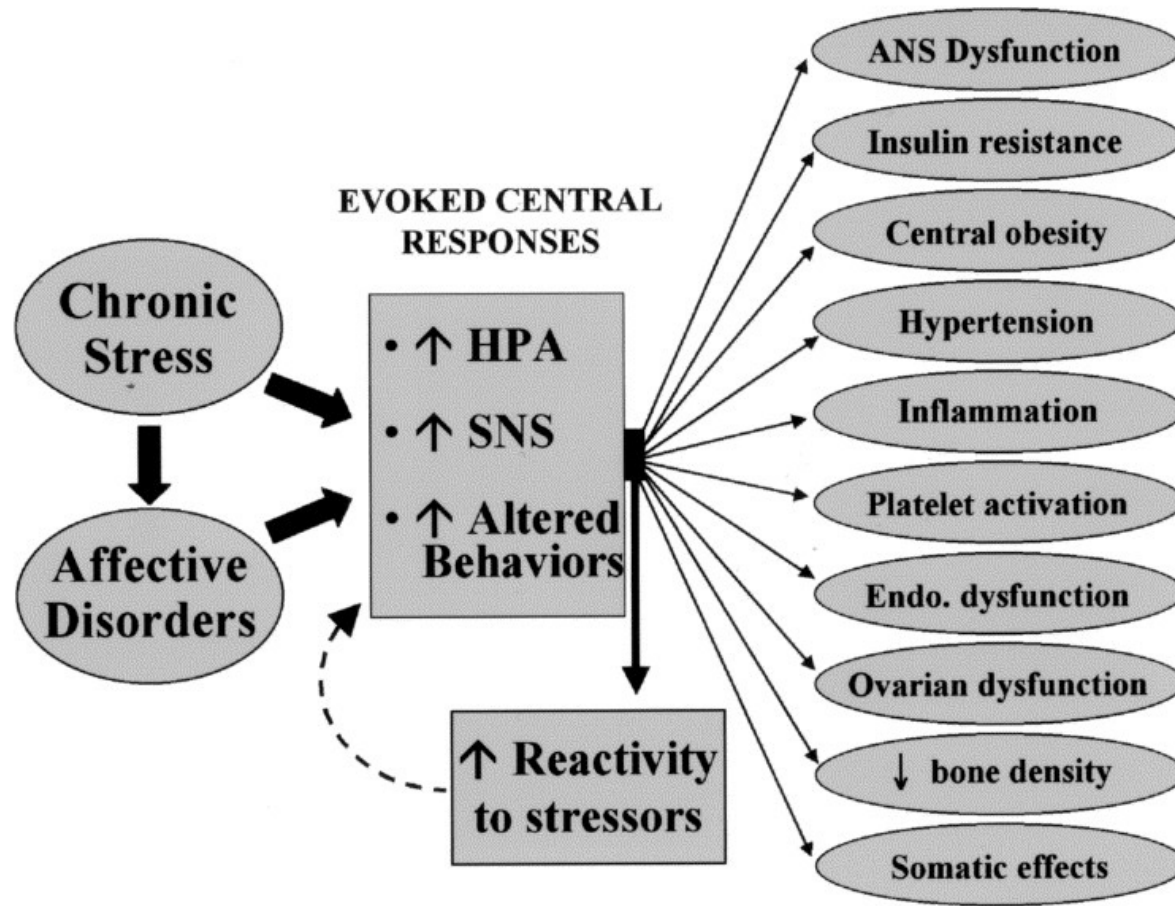
Influence of oxidative stress and the interface of ageing and chronic degenerative diseases

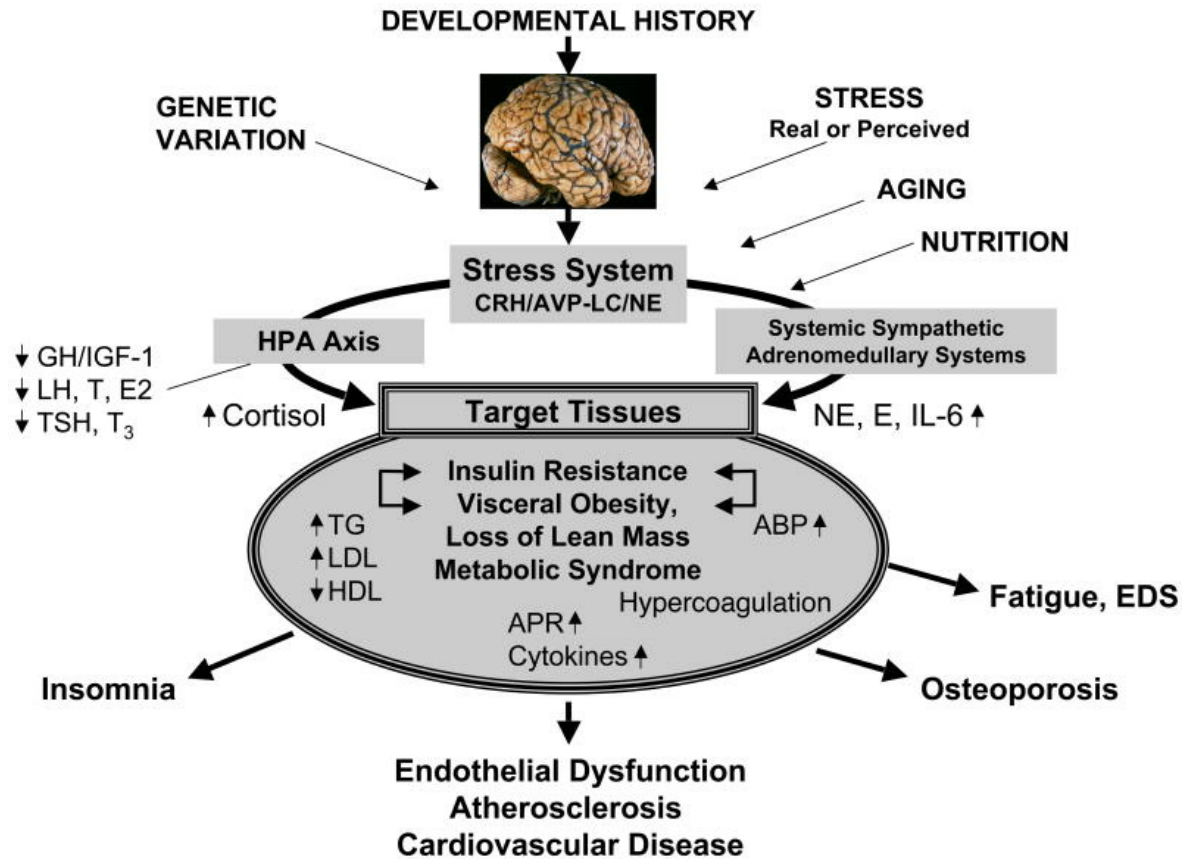


The accretion of oxidative stress and the defective antioxidant defence system contributes to elevated membrane alterations, inflammation, cell senescence, and cell apoptosis. This may subsequently contribute to chronic degenerative diseases

Leyane TS, et al. Int J Mol Sci. 2022;23:7273

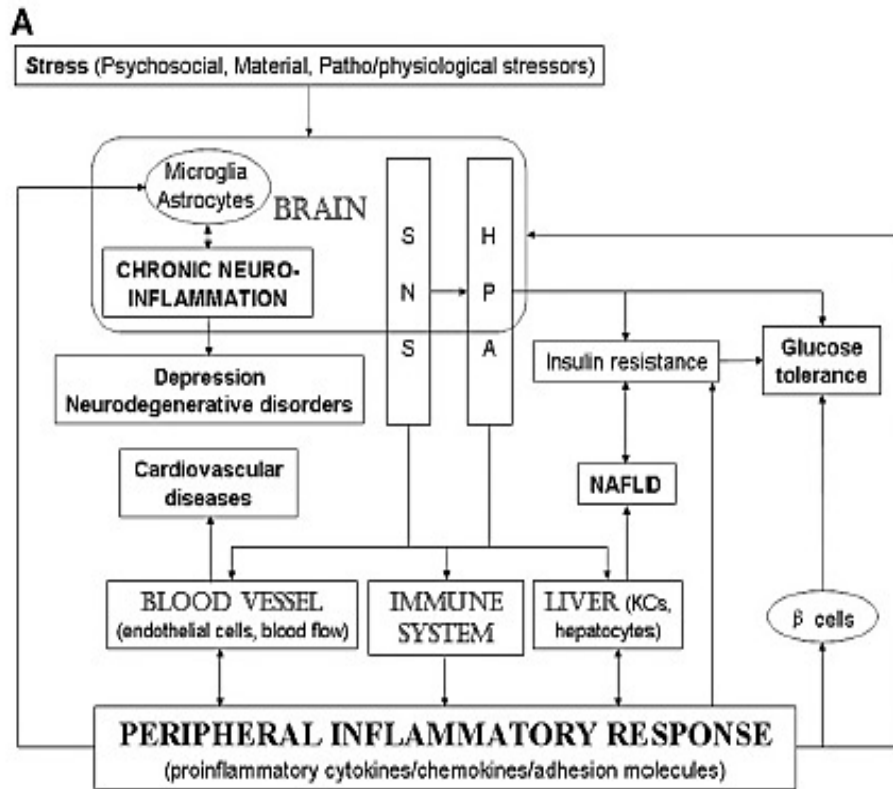




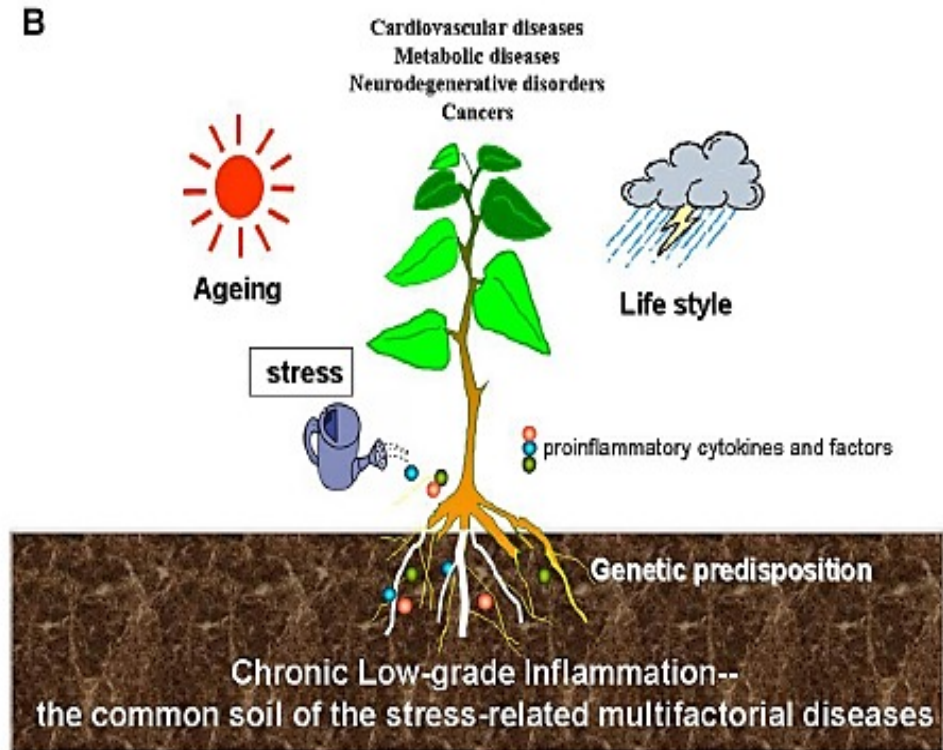


Endogenous/exogenous inputs to the stress system and their effects on the metabolic and cardiovascular systems and bone
 ABP: Arterial blood pressure; APR: Acute phase reactants; AVP: Arginine vasopressin; CRH: Corticotropin-releasing hormone; E2: Estradiol;
 EDS: Excessive daytime sleepiness; GH: Growth hormone; HDL: High-density lipoprotein; HPA Axis: Hypothalamic-pituitary-adrenal axis; IGF-
 1: Insulin-like growth factor-1; IL-6: Interleukin-6; LC: Locus caeruleus; LDL: Low-density lipoprotein; LH: Luteinizing hormone;
 NE: Norepinephrine; T: Testosterone; T3: Triiodothyronine; TG: Triglyceride; TSH: Thyroid-stimulating hormone.
 Chrousos and Kino Ann NY Acad Sci 1179:153-166,2009

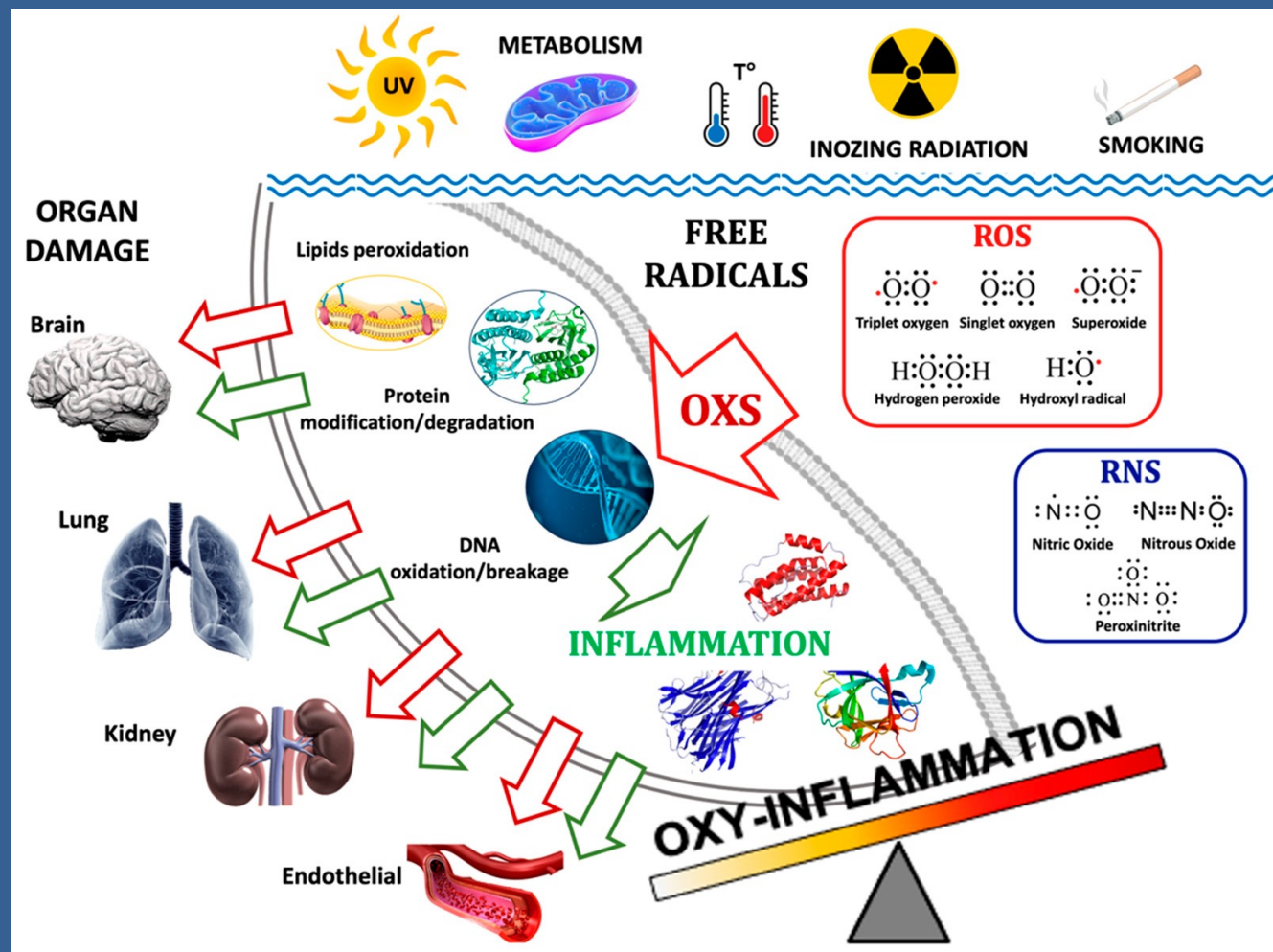




(SNS) sympathetic nervous system; (HPA) hypothalamic-pituitary-adrenal axis; (NAFLD) non-alcoholic fatty liver disease



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pathways of the formation of Oxy-Inflammation and organ damage. Environmental triggers such as exposure to UV and ionizing radiation, metabolism, water/body temperature, and smoking can produce free radicals: ROS (e.g., 3O_2 , O_2 , O_2^- , H_2O_2 , $HO\cdot$) and RNS (e.g., NO , N_2O , $ONOO^-$). Their accumulations can lead to lipids cellular membrane degradation, misfolded proteins, and DNA oxidation/breakage. The inflammation triggered by Oxi-Inflammation is the cause of many types of organ damage and acute/chronic diseases

Vezzoli et al. Int J Mol Sci. 2024;25(5):3060.



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La variazione del profilo infiammatorio sistemico rappresenta un potenziale biomarcatore della risposta dell'organismo allo stress iperbarico ed è stata proposta come parametro per il monitoraggio della qualità della decompressione e la stima del rischio iperbarico nella pratica subacquea.

FREE RADICAL RESEARCH
2019, VOL. 53, NO. 5, 522-534
<https://doi.org/10.1080/10715762.2019.1612890>



ORIGINAL ARTICLE



Effect of hyperoxia on the immune status of oxygen divers and endurance athletes

Frauke Tillmans^a, Roshanak Sharghi^{b*}, Tatjana Noy^{a*}, Wataru Kähler^a, Sebastian Klapa^a, Simon Sartiso^a, Susanne Sebens^{b,†} and Andreas Koch^{a,†}

Physiol Genomics 46: 647-654, 2014.
First published July 8, 2014; doi:10.1152/physiolgenomics.00028.2014.

Scuba diving induces nitric oxide synthesis and the expression of inflammatory and regulatory genes of the immune response in neutrophils

Antoni Sureda,¹ Juan M. Batle,¹ Xavier Capó,¹ Miquel Martorell,¹ Alfredo Córdova,² Josep A. Tur,¹ and Antoni Pons¹

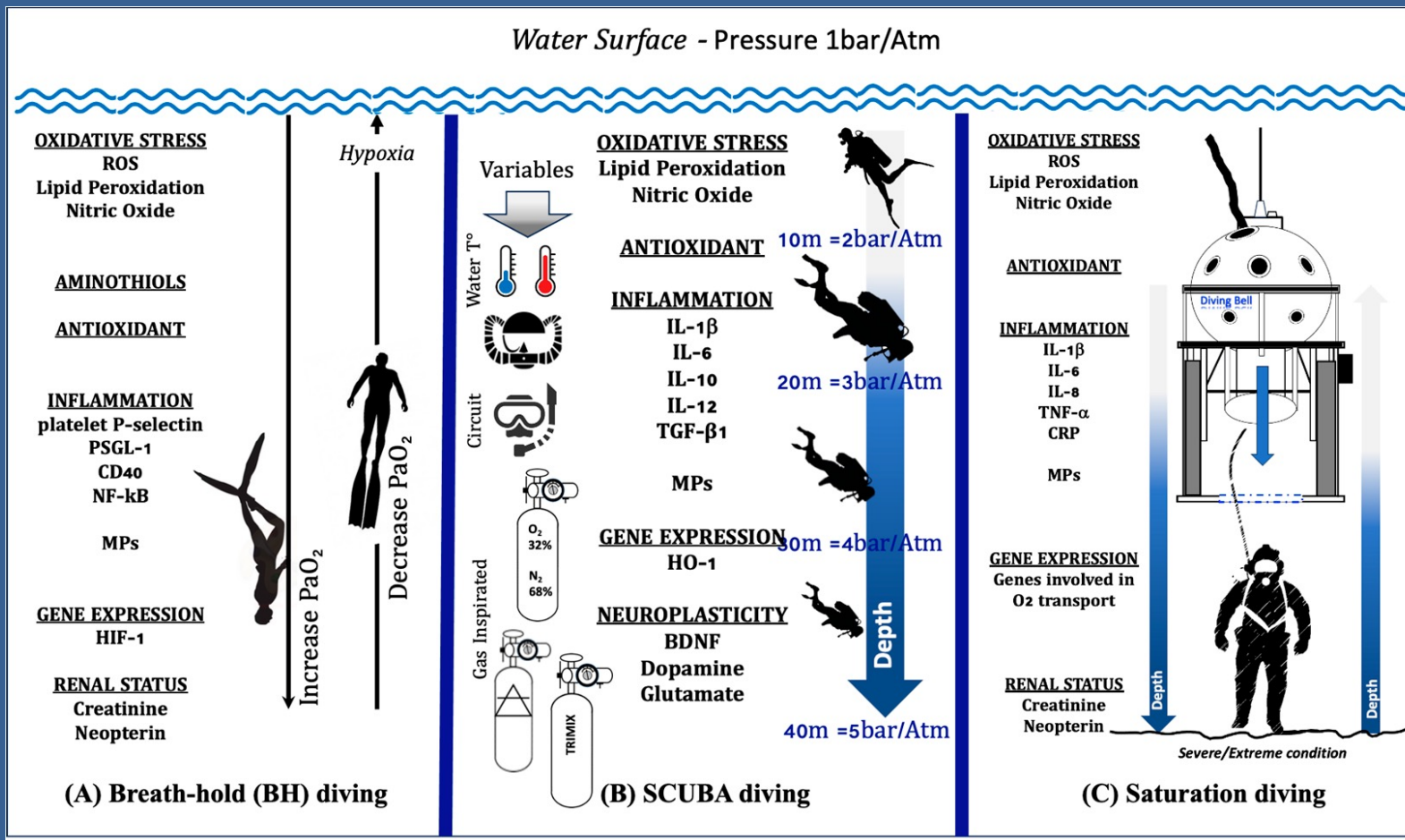
Physiol Genomics 45: 965-972, 2013.
First published August 20, 2013; doi:10.1152/physiolgenomics.00164.2012.

Acute and potentially persistent effects of scuba diving on the blood transcriptome of experienced divers

Ingrid Eftedal,¹ Marko Ljubkovic,² Arnar Flatberg,³ Arve Jørgensen,¹ Alf O. Brubakk,¹ and Zeljko Djicic²



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The "diving response", including physiological adaptation, cardiovascular stress

Esposizione a elevata pO₂



- > Accentua lo stress ossidativo
- > Stimola Infiammazione
- > Risposte patofisiologiche in acuto abbastanza conosciute
- > Cambiamenti persistenti nel tempo in seguito a esposizione cronica?
- > Fattori di rischio per lo sviluppo di malattie cronico-degenerative?
- > Possibili strategie di prevenzione?

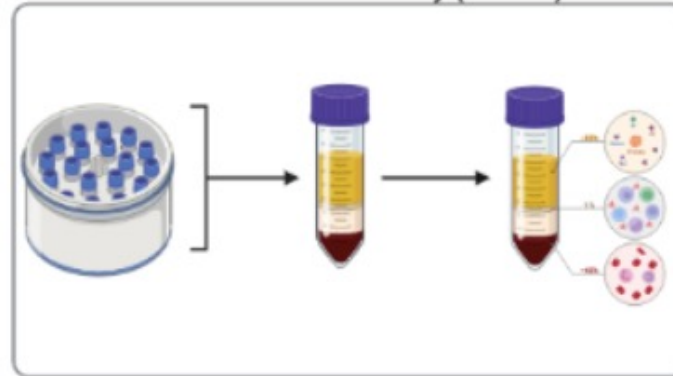
MONONUCLEAR CELL SEPARATION by BUFFY COAT



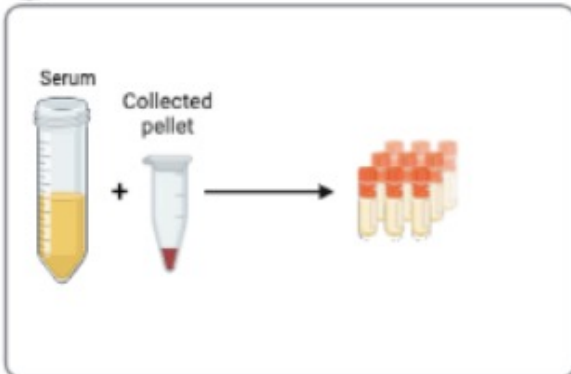
1 Blood collection from patients



2 Buffy Coat- Serum collection (ELISA) and mononuclear cell recovery (RT-PCR)



3 Store in eppendorf



4 Freeze



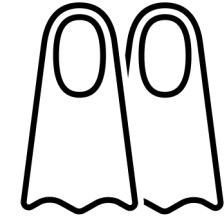
1. Centrifugare il campione di sangue periferico a 1200 rpm per 10 min a 4°C.
2. Recuperare il plasma per ogni campione di sangue (circa 250ul ciascuna eppendorf) e conservarlo a -80°C per analizzare la presenza di citochine tramite ELISA.
3. Recuperare con una Pasteur sterile le cellule mononucleate (anello bianco) e raccoglierlo in un tubo sterile da 15ml (circa 0,5 ml ogni campione).
4. Aggiungere 0,800ml di lysis buffer per ciascun campione (Buffer EL-ERYthrocyte lysis buffer cat. n. 79217, Qiagen) e lasciare a 4°C (in ghiaccio) per 20 min agitando per inversioni ogni 10 min.
5. Centrifugare a 1200 rpm per 10 min a 4 °C.
6. Eliminare il surnatante aggiungere 0.4ml di lysis buffer a 4°C per 5 min.
7. Centrifugare a 1200 rpm per 10 min a 4°C ed eliminare il surnatante.
8. Sospendere con 1 ml PBS (1X) in una eppendorf da 1,5ml e centrifugare a 1300 rpm per 1 min a TA.
9. Scartare il surnatante e aggiungere 700ul di Qiazol poi congelare a -80°C.



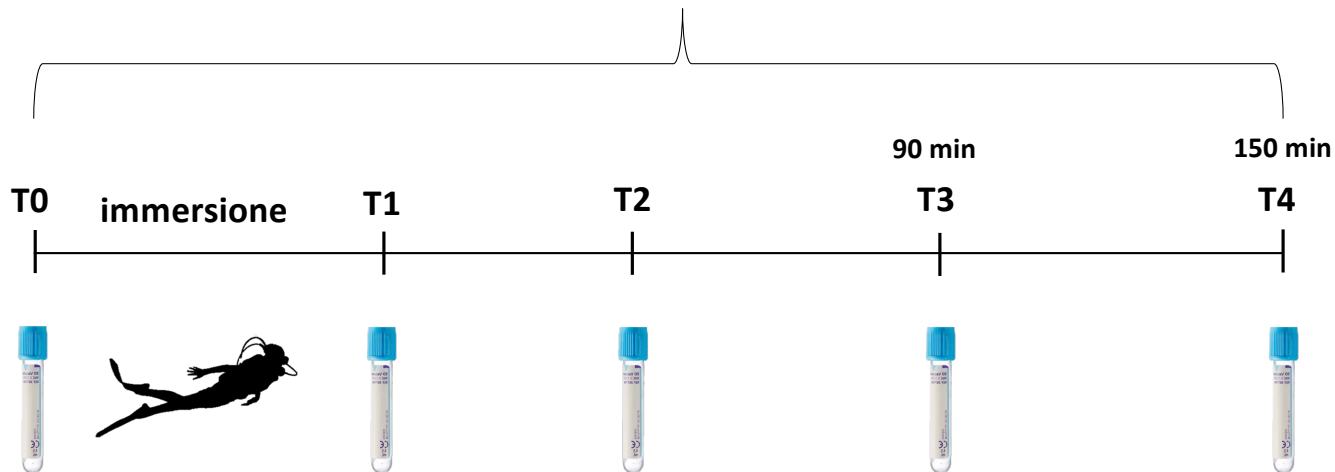
RT-PCR

Seduta sperimentale
Montegrotto 2020

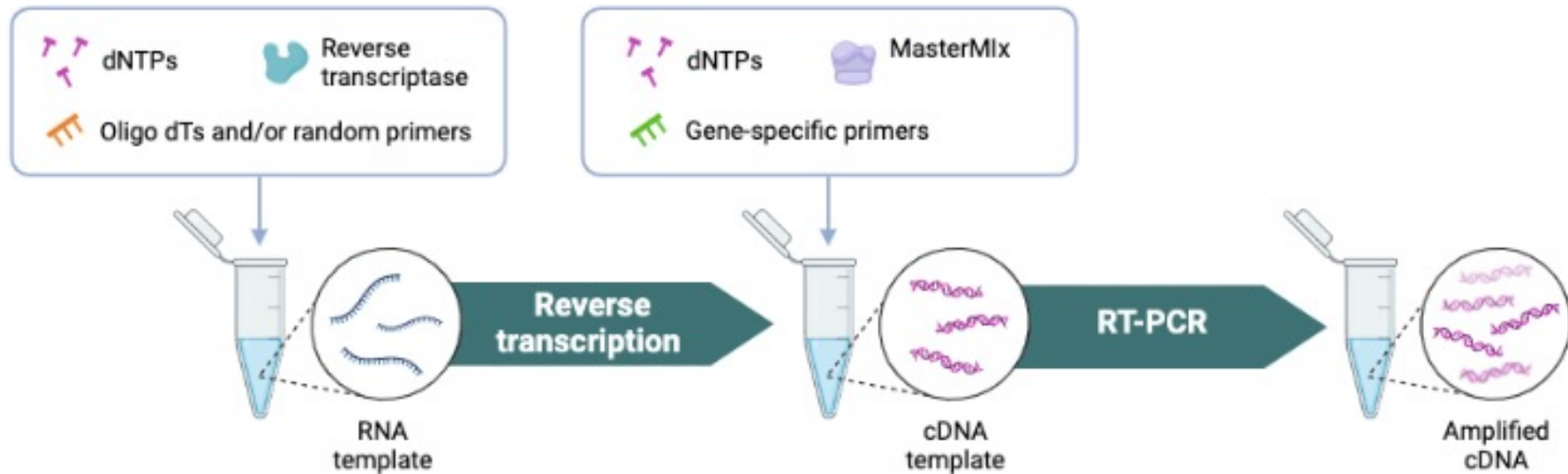
Profondità immersione (m)	20(A)	30(B)	40©
T0	(1)8,3	8,3	8,3
T1	(2)9,15	9,15	9,45
T2	(3)10,3	10,3	11
T3	(4)12	12	12,3
T4	(5)13,3	13,3	14



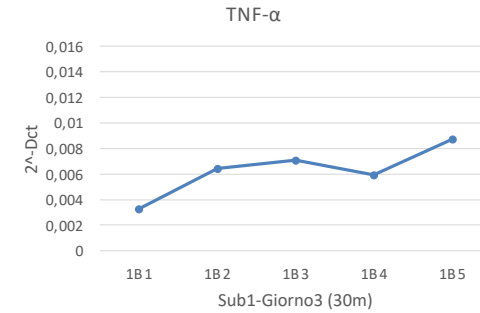
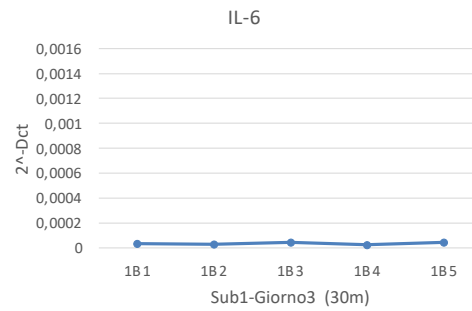
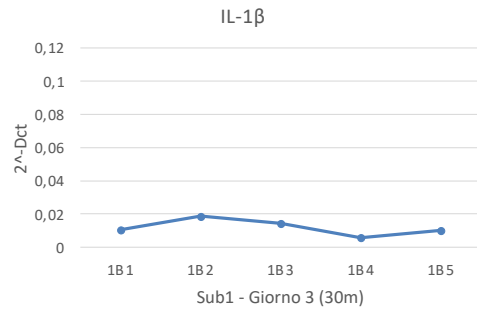
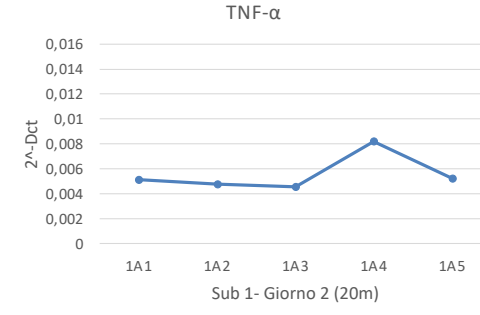
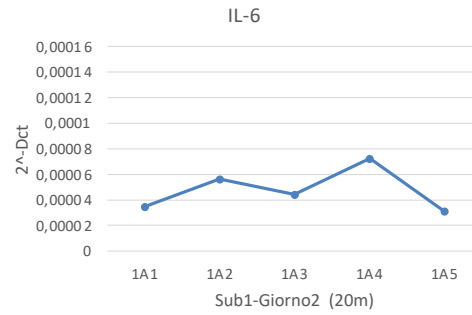
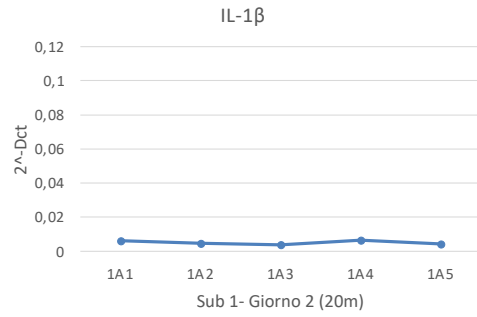
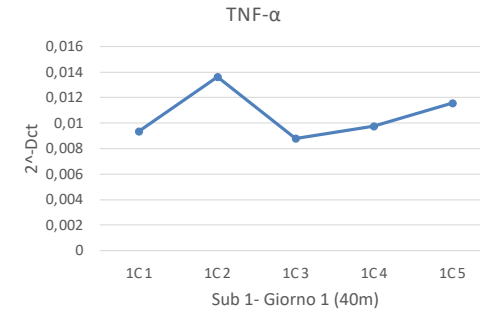
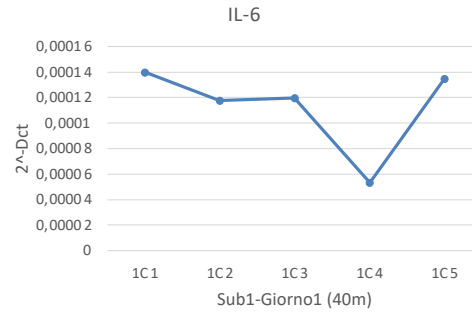
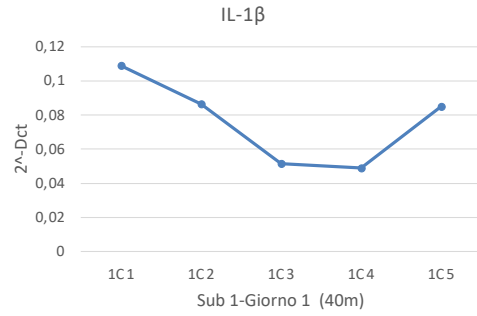
Per 3 giorni consecutivi a diverse profondità



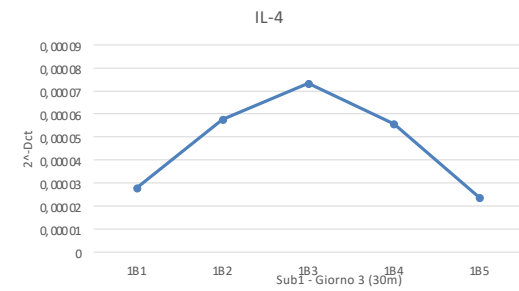
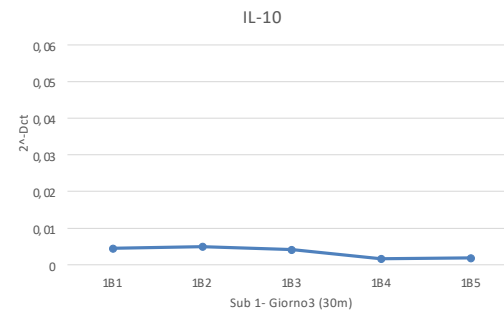
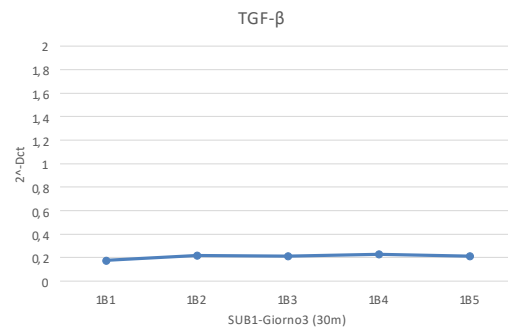
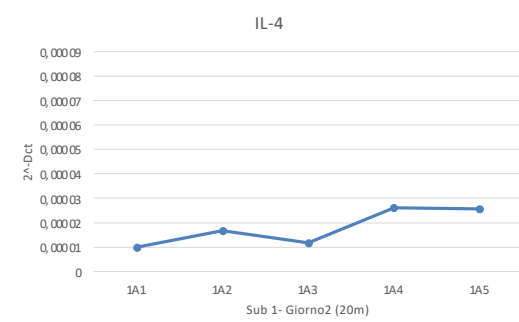
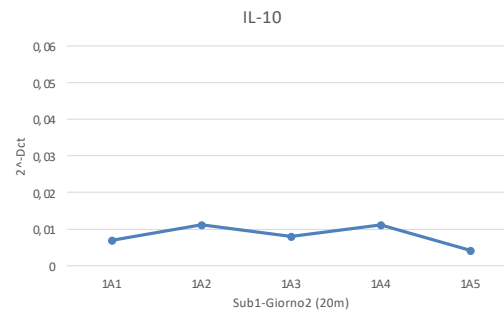
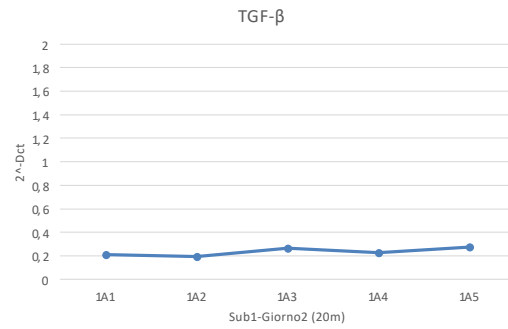
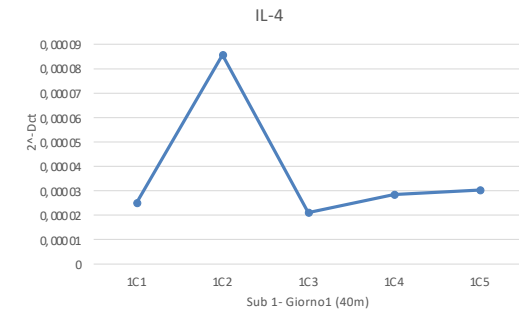
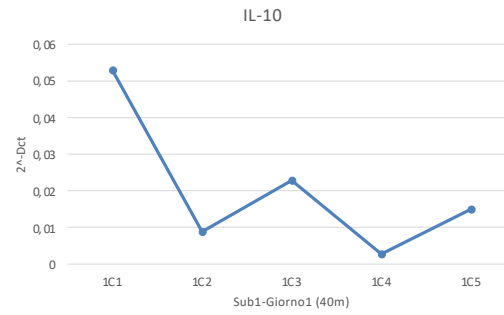
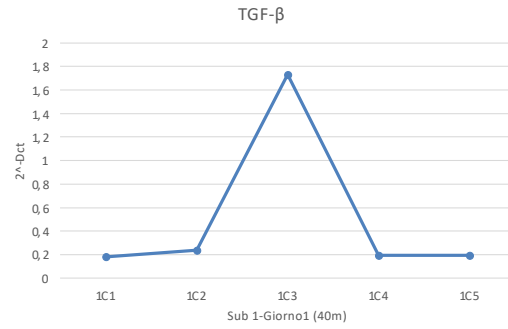
RT-PCR: Analisi dell'espressione dell'mRNA delle citochine Pro e Anti-Infiammatorie



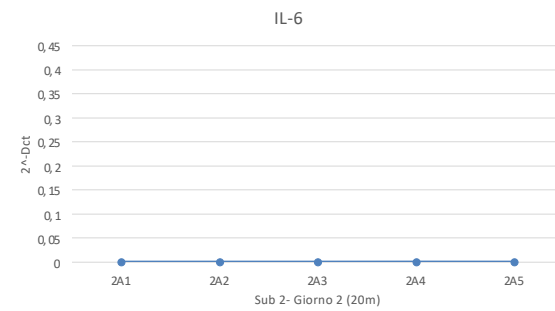
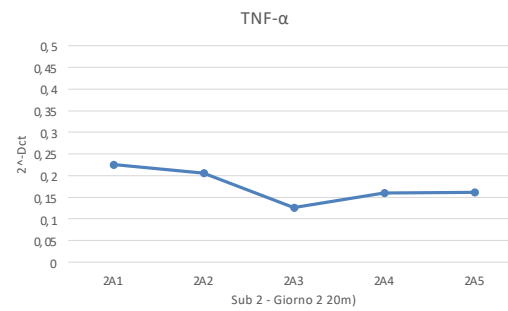
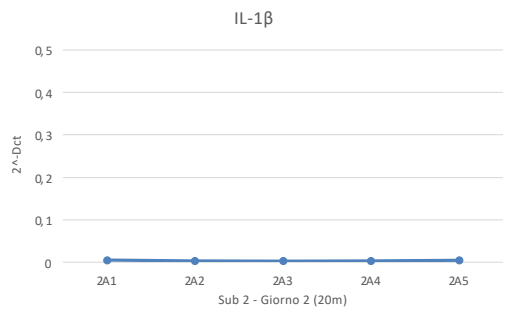
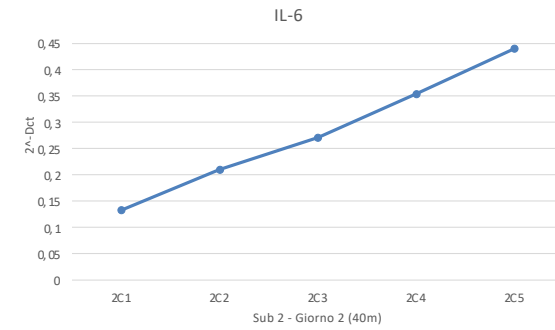
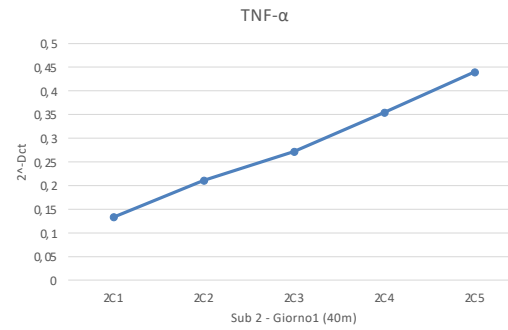
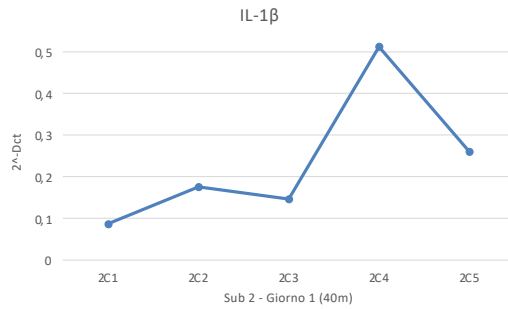
Citochine pro-infiammatorie SUB1



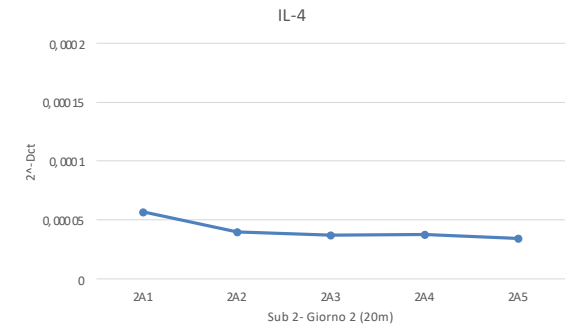
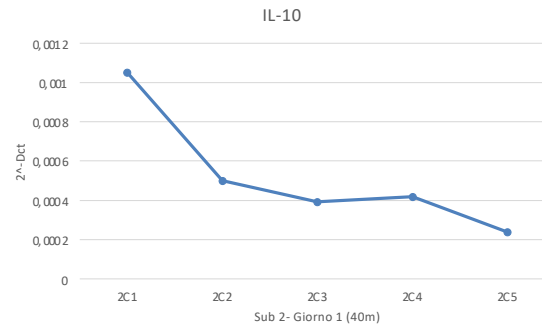
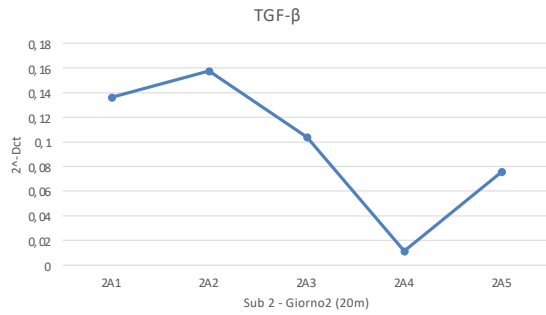
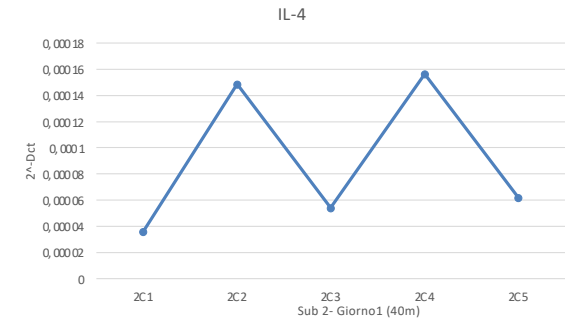
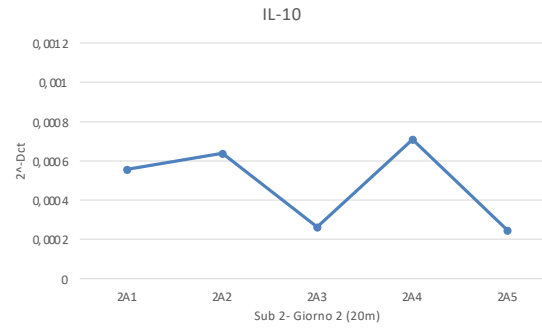
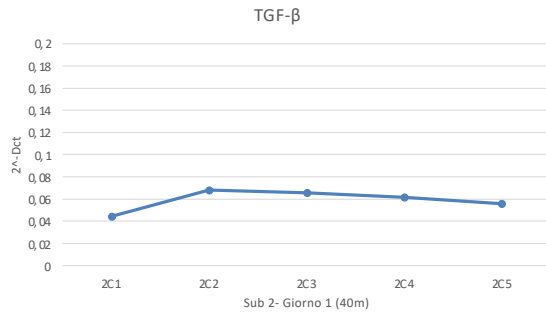
Citochine anti-infiammatorie SUB1



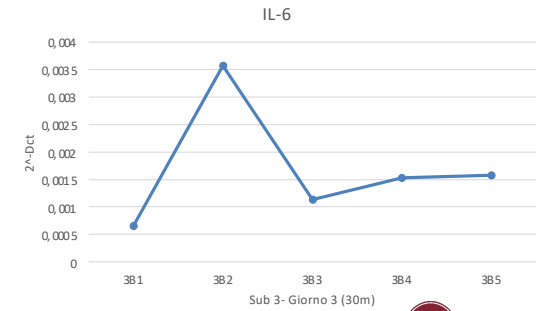
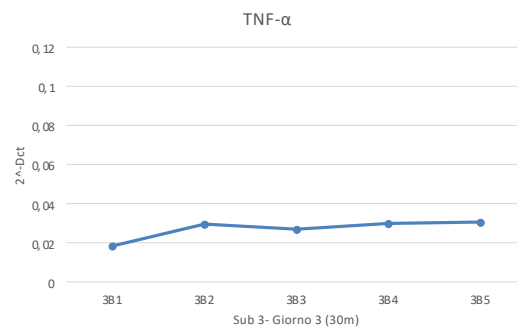
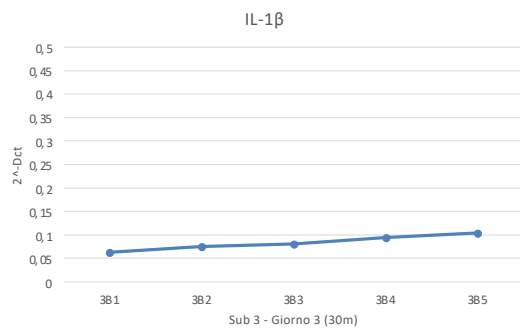
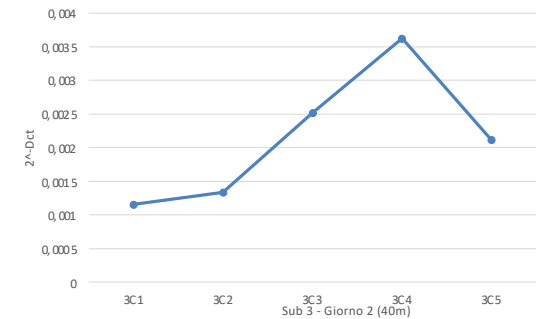
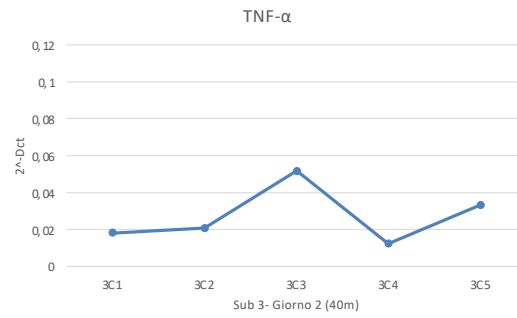
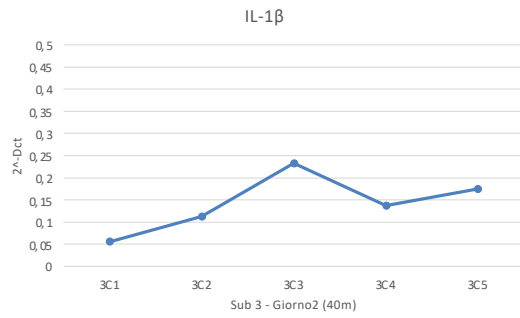
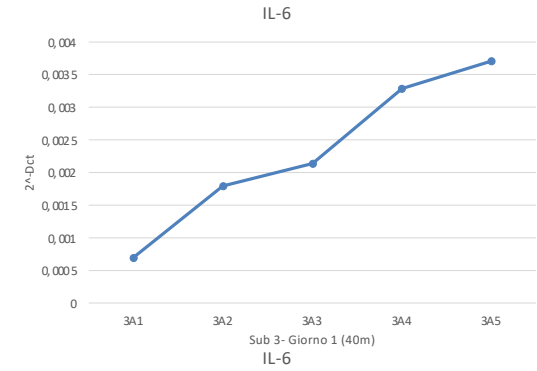
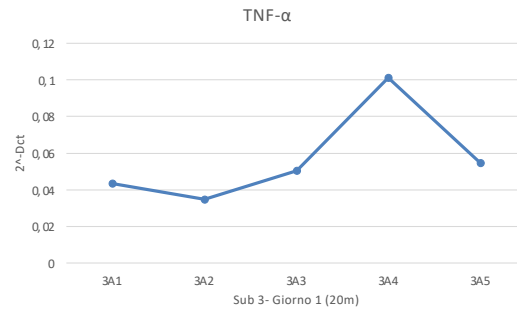
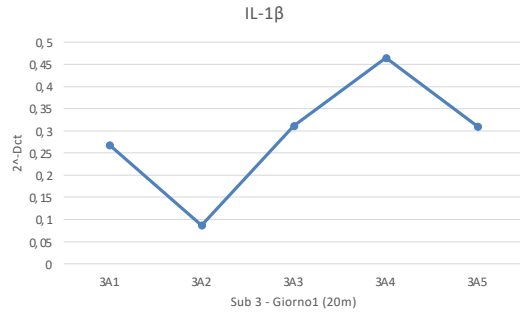
Citochine pro-infiammatorie SUB2



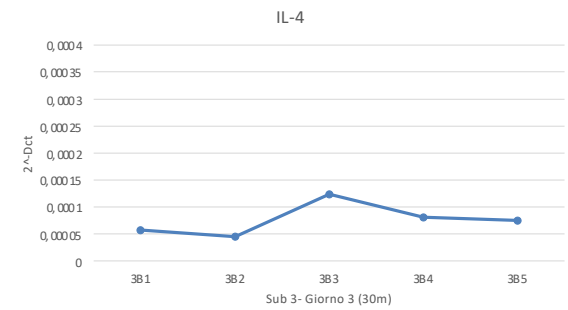
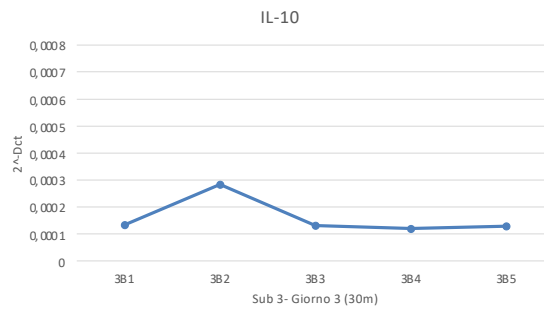
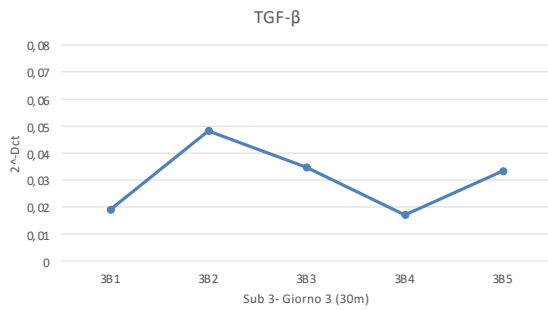
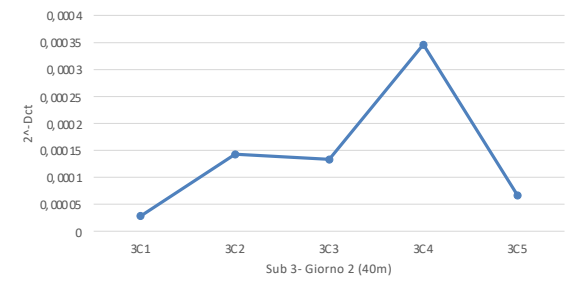
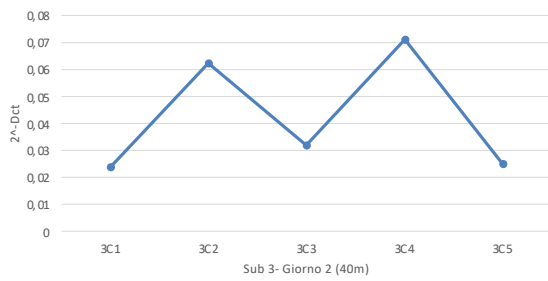
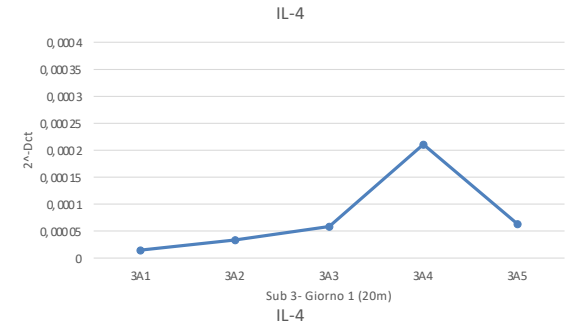
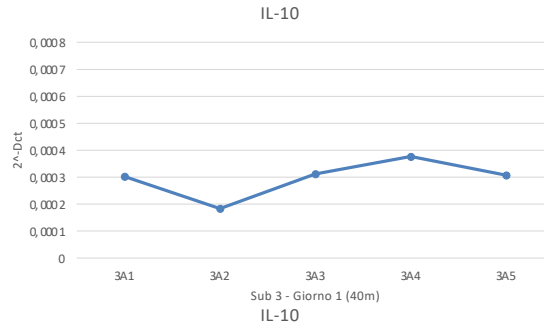
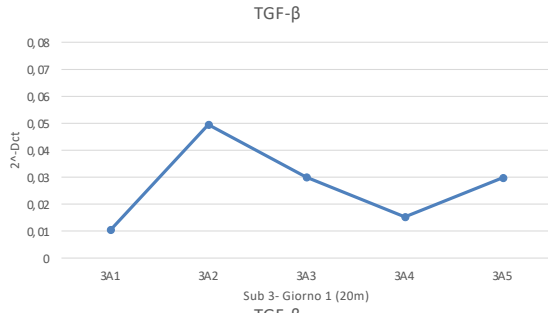
Citochine anti-infiammatorie SUB2



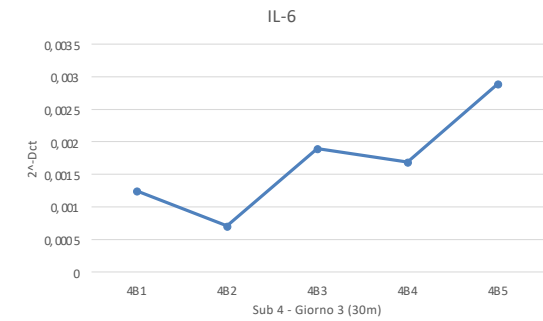
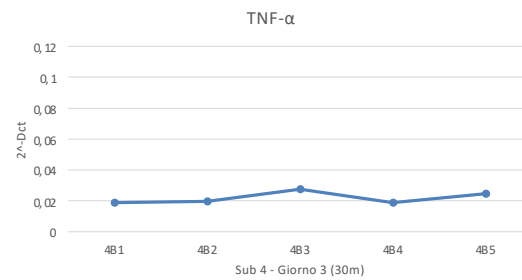
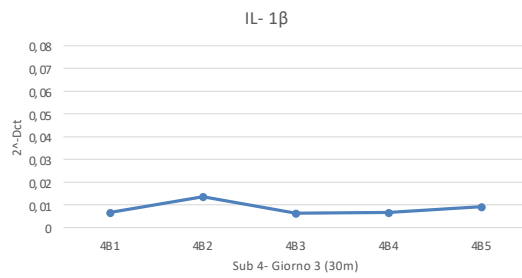
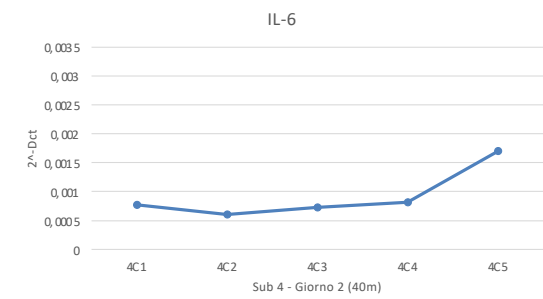
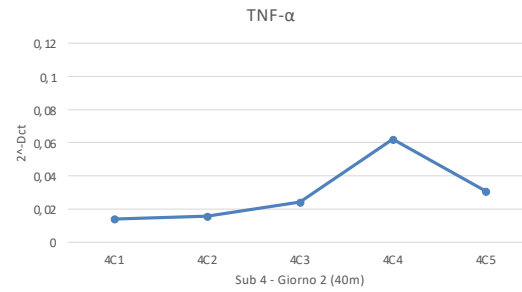
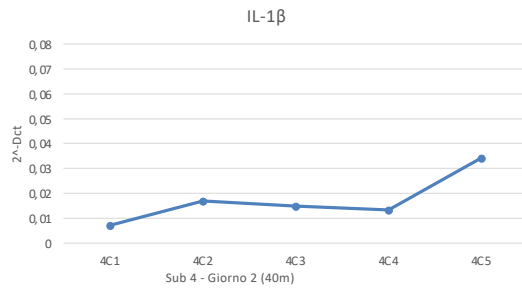
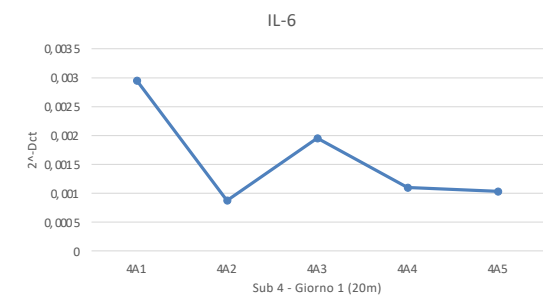
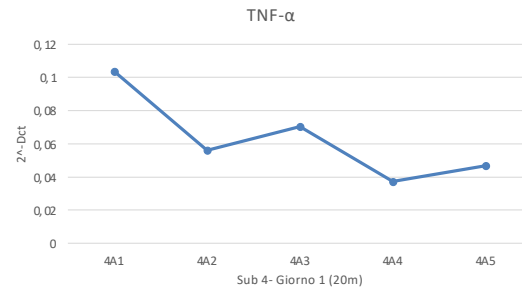
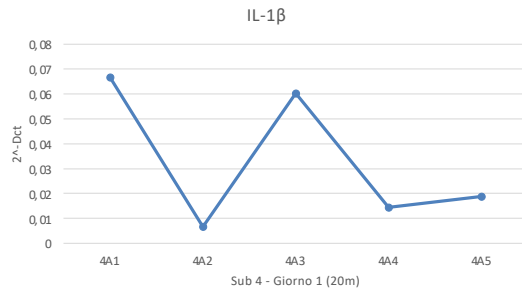
Citochine pro-infiammatorie SUB3



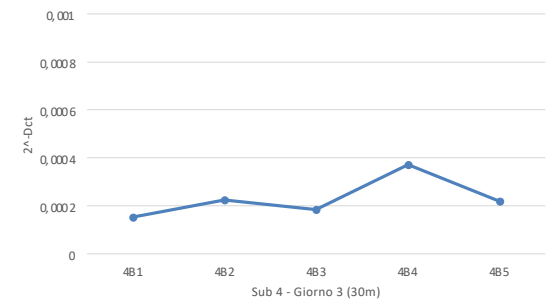
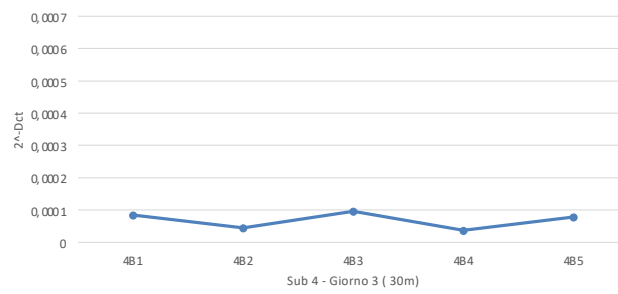
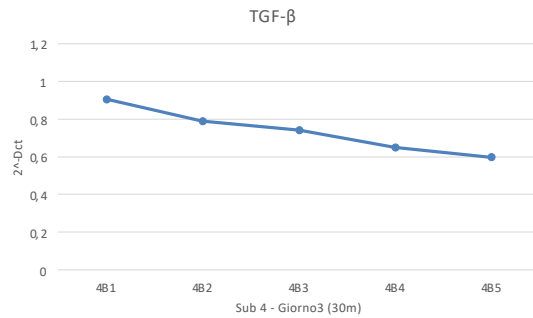
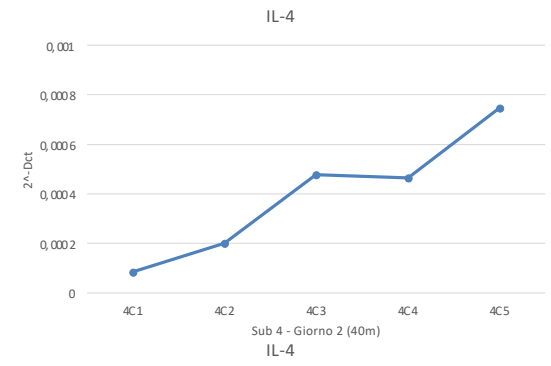
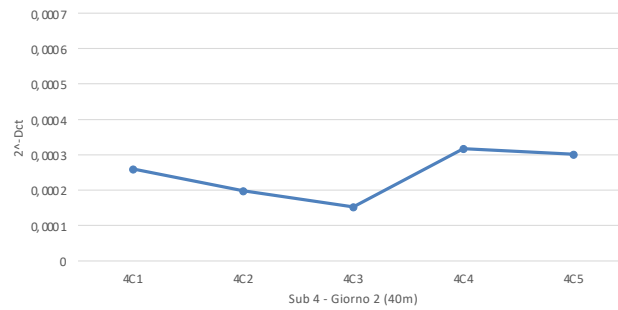
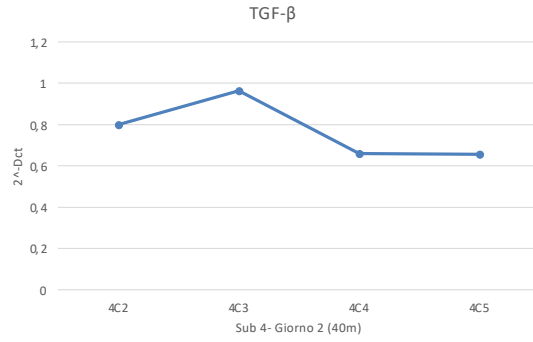
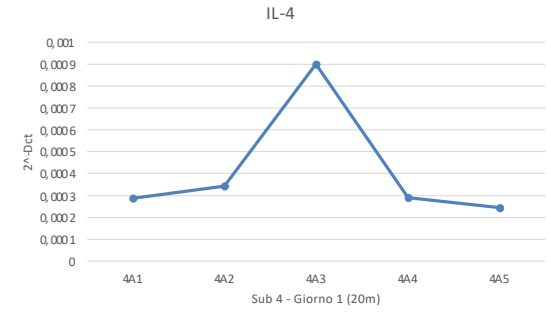
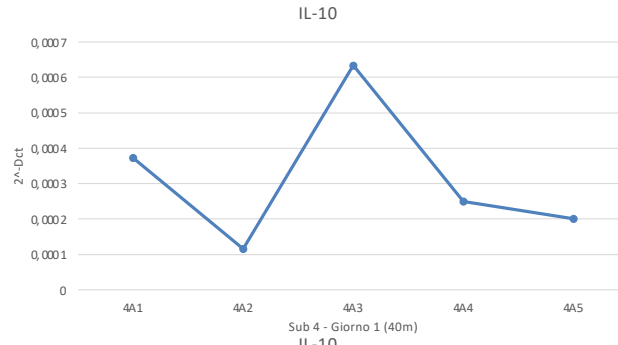
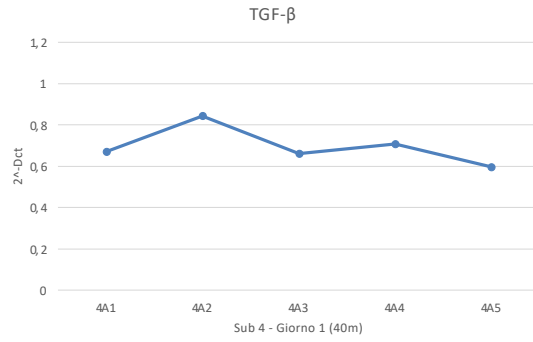
Citochine anti-infiammatorie SUB3



Citochine pro-infiammatorie SUB4

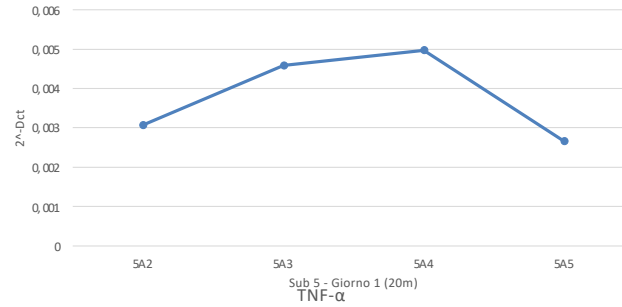


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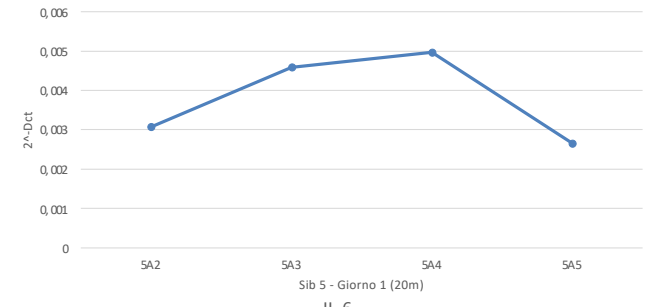


Citochine pro-infiammatorie SUB5

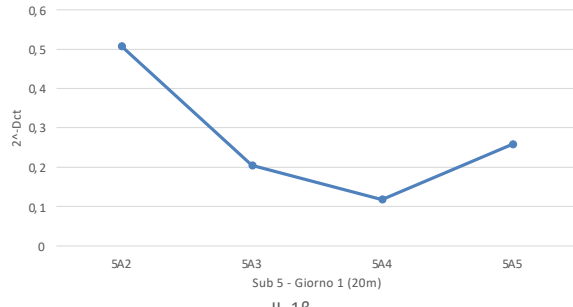
TNF- α



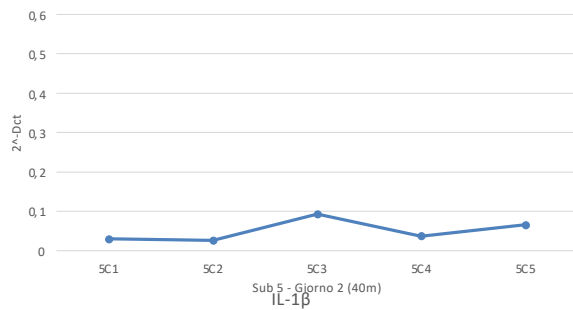
IL-6



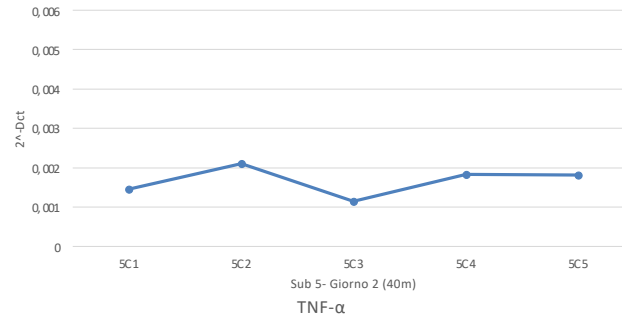
IL-1 β



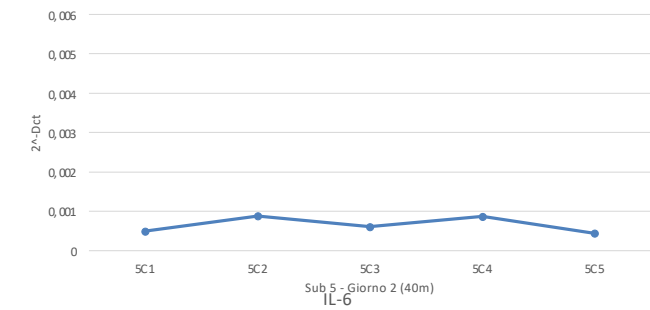
IL-1 β



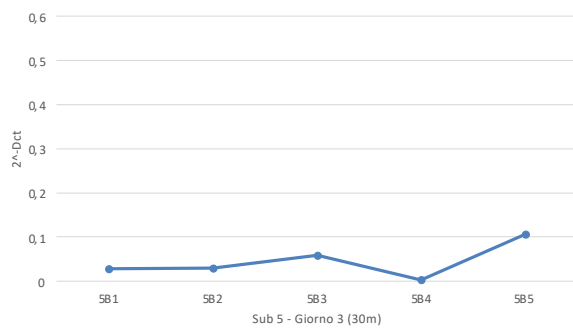
TNF- α



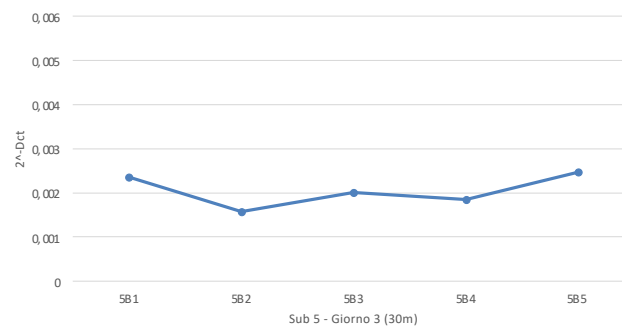
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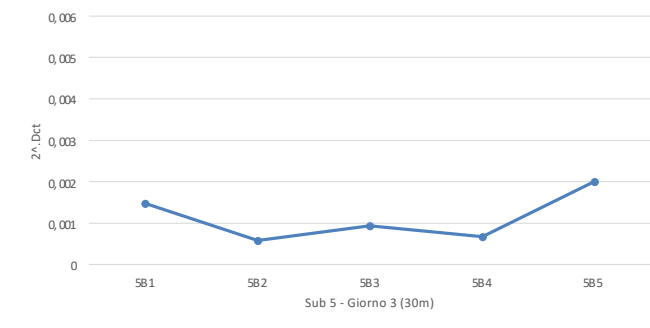
IL-1 β



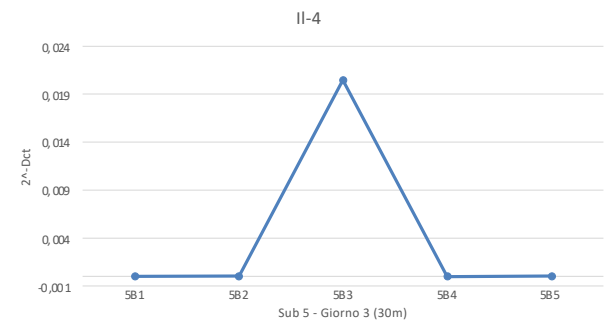
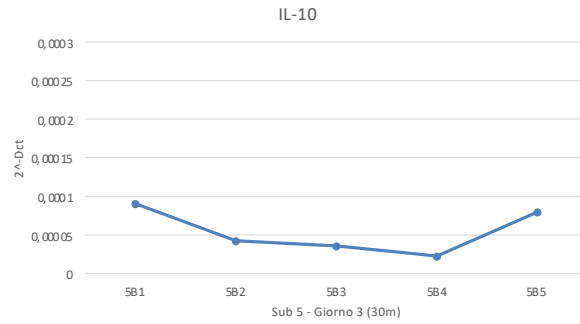
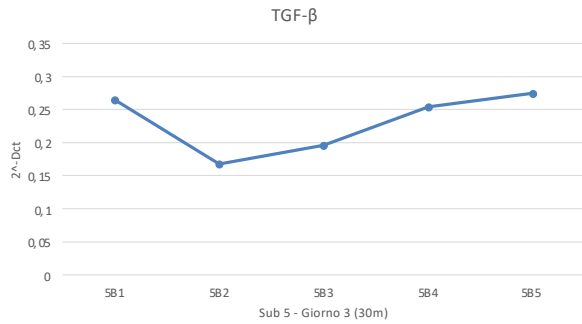
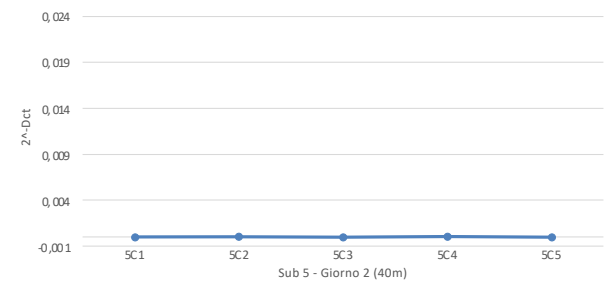
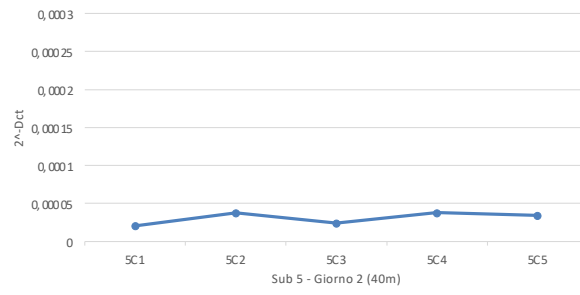
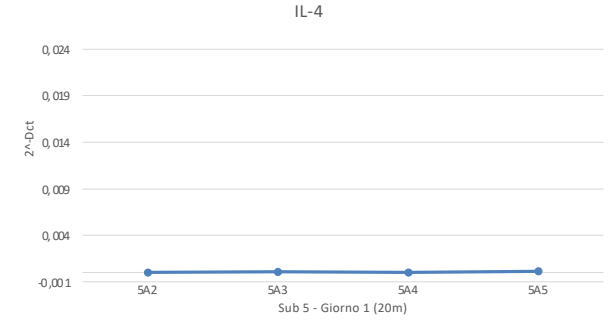
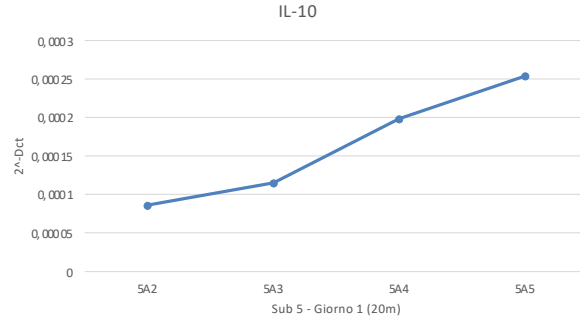
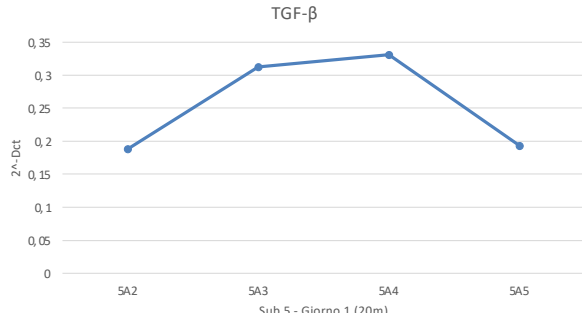
TNF- α



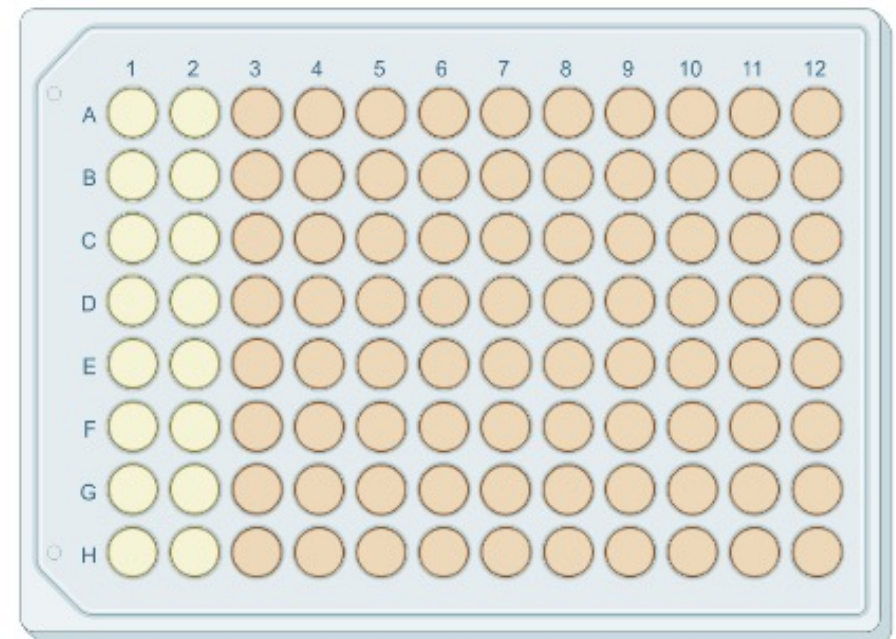
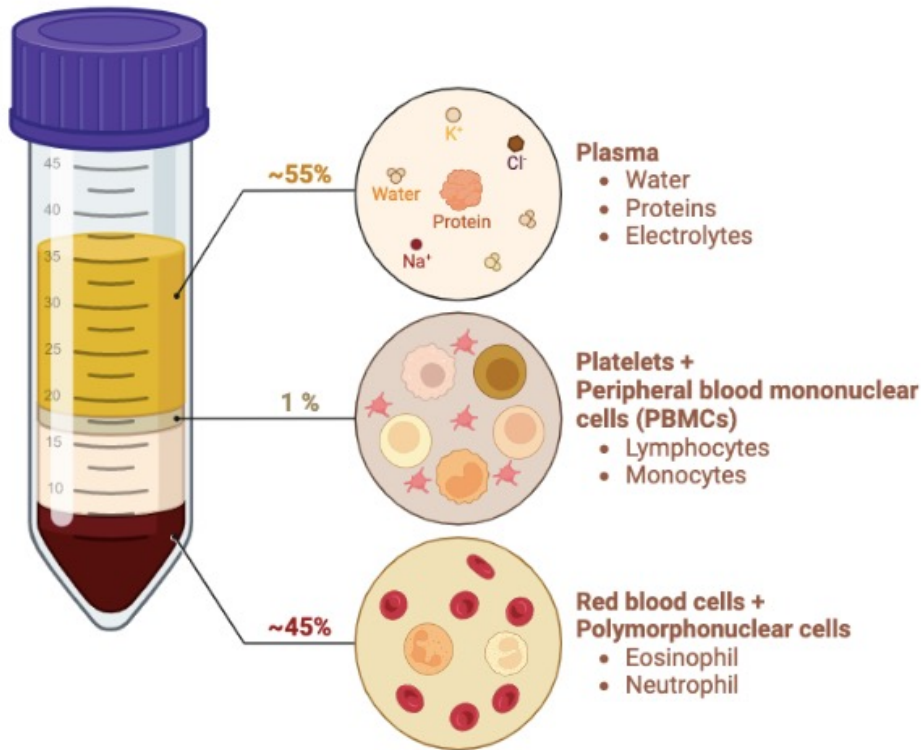
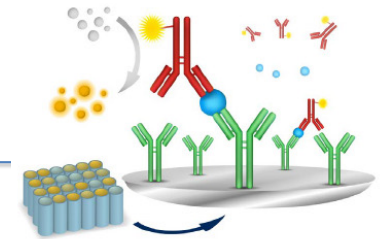
IL-6



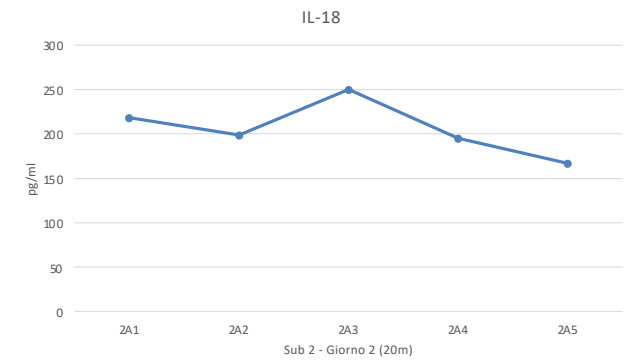
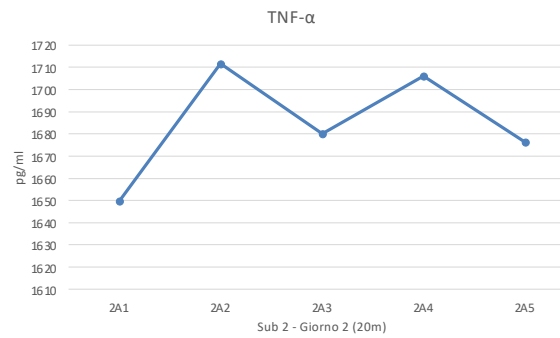
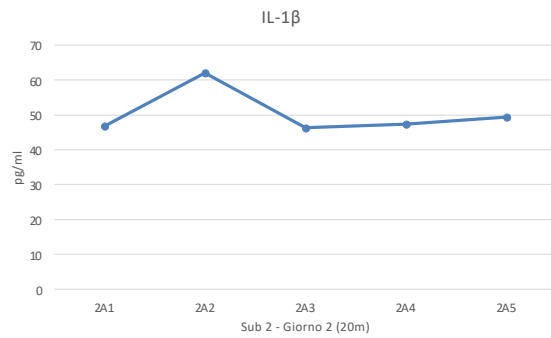
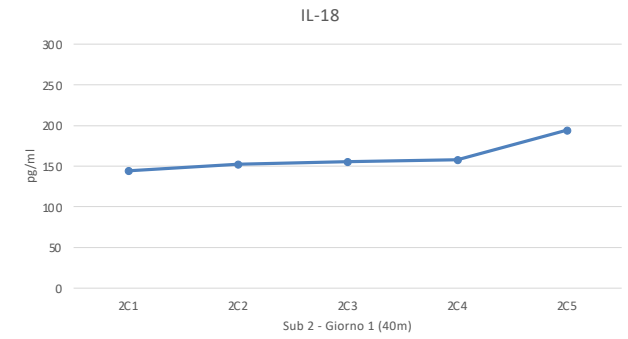
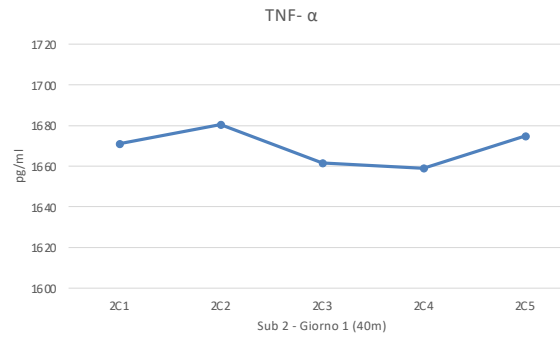
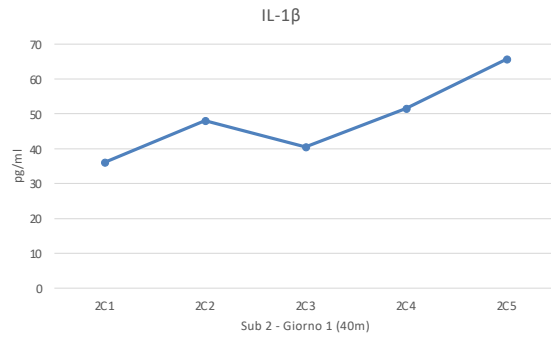
Citochine anti-infiammatorie SUB5

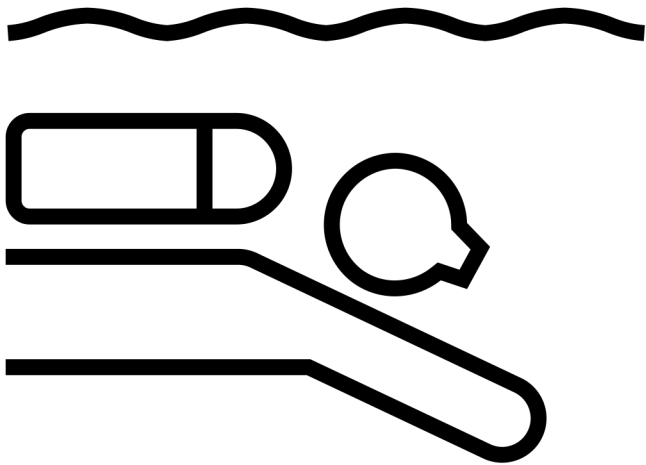


ELISA: Analisi dell'espressione delle citochine Pro e Anti-Infiammatorie nel plasma



Citochine pro-infiammatorie SUB2

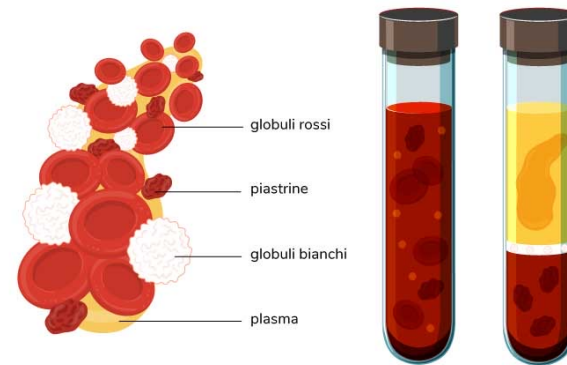
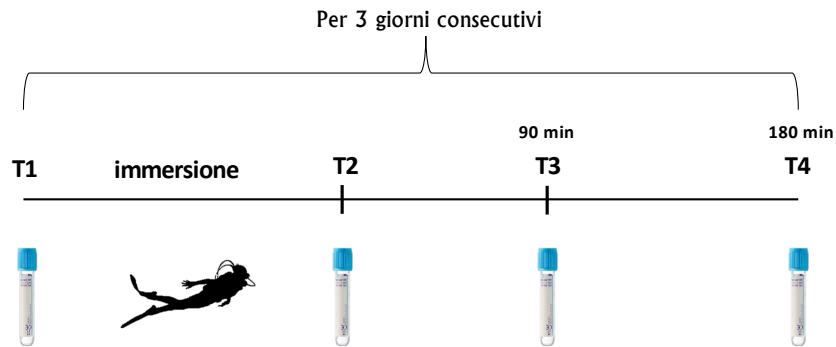




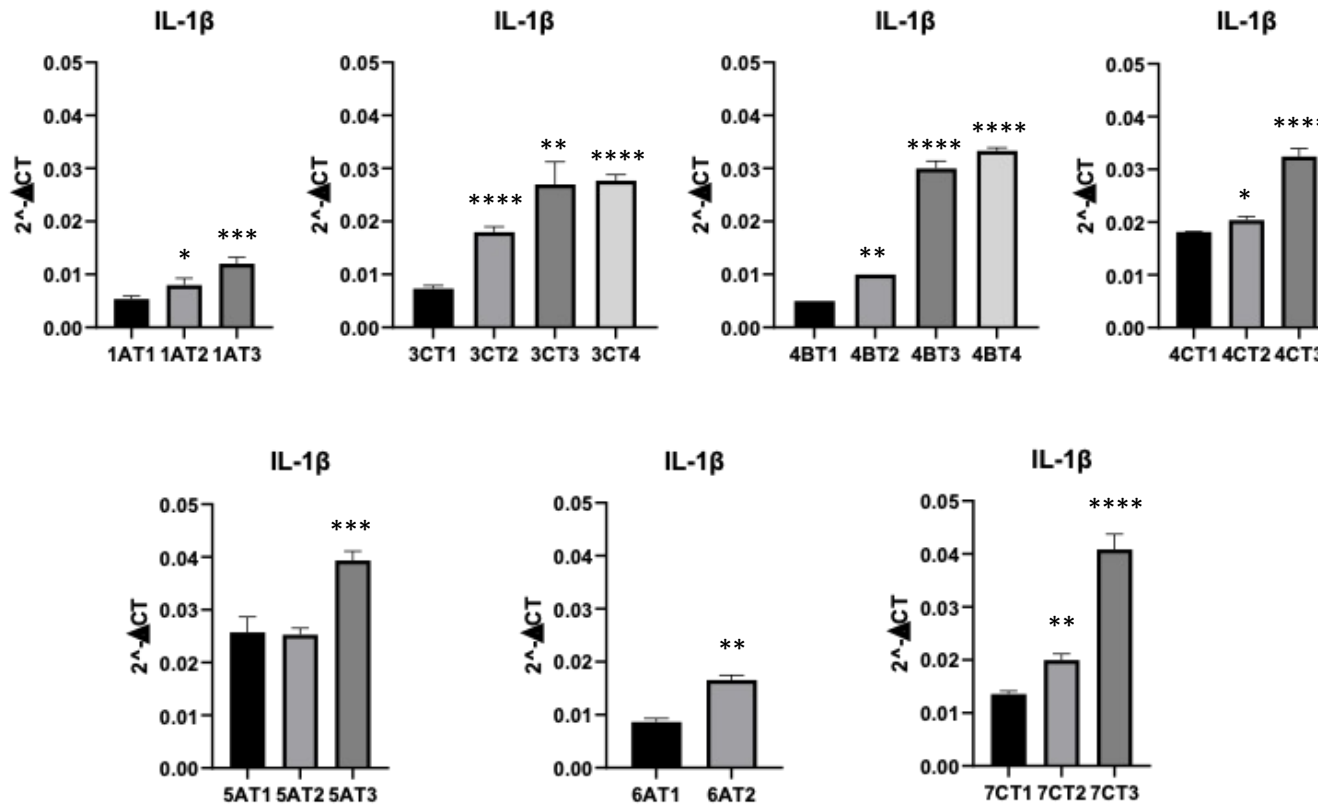
Montegrotto 2024

7-11 Aprile 2024

- Soggetti: Tempi (T): Profondità:
- 1 1. Pre-immersione A. -20m
 - 2 2. Post-immersione B. -30m
 - 3 3. 90min C. -40m
 - 4 4. 180 min
 - 5
 - 6 Esempio:
 - 7 1AT3 = Sog.1, -20m, 90 min post immersione



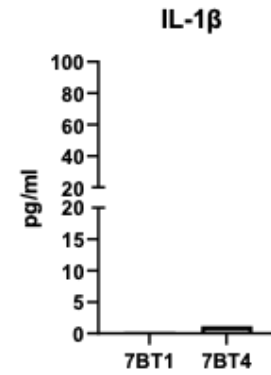
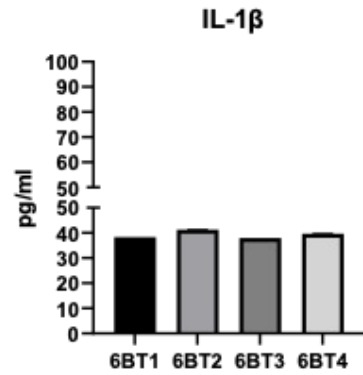
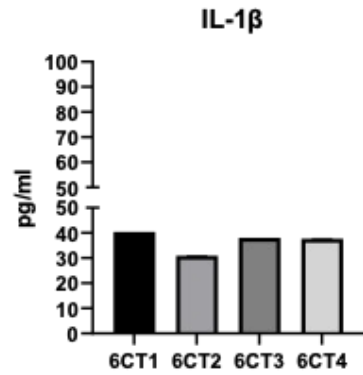
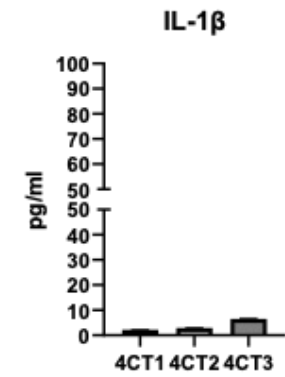
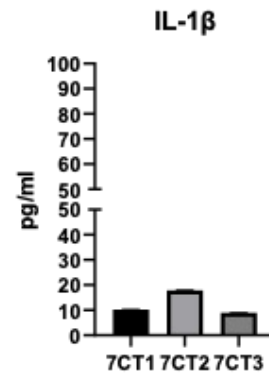
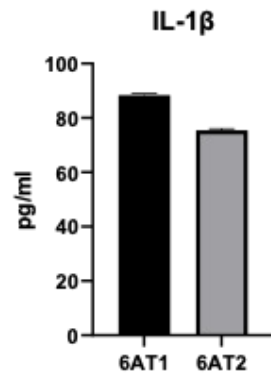
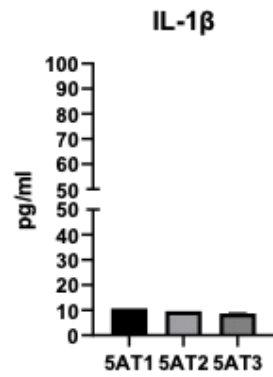
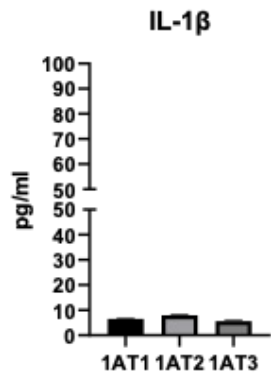
RT-PCR IL-1 β



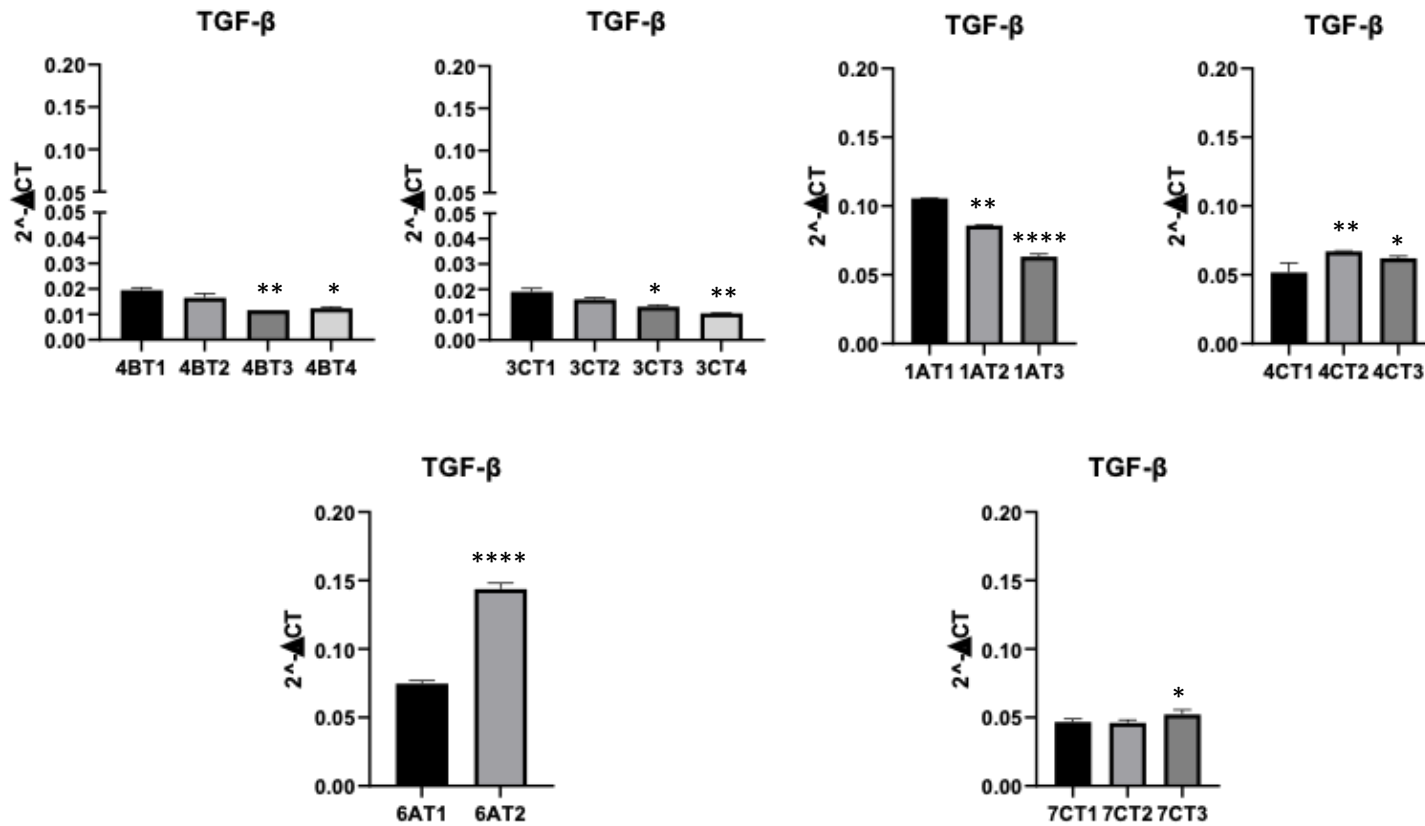
* Vs T1

L'analisi statistica è stata effettuata utilizzando il t-test di Student. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$

ELISA IL-1 β



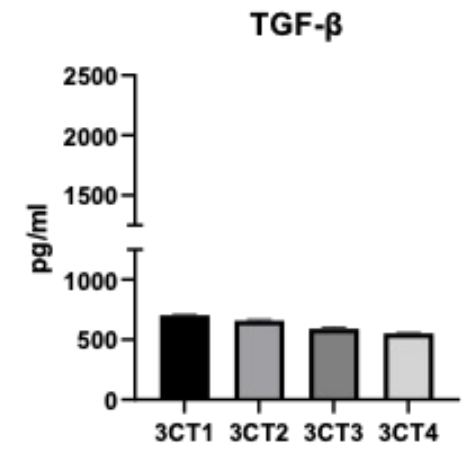
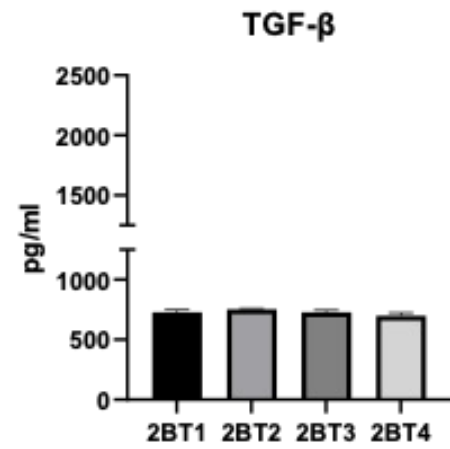
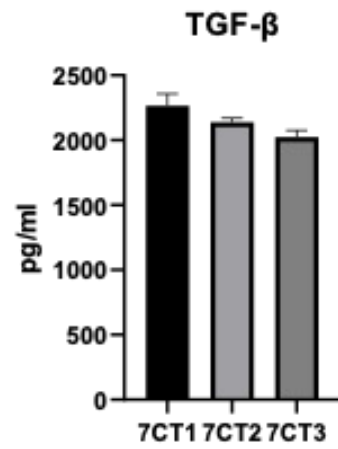
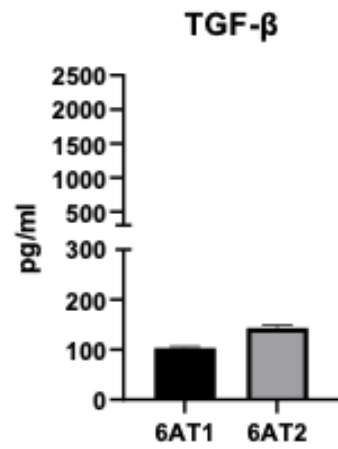
RT-PCR TGF- β

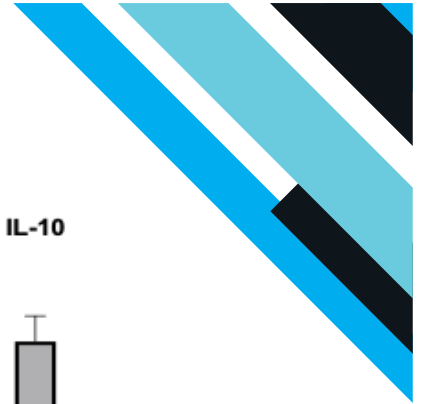


* Vs T1

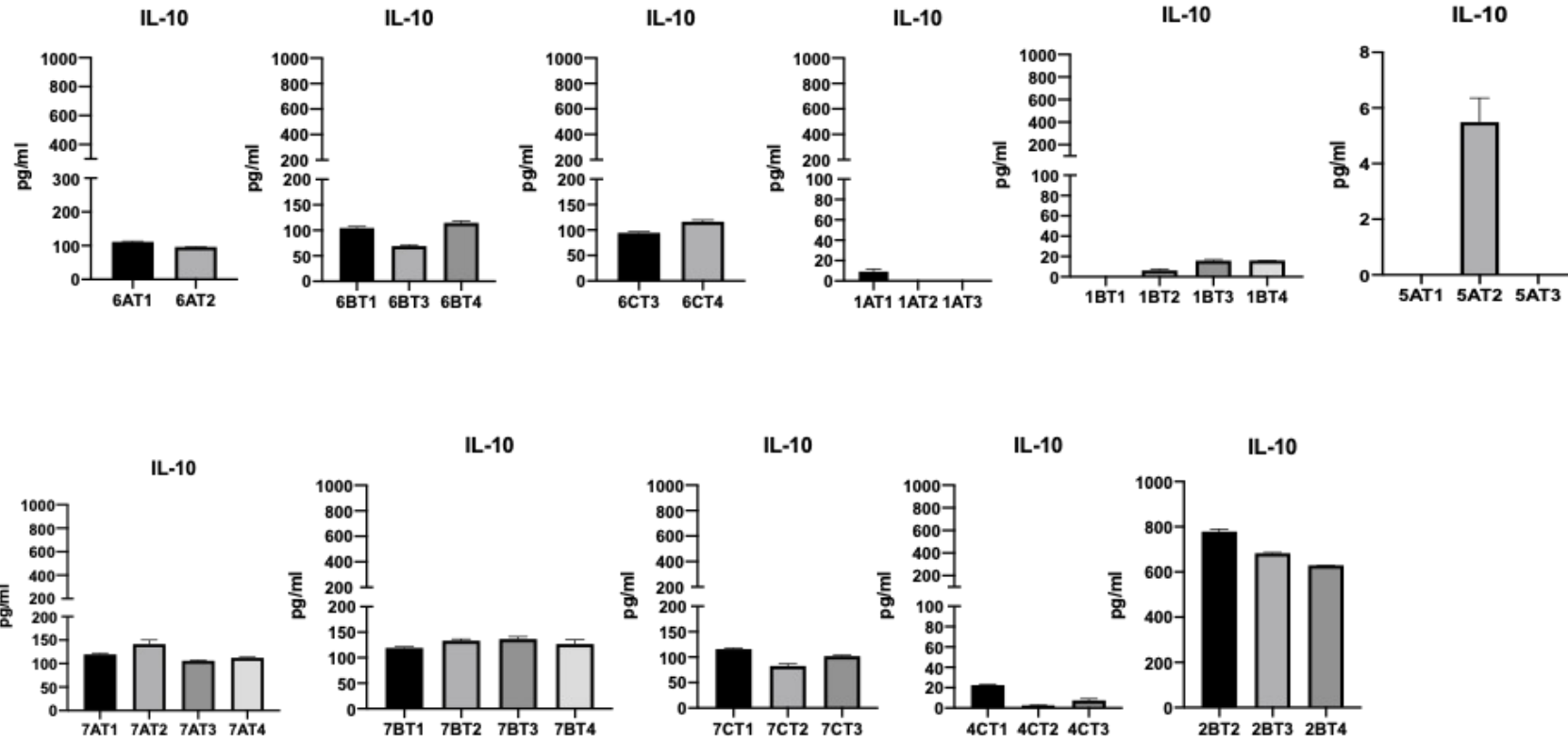
L'analisi statistica è stata effettuata utilizzando il t-test di Student. * $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$

ELISA TGF- β



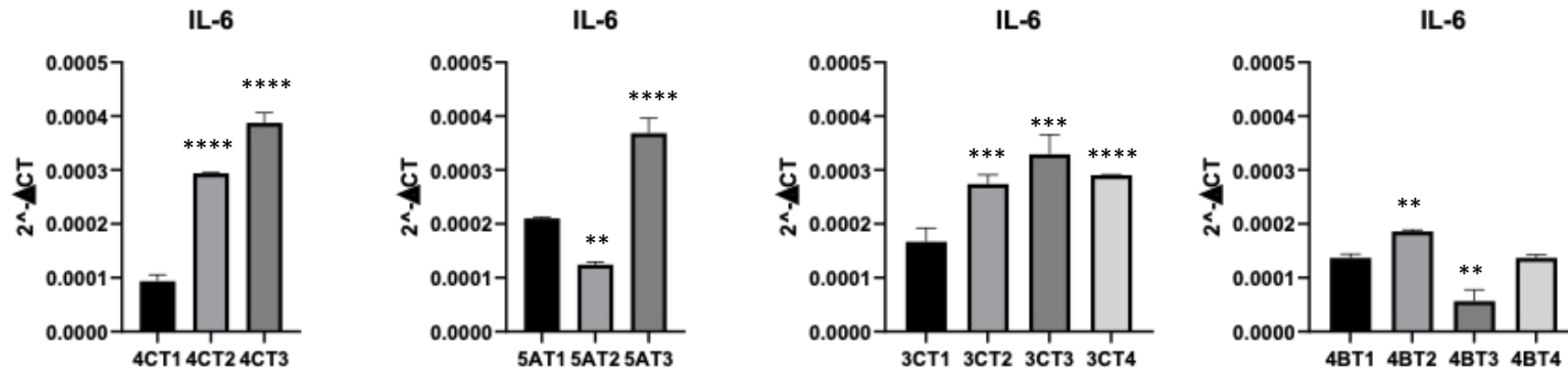


ELISA IL-10





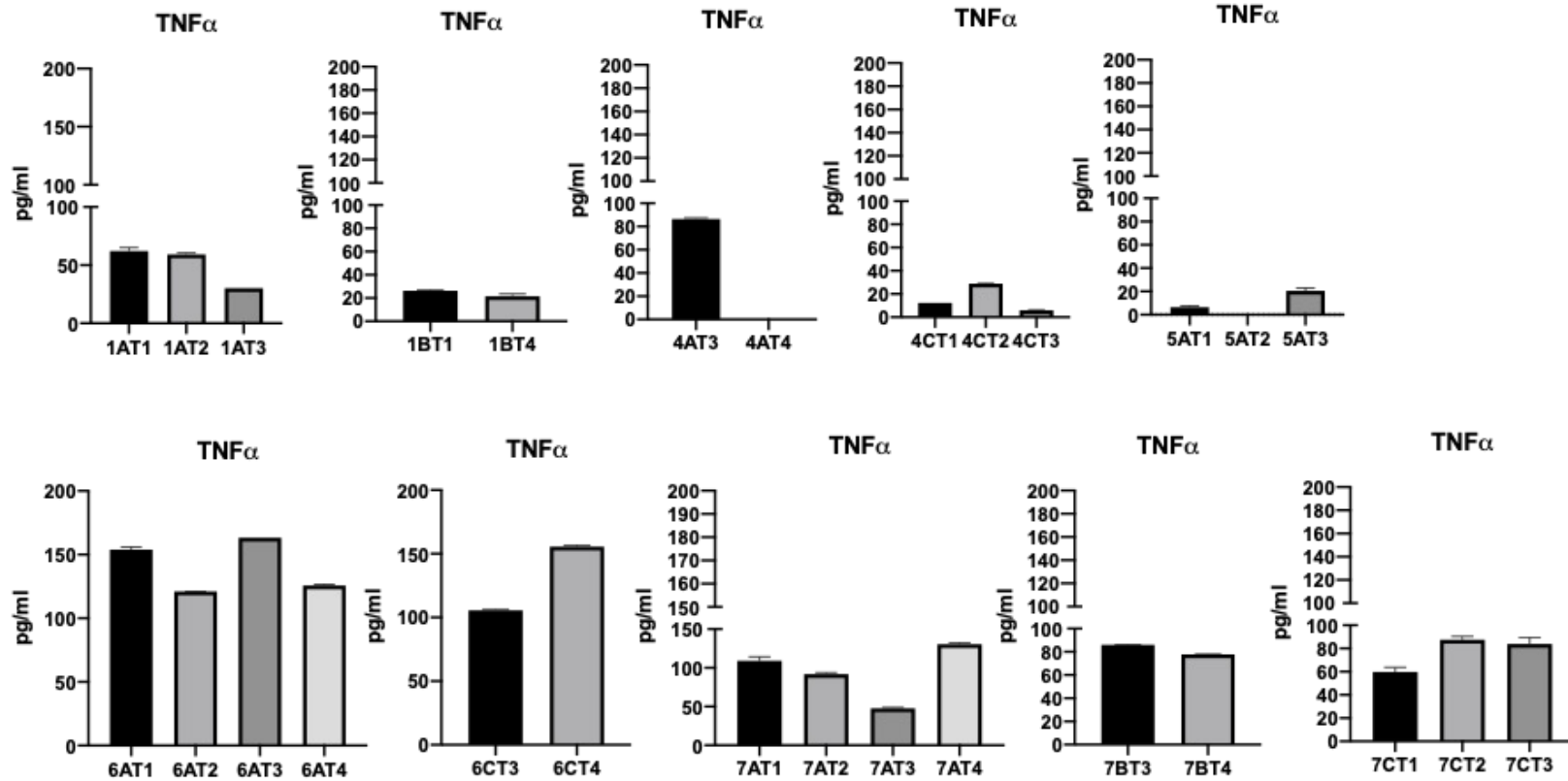
RT-PCR IL-6



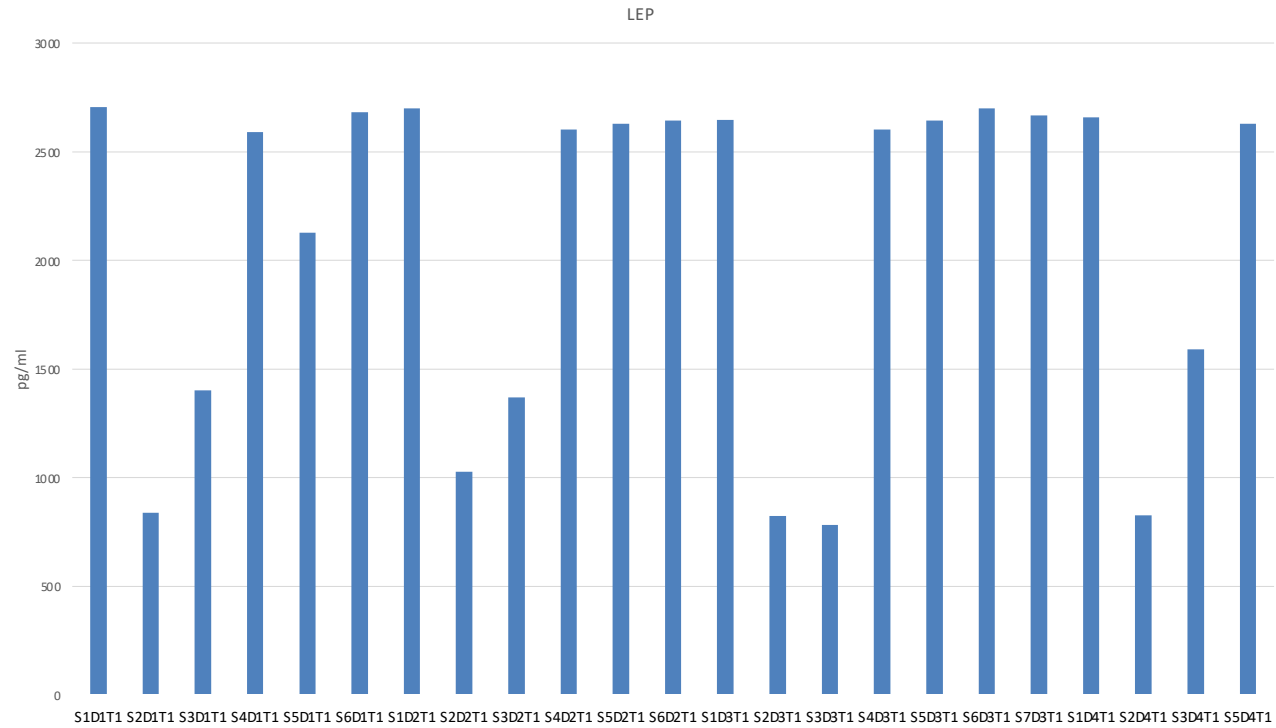
* Vs T1

L'analisi statistica è stata effettuata utilizzando il t-test di Student. ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$

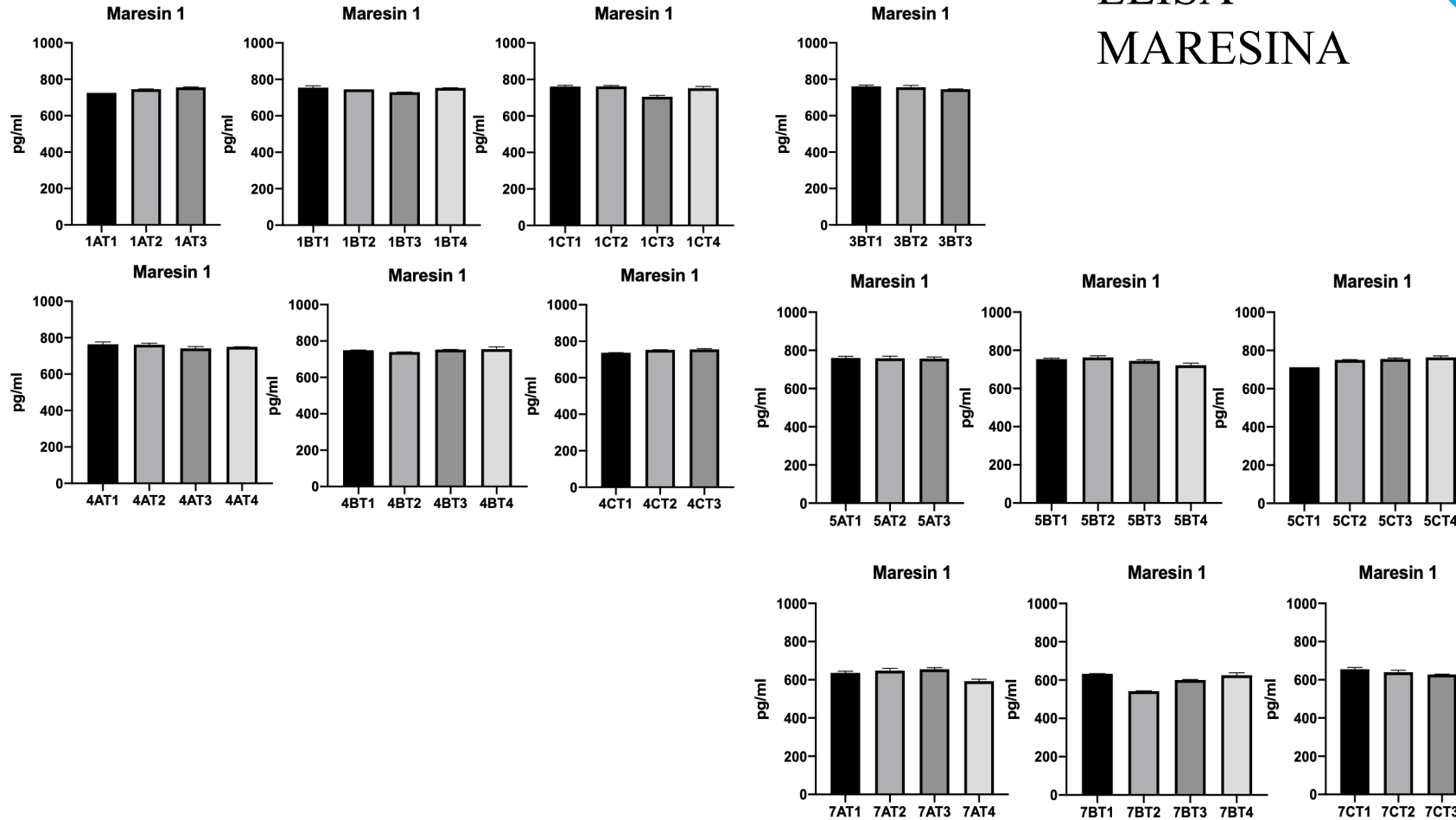
ELISA TNF- α



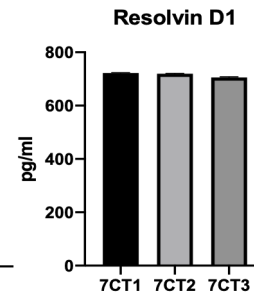
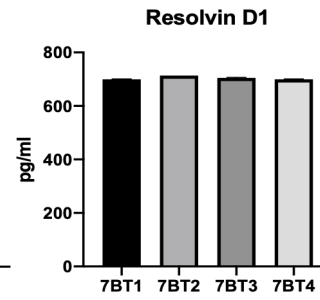
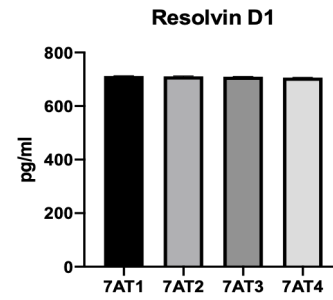
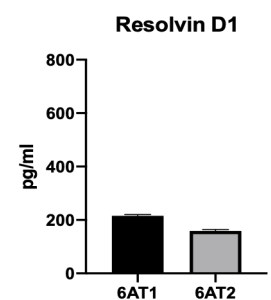
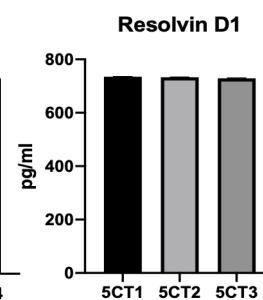
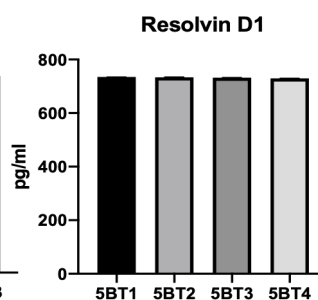
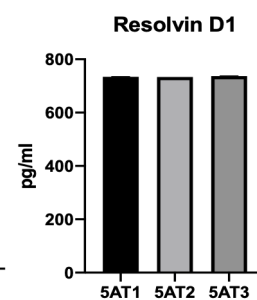
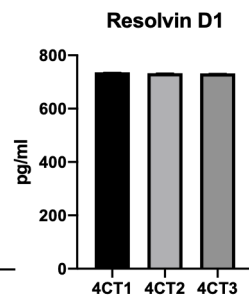
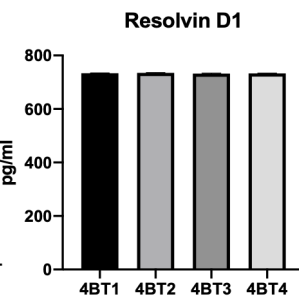
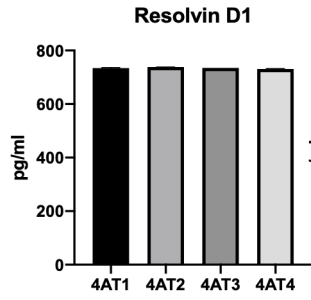
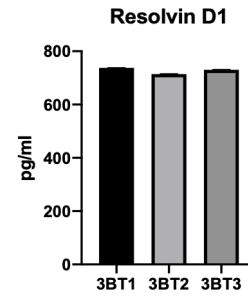
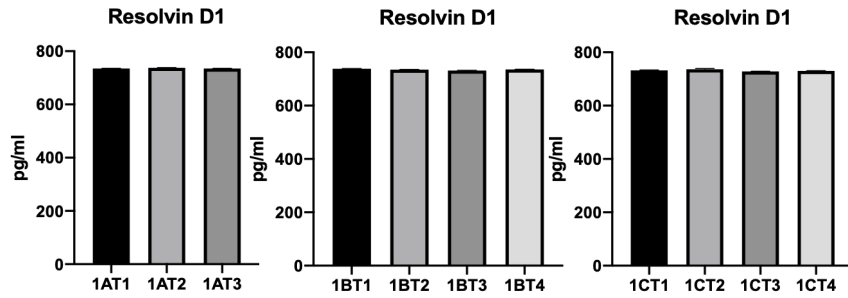
LEPTINA



ELISA MARESINA



ELISA RESOLVINA



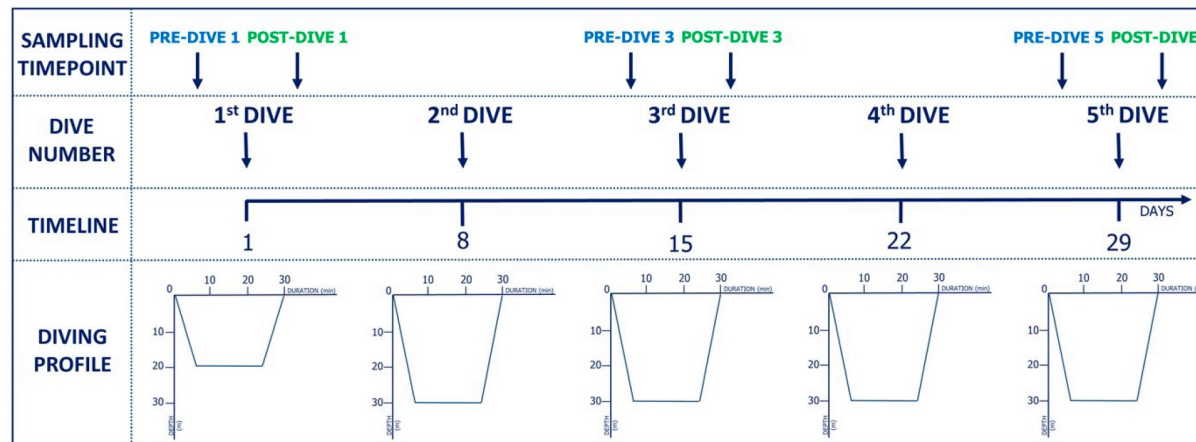
**FIGURE 1** Study design and blood collection time points

TABLE 1 Results of pituitary-target organ axis hormones levels before and after the first, third, and fifth dive.

Parameter (unit)	DIVE 1		DIVE 3		DIVE 5		P (1 vs. 3 vs. 5)	
	Pre-dive	Post-dive	Pre-dive	Post-dive	Pre-dive	Post-dive	Pre-dive	Post-dive
ACTH (pmol/L)	6.9 (4.5–8.6)	3.4 (2.2–4.5)	6.1 (3.4–9.6)	4.1 (2.8–5.7)	5.3 (4.0–7.9)	3.6 (2.5–4.6)	0.109	0.135
P (post vs. pre)	↓ 0.001*		↓ 0.004*		↓ 0.002*			
Cortisol (nmol/L)	295.8 (244.9–350.3)	223.0 (189.1–270.9)	307.7 (256.2–355.6)	199.3 (174.6–300.4)	276.1 (217.5–389.0)	213.3 (163.8–338.0)	0.807	0.807
P (post vs. pre)	↓ 0.006*		↓ 0.019*		↓ 0.022*			
TSH (mIU/L)	1.09 (0.67–1.92)	1.33 (0.77–1.92)	1.11 (0.70–1.88)	1.45 (0.97–2.08)	1.04 (0.71–1.74)	1.27 (0.85–1.78)	0.500	0.926
P (post vs. pre)	0.133		0.055		0.133			
fT4 (pmol/L)	12.1 (11.5–12.9)	12.3 (11.7–13.0)	12.7 (11.4–13.4)	12.6 (11.4–13.2)	12.2 (11.4–13.1)	12.4 (11.5–12.8)	0.199	0.735
P (post vs. pre)	0.402		0.272		0.972			
Prolactin (mIU/L)	135.4 (112.5–187.3)	128.0 (98.3–167.3)	139.0 (101.6–198.2)	163.5 (102.5–229.4)	142.3 (124.1–196.4)	155.4 (99.9–220.2)	0.109	0.071
P (post vs. pre)	0.124		0.272		0.683			
Testosterone (nmol/L)	15.7 (14.0–21.0)	13.6 (12.5–17.6)	16.1 (13.9–22.8)	15.6 (13.5–19.0)	17.4 (15.7–20.4)	16.5 (14.6–18.9)	0.607	0.607
P (post vs. pre)	↓ < 0.001*		0.245		0.074			
GH (mIU/L)	0.55 (0.28–5.59)	1.5 (0.34–3.83)	0.44 (0.17–4.25)	1.64 (0.54–5.20)	0.69 (0.20–1.56)	0.64 (0.16–2.42)	0.410	0.265
P (post vs. pre)	0.826		0.551		0.552			

ACTH, adrenocorticotrophic hormone; TSH, thyroid-stimulating hormone; fT4, free thyroxine; GH, growth hormone.

↓ A statistically significant decrease.

* A statistically significant difference between pre- and post-dive (Wilcoxon test).

CONCLUSIONI

I nostri risultati mostrano che l'attività iperbarica influisce sugli equilibri omeostatici del nostro organismo. In alcuni soggetti con effetti positivi (diminuzione delle citochine pro-infiammatorie e aumento delle citochine anti-infiammatorie) confermando i risultati di altri studi in cui **l'attività iperbarica veniva assimilata a mindfulness e biofeedback** per la proprietà di spostare gli equilibri anche **a livello del SNA**, stimolandone la **componente parasimpatica** e pertanto promuovendone l'attività anti-infiammatoria

In altri soggetti i risultati, sia a livello di mRNAs che di test immunochimici (ELISA) mostravano comportamenti opposti con un aumento dei mediatori infiammatori.

In conclusione i risultati non potevano raggiungere una significatività statistica sia per la scarsa numerosità del campione, sia per i risultati ottenuti, a volte opposti tra i gruppi, ma congruenti nello stesso soggetto.

Medicina personalizzata o di precisione

Necessità di **addestrare l'AI** per l'implementazione di algoritmi in grado di comprendere i numerosi dati ottenuti dagli studi condotti sulla tematica e in grado di elaborare **ipotesi predittive per la valutazione del rischio** individuale. Questo sarà possibile soltanto con analisi di big data per un machine learning efficace

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Grazie per l'attenzione!!!

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