Reazioni infiammatorie autoimmuni indotte dai vaccini genetici contro la COVID-19 in tessuti terminalmente differenziati

InfoVax Evidence Based

21 gennaio 2024

Panagis Polykretis, Biologo, PhD in Biologia Strutturale

Autoimmunità

Merriam-Webster | Dictionary | Thesaurus | autoimmunity | Games & Quizzes | Word of the Day | Grammar | Wordplay | Word Finder | More

Medical

Definition

Entries Near

Show More

Save Word

autoimmunity noun

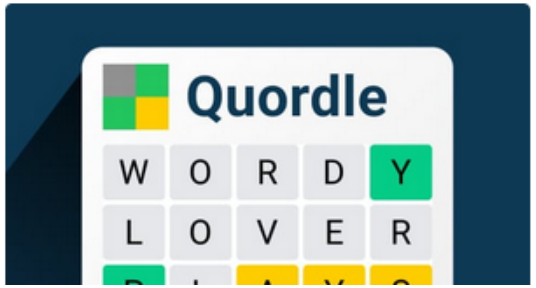
au·to·im·mu·ni·ty ˌȯt-ō-im-ˈyü-nət-ē

plural **autoimmunities**

: a condition in which the body produces an immune response against its own tissue constituents

Dictionary Entries Near *autoimmunity*

autoimmune hepatitis
autoimmunity
autoimmunization



Fonte: www.merriam-webster.com/medical/autoimmunity

Il processo di presentazione dell'antigene

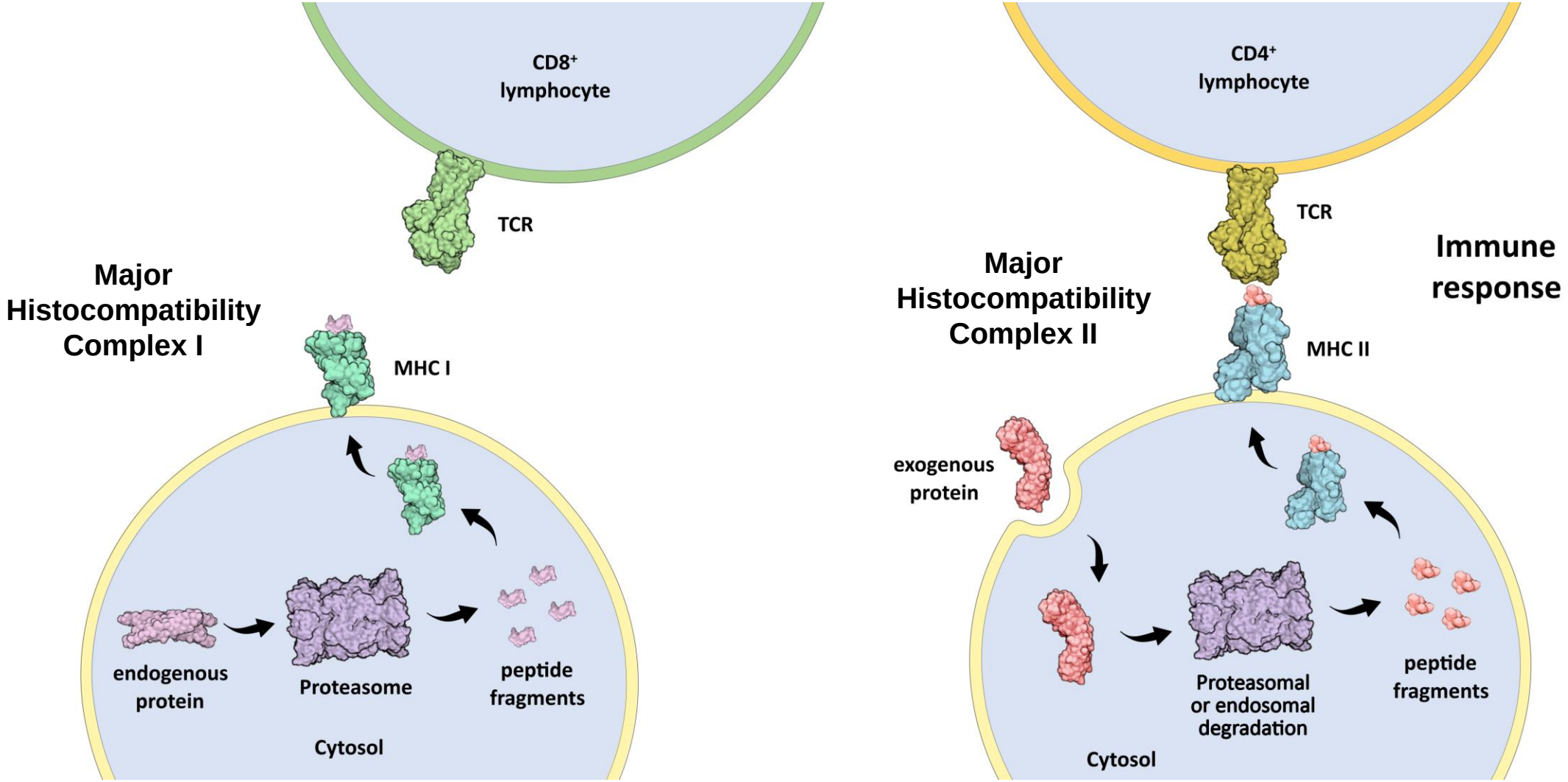
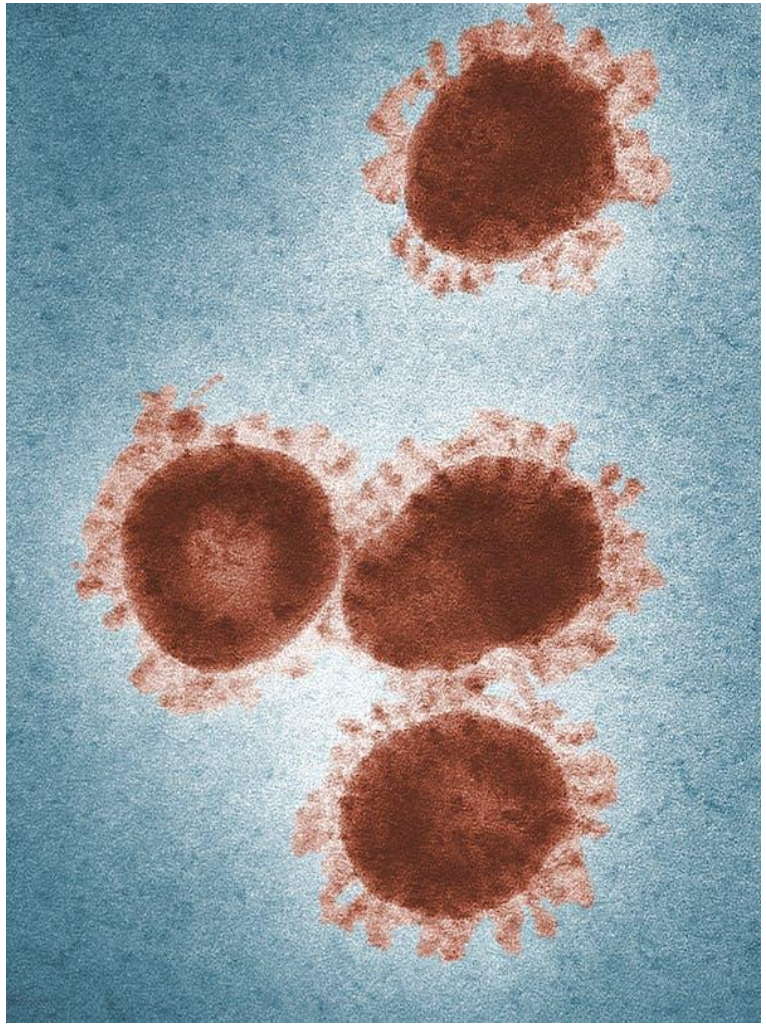


Immagine tratta e modificata da **Polykretis**, *Scand J Immunol*, 2022.

Il ruolo delle infezioni virali nello sviluppo di malattie autoimmuni



CRITICAL REVIEWS IN MICROBIOLOGY
https://doi.org/10.1080/1040841X.2019.1614904

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

Check for updates

The role of viral infections in the development of autoimmune diseases

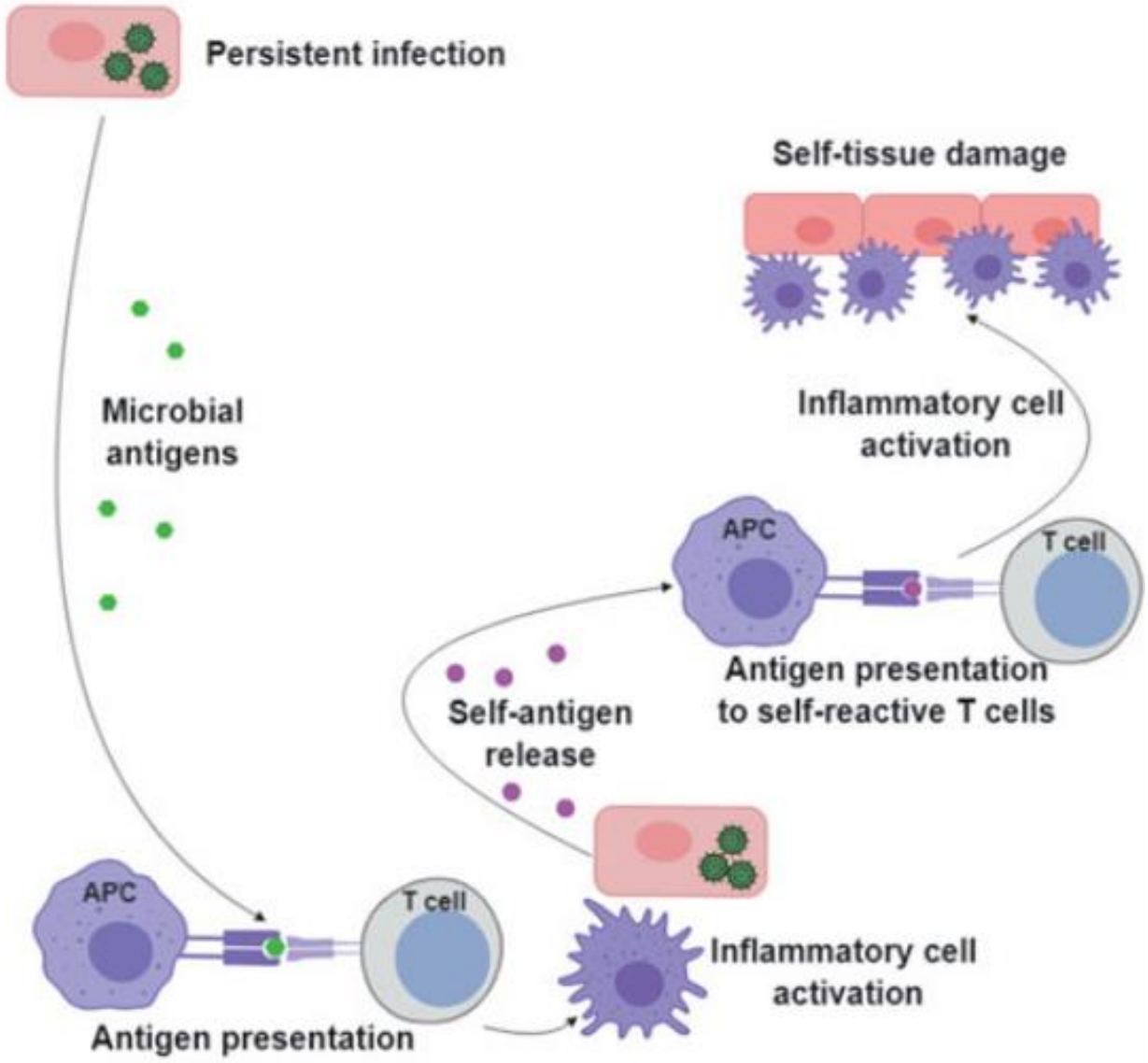
Hadi M. Hussein[a,b] and Elias A. Rahal[a,b]

[a]Department of Experimental Pathology, Immunology and Microbiology, Faculty of Medicine, American University of Beirut, Beirut, Lebanon; [b]Center for Infectious Diseases Research (CIDR), American University of Beirut, Beirut, Lebanon

(Husebye et al. 2018). Viral infection has been associated with multiple autoimmune diseases. These infections typically trigger several immune processes some of which could overwhelm the immune regulatory mechanisms. This may result in immune reactions directed to viral as well as host antigens potentially resulting in tissue damage. Several mechanisms, including molecular mimicry, bystander activation of T-cells and epitope spreading have been the primary ways of explaining how a viral infection might induce a series of reactions resulting in an autoimmune disease.

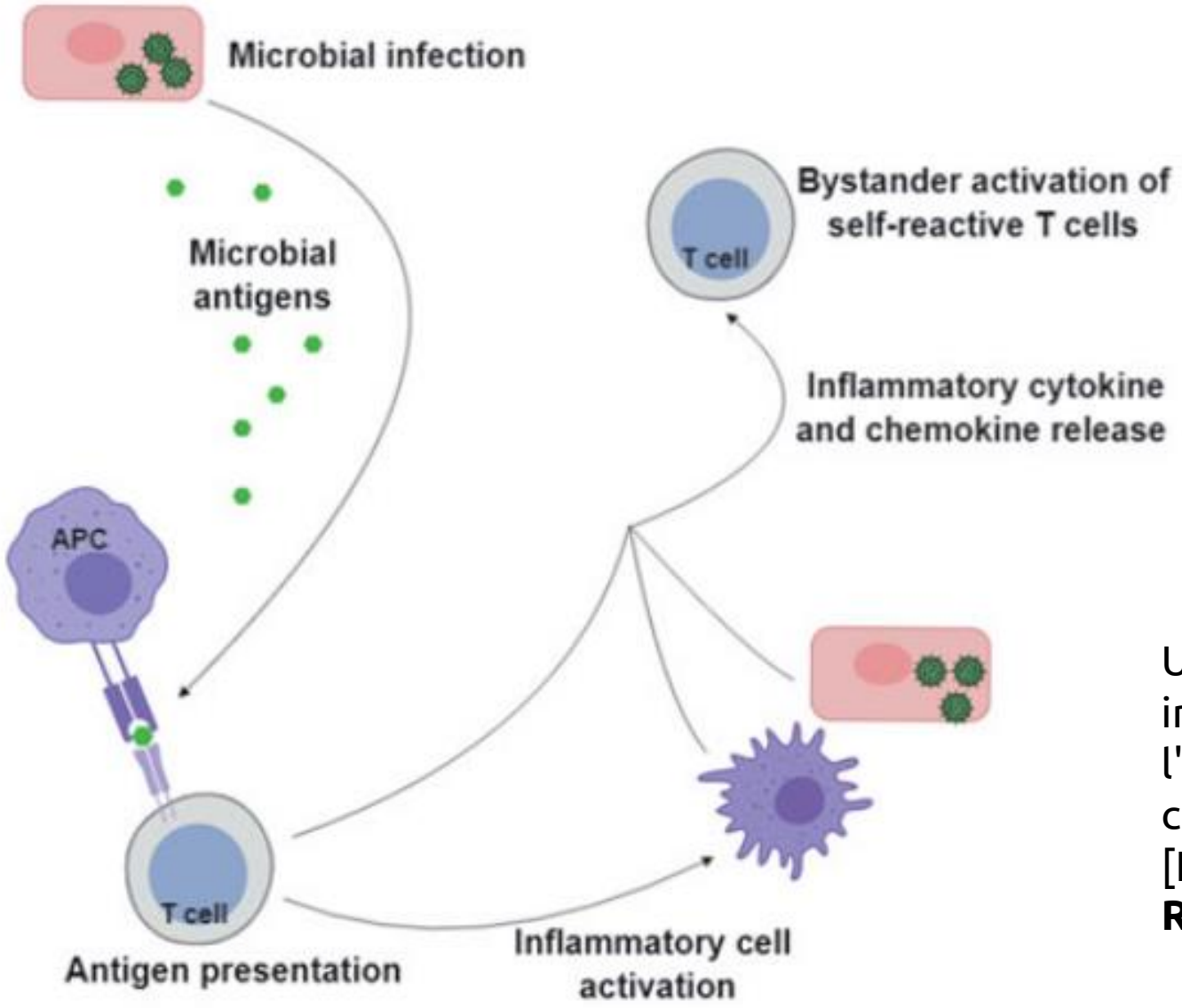
Immagine tratta da: www.pexels.com; citazione tratta da: **Hussein** & **Rahal**, *Crit. Rev. Microbiol.*, 2020.

(i) Diffusione degli epitopi



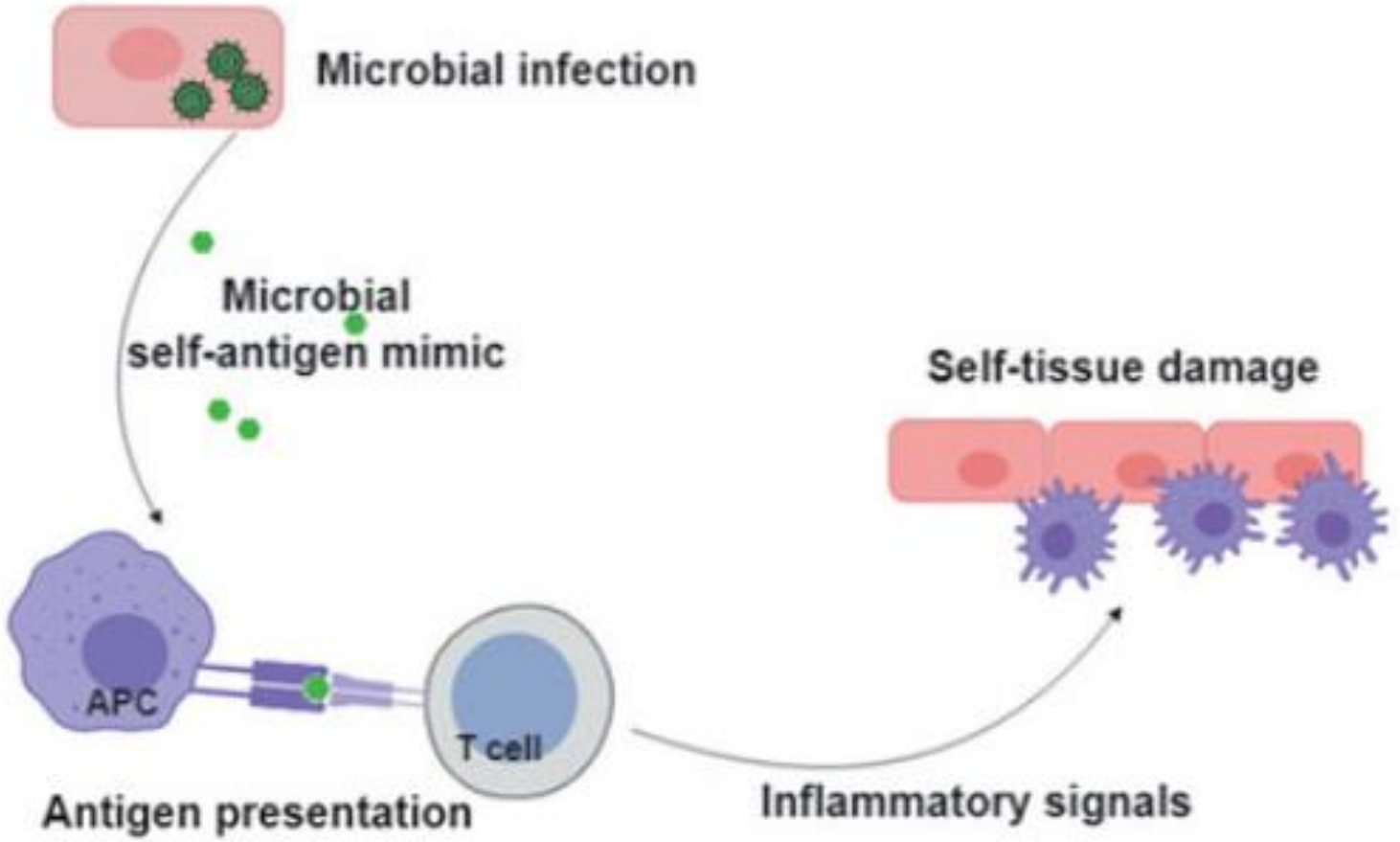
Un'infezione persistente provoca l'assorbimento di antigeni microbici da parte delle cellule presentanti l'antigene (**APC**) e la presentazione di questi antigeni a linfociti T specifici. La conseguente cascata infiammatoria provoca danno tissutale e assorbimento di antigeni self da parte delle APC. La presentazione di questi antigeni self alle cellule T autoreattive provoca quindi una reazione autoimmune contro i propri tessuti [Immagine tratta e modificata da: **Hussein & Rahal**, *Crit. Rev. Microbiol.*, 2020].

(ii) Attivazione bystander



Un'infezione microbica può innescare segnali infiammatori che inavvertitamente determinano l'attivazione di cellule T autoreattive, con conseguente attivazione di processi autoimmuni [Immagine tratta e modificata da: **Hussein & Rahal**, *Crit. Rev. Microbiol.*, 2020].

(iii) Mimetismo molecolare



Gli antigeni microbici possono condividere una somiglianza antigenica con gli antigeni self. La presentazione di queste “mimi” autoantigenici da parte delle APC linfociti T che riconoscono sia la replica microbica che il rispettivo autoantigene, può causare una reazione autoimmune [credito immagine: tratto e modificato da **Hussein & Rahal**, *Crit. Rev. Microbiol.*, 2020].

Infezione da SARS-CoV-2 come fattore scatenante dell'autoimmunità

Received: 22 September 2020 | Revised: 2 December 2020 | Accepted: 4 December 2020

DOI: 10.1111/cts.12953

ARTICLE

SARS-CoV-2 infection as a trigger of autoimmune response

Maria C. Sacchi[1] | Stefania Tamiazzo[1] | Paolo Stobbione[2] | Lisa Agatea[3] | Piera De Gaspari[4] | Anna Stecca[3] | Ernesto C. Lauritano[5] | Annalisa Roveta[6] | Renato Tozzoli[7] | Roberto Guaschino[1] | Ramona Bonometti[5]

European Review for Medical and Pharmacological Sciences 2020; 24: 9695-9697

The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection

R. BONOMETTI[1], M.C. SACCHI[2], P. STOBBIONE[3], E.C. LAURITANO[1], S. TAMIAZZO[2], A. MARCHEGIANI[4], E. NOVARA[5], E. MOLINARO[5], I. BENEDETTI[6], L. MASSONE[4], A. BELLORA[4], R. BOVERIO[1]

[1]Department of Emergency Medicine, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy
[2]Autoimmunology and Analysis Laboratory Unit, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy
[3]Department of Rheumatology, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy
[4]Geriatric Division, Santi Antonio e Biagio e Cesare Arrigo Hospital, Alessandria, Italy
[5]Department of Emergency Medicine, IRCCS San Matteo Hospital Foundation University of Pavia, Pavia, Italy
[6]Department of Internal Medicine, IRCCS San Matteo Hospital Foundation University of Pavia, Pavia, Italy

Citation: Clin Transl Sci (2020) 13, 1077–1086; doi:10.1111/cts.12805

ARTICLE

Clinical and Autoimmune Characteristics of Severe and Critical Cases of COVID-19

Yaqing Zhou[1], Tao Han[2,*], Jiaxin Chen[1], Can Hou[1], Lei Hua[1], Shu He[1], Yi Guo[1], Sheng Zhang[1], Yanjun Wang[1], Jinxia Yuan[1], Chenhui Zhao[1], Jing Zhang[1], Qiaowei Jia[1], Xiangrong Zuo[2], Jinhai Li[2], Liansheng Wang[1], Quan Cao[2,*] and Enzhi Jia[1,*]

In this study we report on the clinical and autoimmune characteristics of severe and critical novel coronavirus pneumonia caused by severe acute respiratory syndrome–associated coronavirus 2 (SARS-CoV-2). The clinical, autoimmune, and laboratory characteristics of 21 patients who had laboratory-confirmed severe and critical cases of coronavirus disease 2019 (COVID-19) from the intensive care unit of the Huangshi Central Hospital, Hubei Province, China, were investigated. A total of 21 patients (13 men and 8 women), including 8 (38.1%) severe cases and 13 (61.9%) critical cases, were enrolled. Cough (90.5%) and fever (81.0%) were the dominant symptoms, and most patients (76.2%) had at least one coexisting disorder on admission. The most common characteristics on chest computed tomography were ground-glass opacity (100%) and bilateral patchy shadowing (76.2%). The most common findings on laboratory measurement were lymphocytopenia (85.7%) and elevated levels of C-reactive protein (94.7%) and interleukin-6 (89.5%). The prevalence of anti–52 kDa SSA/Ro antibody, anti–60 kDa SSA/Ro antibody, and antinuclear antibody was 20%, 25%, and 50%, respectively. We also retrospectively analyzed the clinical and laboratory data from 21 severe and critical cases of COVID-19. Autoimmune phenomena exist in COVID-19 subjects, and the present results provide the rationale for a strategy of preventing immune dysfunction and optimal immunosuppressive therapy.

Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19

COVID-19 grave e tempesta citochinica

Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause of COVID-19, which has affected more than 6 million people worldwide causing more than 400 000 deaths. The disease affects predominantly the upper and lower respiratory tracts causing severe pulmonary disease which often evolves to a multiorgan systemic disease.[1] This is evidenced by thromboembolic lesions of the heart and lungs, pulmonary haemorrhage, muscle weakness, hyperbilirubinaemia and lymphopenia suggesting that COVID-19 affects epithelial barriers, endothelial cells, coagulation, fibrinolysis and the immune system.[2] In patients who are severely ill, innate immune hyperactivity causes a cytokine storm which disturbs microcirculation resulting in shock and acute respiratory distress syndrome.[3] Systemic disease perpetuation may be due to the virus itself, infecting cells via ACE2 receptor or, following the cytokine storm, due to autoinflammatory and/or autoimmune mechanisms.[4]

the exception of hydroxychloroquine (28/29 treated), were not treated with any immunomodulatory drugs.

The small sample size did not allow procurement of any statistically significant clinicolaboratory associations. Despite this and the lack of preinfection serological data, the presence of several systemic autoimmune reactivities in almost 70% of the patients suggests a post-SARS-CoV-2 or para-SARS-CoV-2 infectious autoimmune activation. This is not surprising, as cytokines present in the cytokine storm, for example, interleukin-6, can drive autoinflammatory reactions and autoimmunity, probably via pre-existing natural B cell clones or molecular mimicry. The possible autoimmune mechanism merits further investigation, therefore an autoimmune surveillance in larger cohorts is necessary to investigate possible mechanisms of COVID-19 perpetuation and to inform ongoing convalescence plasma therapeutic trials.[7 8] As several of the reported autoantibodies are disease markers and can be pathogenic, one should be cautious before transferring autoantibodies, along with neutralising antibodies, into severely affected patients.

Panayiotis G Vlachoyiannopoulos,[1] **Eleni Magira**,[2] **Haris Alexopoulos**,[1] **Edison Jahaj**,[2] **Katerina Theophilopoulou**,[1] **Anastasia Kotanidou**,[2] **Athanasios G Tzioufas**[1]

Tratto da: **Vlachoyiannopoulos** et al., *Ann Rheum Dis*, 2020.

Meccanismo d’immunizzazione dei vaccini a mRNA contro la COVID-19

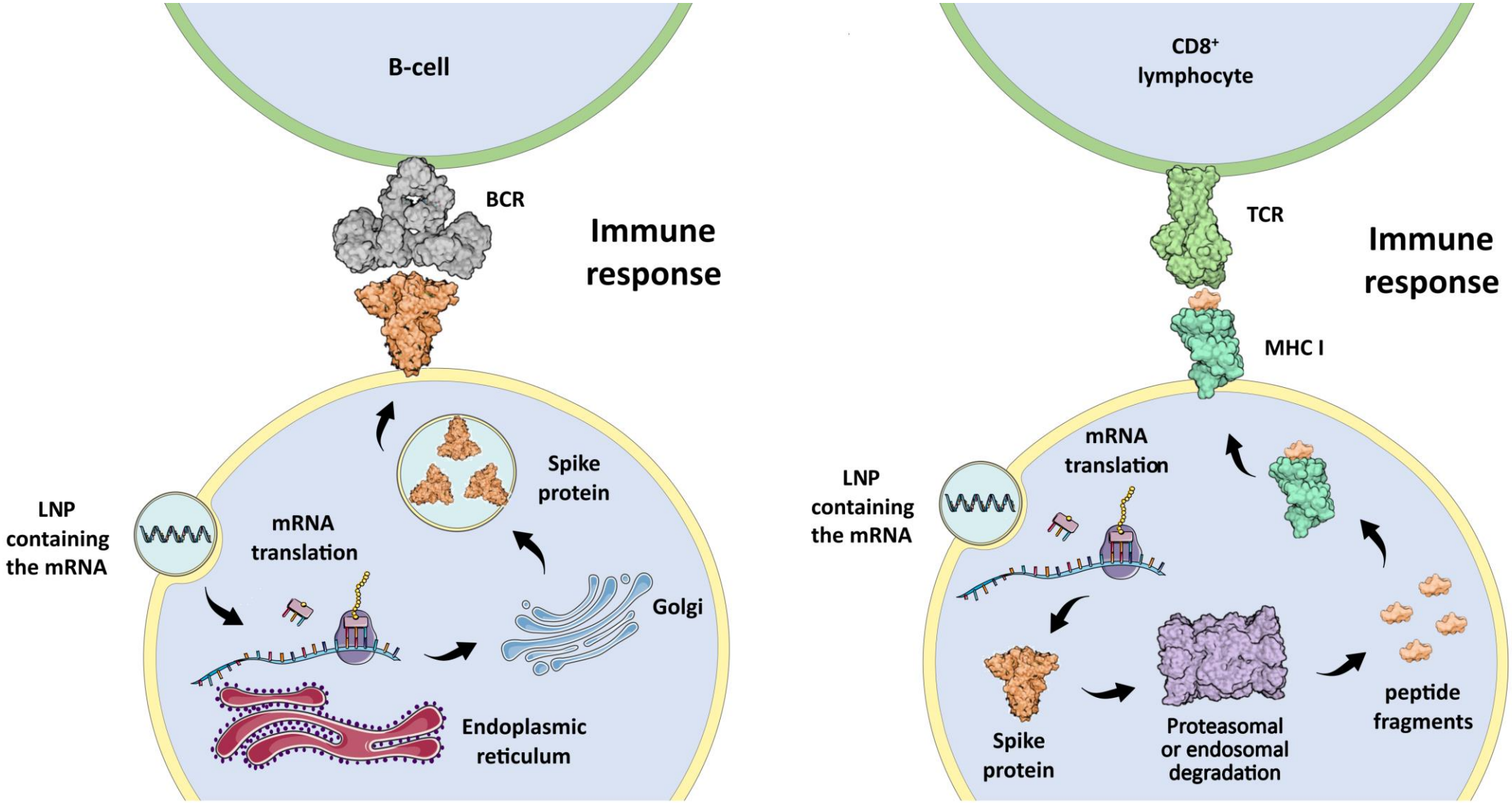


Immagine tratta e modificata da: **Polykretis**, *Scand J Immunol*, 2022.

La questione della biodistribuzione dei vaccini genetici

Received: 21 January 2022 | Revised: 8 March 2022 | Accepted: 13 March 2022

DOI: 10.1111/sji.13160

Scandinavian Journal of Immunology WILEY

LETTER TO THE EDITOR

Role of the antigen presentation process in the immunization mechanism of the genetic vaccines against COVID-19 and the need for biodistribution evaluations

December 2020 to 28 February 2021.[10]

In conclusion, it is essential to underline that every human cell that intakes the LNPs and translates the viral protein (in case of the mRNA vaccines), or that gets infected by the adenovirus and expresses and translates the viral protein (in case of the adenovirus-based vaccines), is inevitably recognized as a threat by the immune system and killed (Figure 1). There are no exceptions to this mechanism. The severity of the resulting damage and the consequences for health depend on the quantity of the cells involved, on the type of tissue and on the strength of the following autoimmune reaction. For instance, if the mRNA contained in the LNPs would get internalized by cardiac myocytes, and such cells would produce the spike protein, the resulting inflammation would likely lead to the necrosis of the myocardium, with an extent proportional to the number of involved cells. Therefore, it is fundamental to perform pharmacokinetic evaluations in humans, in order to determine the exact biodistribution of the vaccines against COVID-19, and thus to identify the possible tissues at threat.

Tratto da: **Polykretis**, *Scand J Immunol*, 2022.

Studio sulla biodistribuzione di Pfizer nei ratti (n° 185350)

Table 1 **Mean (Sexes-Combined) Concentration and Recovery of Total Radioactivity in Whole Blood, Plasma and Tissues Following Single Intramuscular Administration of [^{3}H]-08-A01-C01 to Wistar Han Rats**

Target Dose Level: 50 µg mRNA/Animal; 1.29 mg Total Lipid/Animal

Results expressed as total lipid concentration (µg lipid equiv/g (mL)) and % of administered dose

Sample	Total Lipid Concentration (µg lipid equiv/g (or mL))							% of Administered Dose						
	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h
Adipose tissue	0.057	0.100	0.126	0.128	0.093	0.084	0.181	-	-	-	-	-	-	-
Adrenal glands	0.271	1.484	2.719	2.888	6.803	13.772	18.209	0.001	0.007	0.010	0.015	0.035	0.066	0.106
Bladder	0.041	0.130	0.146	0.167	0.148	0.247	0.365	0.000	0.001	0.001	0.001	0.001	0.002	0.002
Bone (femur)	0.091	0.195	0.266	0.276	0.340	0.342	0.687	-	-	-	-	-	-	-
Bone marrow (femur)	0.479	0.960	1.237	1.236	1.836	2.492	3.771	-	-	-	-	-	-	-
Brain	0.045	0.100	0.138	0.115	0.073	0.069	0.068	0.007	0.013	0.020	0.016	0.011	0.010	0.009
Eyes	0.010	0.035	0.052	0.067	0.059	0.091	0.112	0.000	0.001	0.001	0.002	0.002	0.002	0.003
Heart	0.282	1.029	1.402	0.987	0.790	0.451	0.546	0.018	0.056	0.084	0.060	0.042	0.027	0.030
Injection site	128.253	393.810	311.177	338.039	212.760	194.855	164.929	19.851	52.620	31.574	28.383	21.862	29.126	24.625
Kidneys	0.391	1.161	2.046	0.924	0.590	0.426	0.425	0.050	0.124	0.211	0.109	0.075	0.054	0.057
Large intestine	0.013	0.048	0.093	0.287	0.649	1.104	1.338	0.008	0.025	0.065	0.192	0.405	0.692	0.762
Liver	0.737	4.625	10.972	16.547	26.544	19.240	24.288	0.602	2.871	7.330	11.863	18.050	15.439	16.155
Lung	0.492	1.210	1.834	1.497	1.151	1.039	1.093	0.052	0.101	0.178	0.169	0.122	0.101	0.101
Lymph node (man)	0.064	0.189	0.290	0.408	0.534	0.554	0.727	-	-	-	-	-	-	-
Lymph node (mes)	0.050	0.146	0.530	0.489	0.689	0.985	1.366	-	-	-	-	-	-	-
Muscle	0.021	0.061	0.084	0.103	0.096	0.095	0.192	-	-	-	-	-	-	-
Ovaries (females)	0.104	1.339	1.638	2.341	3.088	5.240	12.261	0.001	0.009	0.008	0.016	0.025	0.037	0.095
Pancreas	0.081	0.207	0.414	0.380	0.294	0.358	0.599	0.003	0.007	0.014	0.015	0.015	0.011	0.019
Pituitary gland	0.339	0.645	0.868	0.854	0.405	0.478	0.694	0.000	0.001	0.001	0.001	0.000	0.000	0.001
Prostate (males)	0.061	0.091	0.128	0.157	0.150	0.183	0.170	0.001	0.001	0.002	0.003	0.003	0.004	0.003
Salivary glands	0.084	0.193	0.255	0.220	0.135	0.170	0.264	0.003	0.007	0.008	0.008	0.005	0.006	0.009
Skin	0.013	0.208	0.159	0.145	0.119	0.157	0.253	-	-	-	-	-	-	-

Sample	Total Lipid Concentration (µg lipid equiv/g (or mL))							% of Administered Dose						
	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h	0.25 min	1 h	2 h	4 h	8 h	24 h	48 h
Small intestine	0.030	0.221	0.476	0.879	1.279	1.302	1.472	0.024	0.130	0.319	0.543	0.776	0.906	0.835
Spinal cord	0.043	0.097	0.169	0.250	0.106	0.085	0.112	0.001	0.002	0.002	0.003	0.001	0.001	0.001
Spleen	0.334	2.471	7.734	10.296	22.091	20.080	23.353	0.013	0.093	0.325	0.385	0.982	0.821	1.030
Stomach	0.017	0.065	0.115	0.144	0.268	0.152	0.215	0.006	0.019	0.034	0.030	0.040	0.037	0.039
Testes (males)	0.031	0.042	0.079	0.129	0.146	0.304	0.320	0.007	0.010	0.017	0.030	0.034	0.074	0.074
Thymus	0.088	0.243	0.340	0.335	0.196	0.207	0.331	0.004	0.007	0.010	0.012	0.008	0.007	0.008
Thyroid	0.155	0.536	0.842	0.851	0.544	0.578	1.000	0.000	0.001	0.001	0.001	0.001	0.001	0.001
Uterus (females)	0.043	0.203	0.305	0.140	0.287	0.289	0.456	0.002	0.011	0.015	0.008	0.016	0.018	0.022
Whole blood	1.970	4.369	5.401	3.049	1.314	0.909	0.420	-	-	-	-	-	-	-
Plasma	3.965	8.132	8.903	6.503	2.360	1.783	0.805	-	-	-	-	-	-	-
Blood:plasma ratio	0.815	0.515	0.550	0.510	0.555	0.530	0.540	-	-	-	-	-	-	-

- =Partial tissue taken therefore not applicable/not applicable

Tratto da: phmpt.org/wp-content/uploads/2022/03/125742_S1_M4_4223_185350.pdf

Report di valutazione del Comirnaty della EMA

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

19 February 2021
EMA/707383/2020 Corr.1*[1]
Committee for Medicinal Products for Human Use (CHMP)

page 47

Assessment report

Comirnaty

Common name: COVID-19 mRNA vaccine (nucleoside-modified)

Procedure No. EMEA/H/C/005735/0000

The biodistribution was also studied in rats using radiolabeled LNP and luciferase modRNA (study 185350). The radiolabeling data, measuring distribution to blood, plasma and selected tissues, of IM injection of a single dose of 50 µg mRNA over a 48-hour period is considered more sensitive than the bioluminescence method and indicate a broader biodistribution pattern than was observed with bioluminescence. Over 48 hours, distribution from the injection site to most tissues occurred, with the majority of tissues exhibiting low levels of radioactivity.

Tratto da: www.ema.europa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-repo rt_en.pdf.

mRNA vaccinale nel sangue

biomedicines

MDPI

Article

Vaccine mRNA Can Be Detected in Blood at 15 Days Post-Vaccination

Tudor Emanuel Fertig [1,2,*], Leona Chitoiu [1], Daciana Silvia Marta [1,3], Victor-Stefan Ionescu [1], Valeriu Bogdan Cismasiu [1], Eugen Radu [2,4], Giulia Angheluta [2], Maria Dobre [1], Ana Serbanescu [5], Mihail Eugen Hinescu [1,2] and Mihaela Gherghiceanu [1,2]

Abstract: COVID-19 mRNA vaccines effectively reduce incidence of severe disease, hospitalisation and death. The biodistribution and pharmacokinetics of the mRNA-containing lipid nanoparticles (LNPs) in these vaccines are unknown in humans. In this study, we used qPCR to track circulating mRNA in blood at different time-points after BNT162b2 vaccination in a small cohort of healthy individuals. We found that vaccine-associated synthetic mRNA persists in systemic circulation for at least 2 weeks. Furthermore, we used transmission electron microscopy (TEM) to investigate SARS-CoV-2 spike protein expression in human leukemic cells and in primary mononuclear blood cells treated in vitro with the BNT162b2 vaccine. TEM revealed morphological changes suggestive of LNP uptake, but only a small fraction of K562 leukemic cells presented spike-like structures at the cell surface, suggesting reduced levels of expression for these specific phenotypes.

Tratto da: **Fertig** et al., *Biomedicines*, 2022.

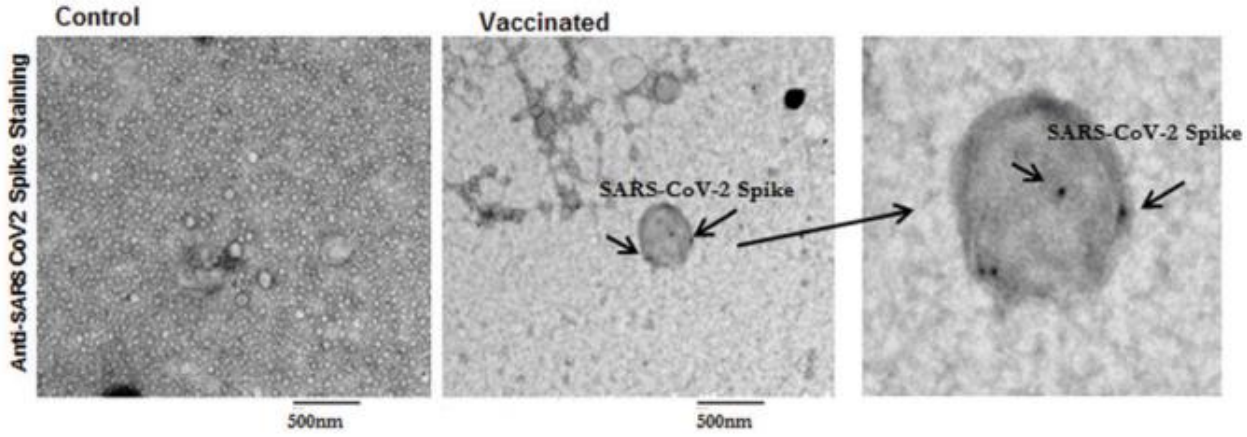
Esosomi che esprimono la proteina spike del vaccino

Cutting Edge

The Journal of Immunology

Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer–BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mRNA Vaccines

Sandhya Bansal,* Sudhir Perincheri,† Timothy Fleming,* Christin Poulson,* Brian Tiffany,* Ross M. Bremner,* and Thalachallour Mohanakumar*



Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) causes severe acute respiratory syndrome. mRNA vaccines directed at the SARS-CoV-2 spike protein resulted in development of Abs and protective immunity. To determine the mechanism, we analyzed the kinetics of induction of circulating exosomes with SARS-CoV-2 spike protein and Ab following vaccination of healthy individuals. Results demonstrated induction of circulating exosomes expressing spike protein on day 14 after vaccination followed by Abs 14 d after the second dose. Exosomes with spike protein, Abs to SARS-CoV-2 spike, and T cells secreting IFN-γ and TNF-α increased following the booster dose. Transmission electron microscopy of exosomes also demonstrated spike protein Ags on their surface. Exosomes with spike protein and Abs decreased in parallel after four months. These results demonstrate an important role of circulating exosomes with spike protein for effective immunization following mRNA-based vaccination. This is further documented by induction of humoral and cellular immune responses in mice immunized with exosomes carrying spike protein. *The Journal of Immunology*, 2021, 207: 2405–2410.

Immagine tratta e modificata da: **Bansal** et al., *J Immunol*, 2021.

Proteina spike vaccinale nei linfonodi

Cell

CellPress
OPEN ACCESS

Article

Immune imprinting, breadth of variant recognition, and germinal center response in human SARS-CoV-2 infection and vaccination

Katharina Röltgen,[1,14] Sandra C.A. Nielsen,[1,14] Oscar Silva,[1,14] Sheren F. Younes,[1,14] Maxim Zaslavsky,[1] Cristina Costales,[1] Fan Yang,[1] Oliver F. Wirz,[1] Daniel Solis,[1] Ramona A. Hoh,[1] Aihui Wang,[1] Prabhu S. Arunachalam,[2] Deana Colburg,[1] Shuchun Zhao,[1] Emily Haraguchi,[1] Alexandra S. Lee,[3] Mihir M. Shah,[3] Monali Manohar,[3] Iris Chang,[3] Fei Gao,[2] Vamsee Mallajosyula,[2] Chunfeng Li,[2] James Liu,[4] Massa J. Shoura,[1] Sayantani B. Sindher,[3] Ella Parsons,[3] Naranjargal J. Dashdorj,[5,6] Naranbaatar D. Dashdorj,[5] Robert Monroe,[7] Geidy E. Serrano,[8] Thomas G. Beach,[8] R. Sharon Chinthrajah,[3,9] Gregory W. Charville,[1] James L. Wilbur,[10] Jacob N. Wohlstadter,[10] Mark M. Davis,[2,11,12] Bali Pulendran,[1,2,11] Megan L. Troxell,[1] George B. Sigal,[10] Yasodha Natkunam,[1] Benjamin A. Pinsky,[1,13] Kari C. Nadeau,[3,9,15] and Scott D. Boyd[1,3,15,16,*]

Prolonged detection of vaccine mRNA in LN GCs and spike antigen in LN GCs and blood following SARS-CoV-2 mRNA vaccination

The biodistribution, quantity, and persistence of vaccine mRNA and spike antigen after vaccination and viral antigens after SARS-CoV-2 infection are incompletely understood but are likely to be major determinants of immune responses. We performed *in situ* hybridization with control and SARS-CoV-2 vaccine mRNA-specific RNAScope probes in the core needle biopsies of the ipsilateral axillary LNs that were collected 7–60 days after the second dose of mRNA-1273 or BNT162b2 vaccination and detected vaccine mRNA collected in the GCs of LNs on days 7, 16, and 37 postvaccination, with lower but still appreciable specific signal at day 60 (Figures 7A–7E). Only rare foci of vaccine mRNA were seen outside of GCs. Axillary LN core needle biopsies of nonvaccinees (n = 3) and COVID-19 patient specimens were negative for vaccine probe hybridization. Immunohistochemical staining for spike antigen in mRNA-vaccinated patient LNs varied between individuals but showed abundant spike protein in GCs 16 days post-second dose, with spike antigen still present as late as 60 days post-second dose. Spike antigen localized in a reticular pattern around the GC cells, similar to staining for follicular dendritic cell processes (Figure 7B).

Tratto da: **Röltgen** et al., *Cell*, 2022.

mRNA vaccinale nei linfonodi e nel tessuto cardiaco di pazienti deceduti

npj | vaccines

www.nature.com/npjvaccines

ARTICLE OPEN

Check for updates

Duration of SARS-CoV-2 mRNA vaccine persistence and factors associated with cardiac involvement in recently vaccinated patients

Aram J. Krauson[1], Faye Victoria C. Casimero[1,2], Zakir Siddiquee[1] and James R. Stone[1,2]✉

At the start of the COVID-19 pandemic, the BNT162b2 (BioNTech-Pfizer) and mRNA-1273 (Moderna) mRNA vaccines were expediently designed and mass produced. Both vaccines produce the full-length SARS-CoV-2 spike protein for gain of immunity and have greatly reduced mortality and morbidity from SARS-CoV-2 infection. The distribution and duration of SARS-CoV-2 mRNA vaccine persistence in human tissues is unclear. Here, we developed specific RT-qPCR-based assays to detect each mRNA vaccine and screened lymph nodes, liver, spleen, and myocardium from recently vaccinated deceased patients. Vaccine was detected in the axillary lymph nodes in the majority of patients dying within 30 days of vaccination, but not in patients dying more than 30 days from vaccination. Vaccine was not detected in the mediastinal lymph nodes, spleen, or liver. Vaccine was detected in the myocardium in a subset of patients vaccinated within 30 days of death. Cardiac ventricles in which vaccine was detected had healing myocardial injury at the time of vaccination and had more myocardial macrophages than the cardiac ventricles in which vaccine was not detected. These results suggest that SARS-CoV-2 mRNA vaccines routinely persist up to 30 days from vaccination and can be detected in the heart.

npj Vaccines (2023)8:141 ; https://doi.org/10.1038/s41541-023-00742-7

with mRNA-1273 and in 6 (46%) of the 13 patients vaccinated with BNT162b2 (Figs. 1b, c, 2). Overall, for both vaccines, vaccine was detected in 8 (73%) of the 11 available axillary lymph nodes samples from the 12 patients dying within 30 days of vaccination compared with no detection of vaccine in any of the axillary lymph nodes samples from the 8 patients dying after 30 days from vaccination ($P = 0.003$, Fisher exact test). For none of the patients was vaccine detected in the liver, spleen, or mediastinal lymph nodes (each $n = 19$). For the 20 cardiac left ventricle and 20 cardiac right ventricle samples, vaccine was detected in 2 samples of left ventricle and 2 samples of right ventricle from a total of three patients. All three of these patients had been vaccinated with BNT162b2 within 30 days of death. All samples positive for vaccine were validated for sequences outside of the dsDNA control sequence (Supplementary Tables 3–4). Since SARS-CoV-2 can involve tissues throughout the body including the heart in the setting of severe respiratory tract infection[22,23], as a further control, all tissue samples with detectable vaccine mRNA were screened for the SARS-CoV-2 virus E gene (Fig. 1d) and were found to be negative for the virus. Vaccine was not detected by RT-qPCR in any of the tissues from the 5 non-vaccinated control patients. Immunohistochemistry for the spike protein in the axillary lymph nodes, left ventricle, right ventricle and liver performed on all 20

Tratto da: **Krauson** et al., *NPJ Vaccines*, 2023.

mRNA vaccinale nel latte materno

Biodistribution of mRNA COVID-19 vaccines in human breast milk

Nazeeh Hanna,[a,b,*] Claudia Manzano De Mejia,[b] Ari Heffes-Doon,[a] Xinhua Lin,[b] Bishoy Botros,[b] Ellen Gurzenda,[b] Christie Clauss-Pascarelli,[c] and Amrita Nayak[a]

[a]Division of Neonatology, Department of Pediatrics, NYU Langone Hospital—Long Island, New York University Grossman Long Island School of Medicine, 259 First Street, Mineola, NY 11501, USA
[b]Women and Children's Research Laboratory, New York University Grossman Long Island School of Medicine, 259 First Street, Mineola, NY 11501, USA
[c]Department of Pharmacy, NYU Langone Hospital—Long Island, New York University Grossman Long Island School of Medicine, 259 First Street, Mineola, NY 11501, USA

Findings Of 13 lactating women receiving the vaccine (20 exposures), trace mRNA amounts were detected in 10 exposures up to 45 h post-vaccination. The mRNA was concentrated in the BM EVs; however, these EVs neither expressed SARS-COV-2 spike protein nor induced its expression in the HT-29 cell line. Linkage analysis suggests vaccine mRNA integrity was reduced to 12–25% in BM.

Interpretation Our findings demonstrate that the COVID-19 vaccine mRNA is not confined to the injection site but spreads systemically and is packaged into BM EVs. However, as only trace quantities are present and a clear translational activity is absent, we believe breastfeeding post-vaccination is safe, especially 48 h after vaccination. Nevertheless, since the minimum mRNA vaccine dose to elicit an immune reaction in infants <6 months is unknown, a dialogue between a breastfeeding mother and her healthcare provider should address the benefit/risk considerations of breastfeeding in the first two days after maternal vaccination.

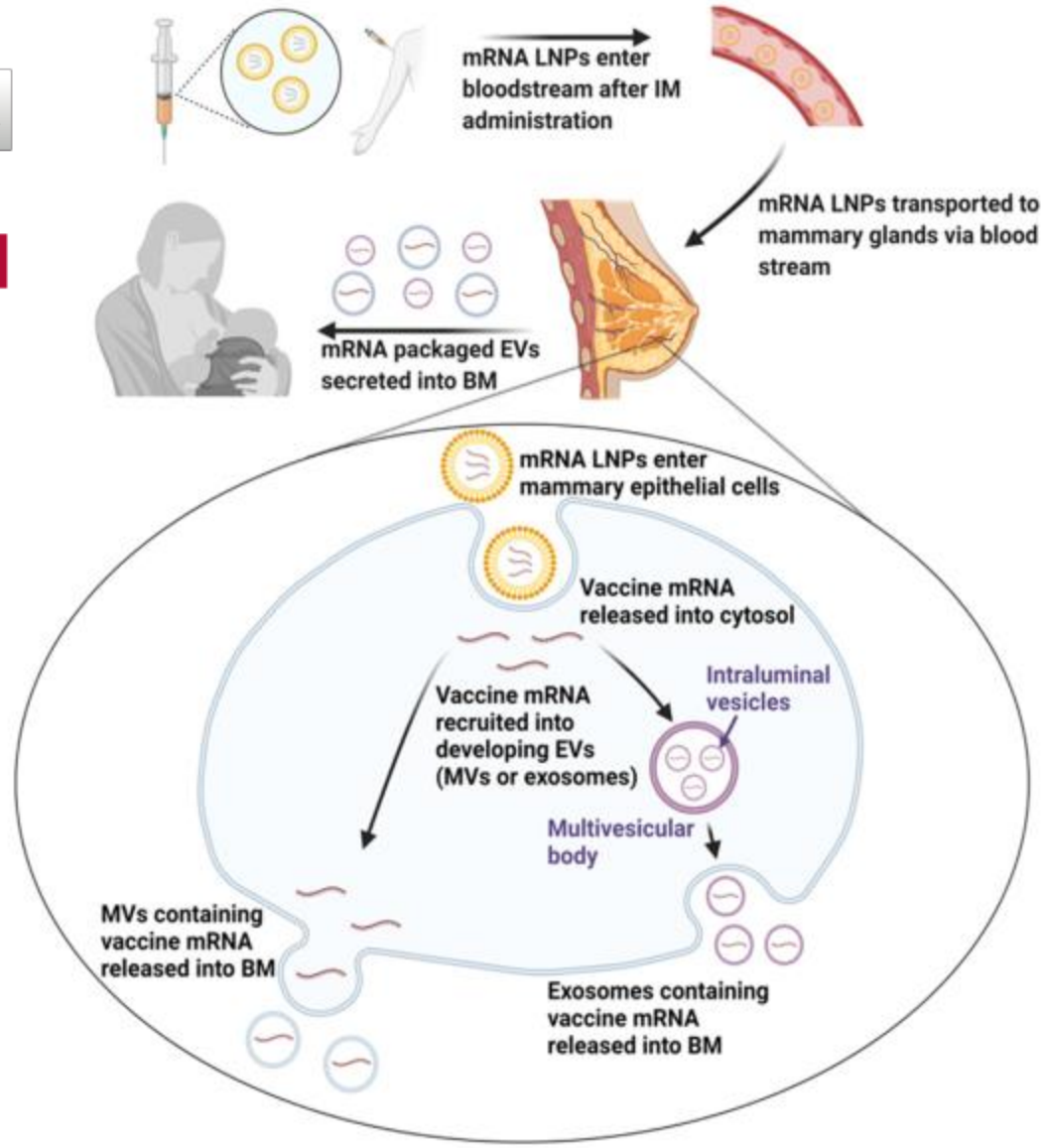
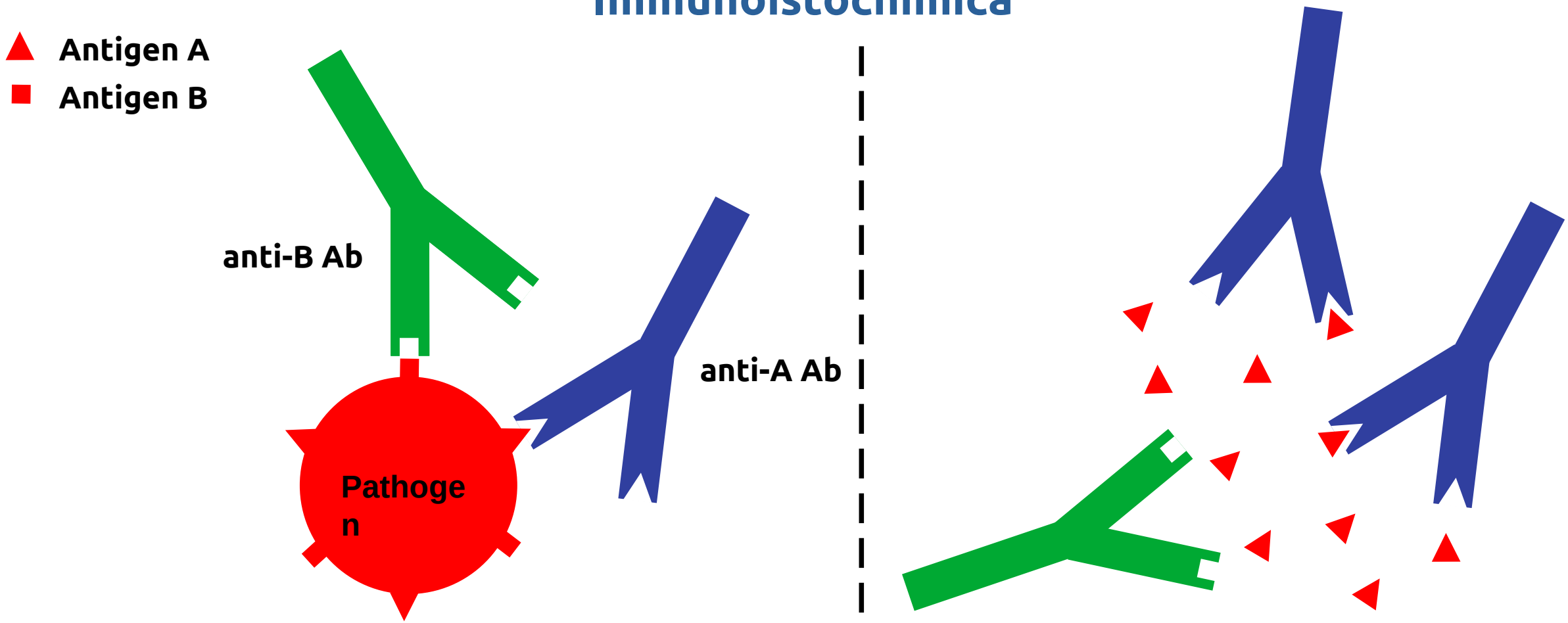


Immagine tratta e modificata da: **Hannah** et al., *eBioMedicine*, 2023.

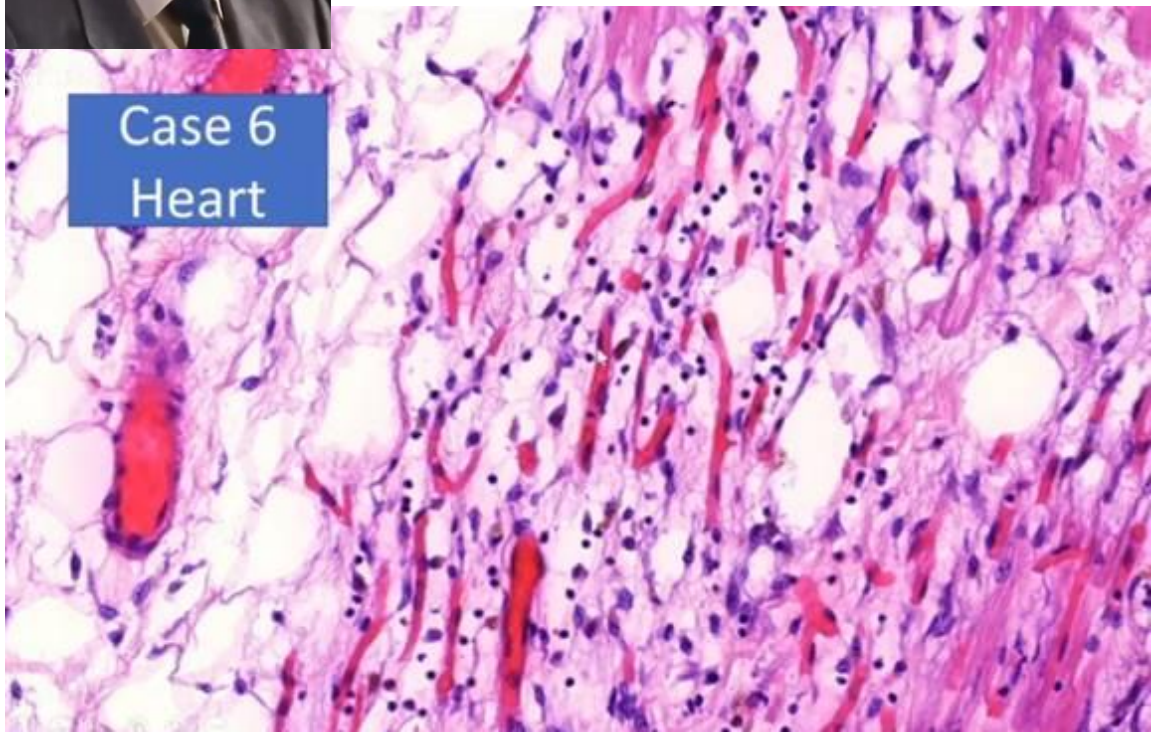
Immunoistochimica

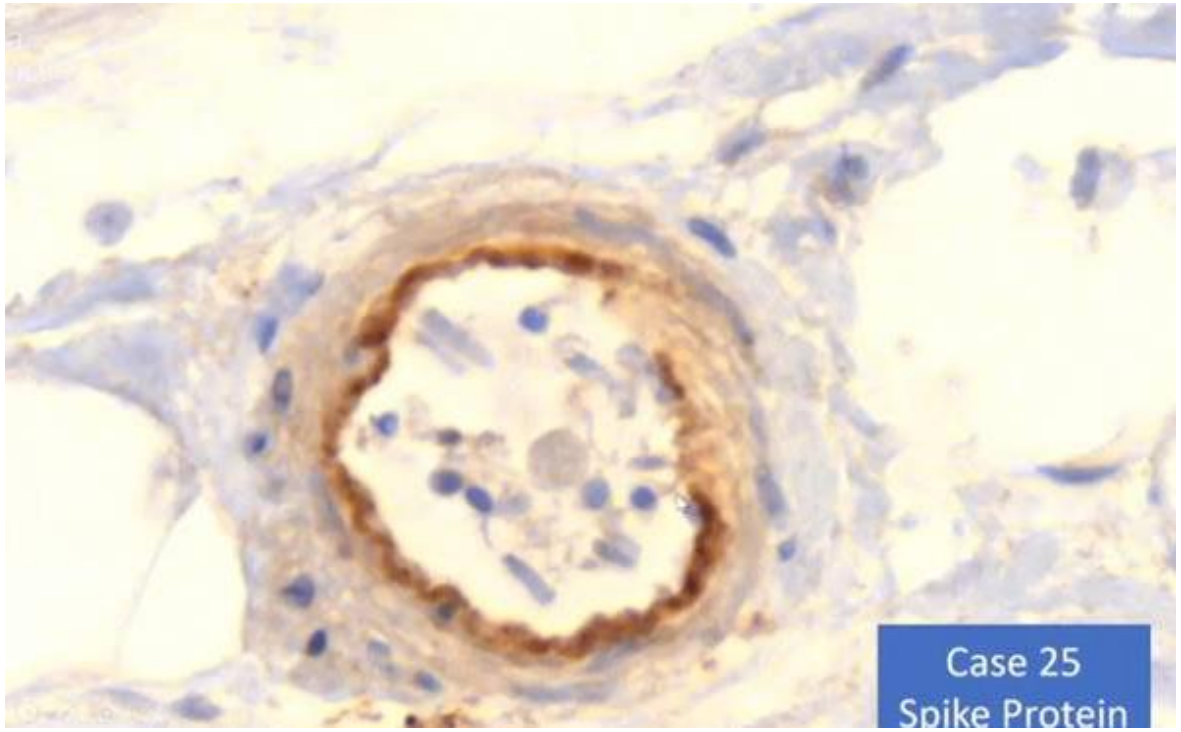


L'immunoistochimica è una tecnica che sfrutta il legame specifico tra un anticorpo (**Ab**) e un antigene per rilevare e localizzare antigeni specifici in una sezione di tessuto. **A sinistra**, l'**Ab anti-A** lega l'**antigene A** (ad esempio la proteina spike del SARS-CoV-2) e l'**Ab anti-B** lega l'**antigene B** (ad esempio la proteina nucleocapside del SARS-CoV-2). **A destra**, solo l'**Ab anti-A** si lega al suo antigene specifico, dimostrando che nel tessuto non c'è stata infezione virale.

I dati istopatologici

Prof. **Arne Burkhardt** (06/01/1944 - 30/05/2023)





(**Sinistra**) Caso di miocardite, in cui le fibre muscolari muoiono ed è rilevabile un denso infiltrato infiammatorio di linfociti; (**destra**) reazione immunoistochimica contro la proteina spike del SARS-CoV-2 nella parete interna di un vaso sanguigno di un paziente con miocardite [Immagini tratte da: corona-blog.net/2022/03/10/reutlinger-autopsie-histologie-studie-nebenwirkungen-und-todesfaelle-durch- die-corona-impfungen/].

Referti istopatologici da autopsie

vaccines

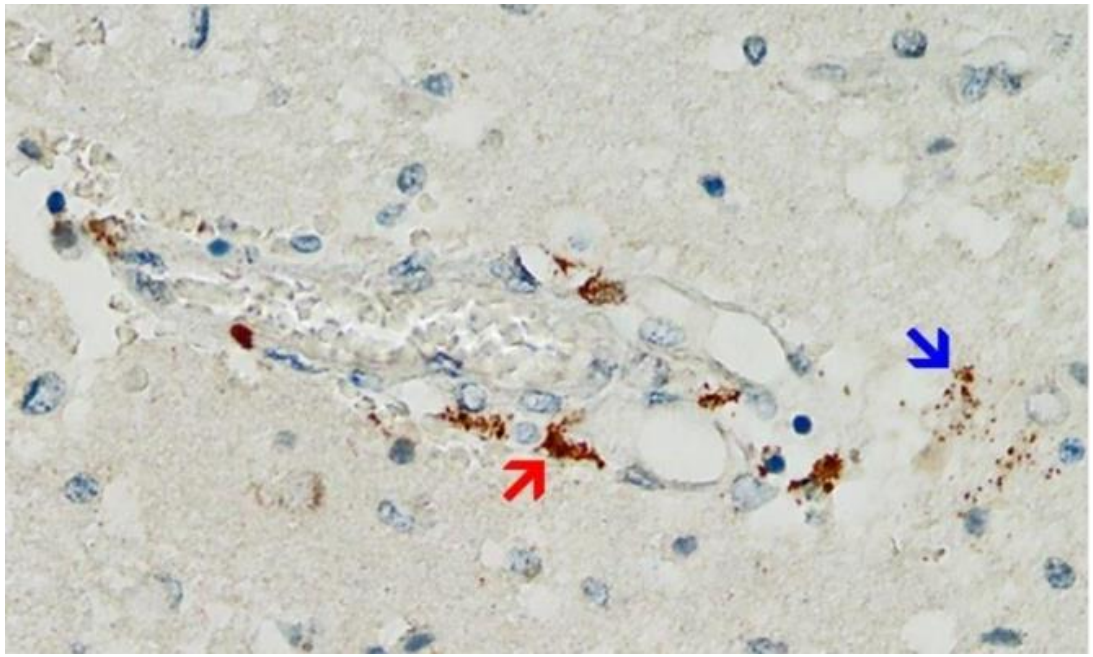
MDPI

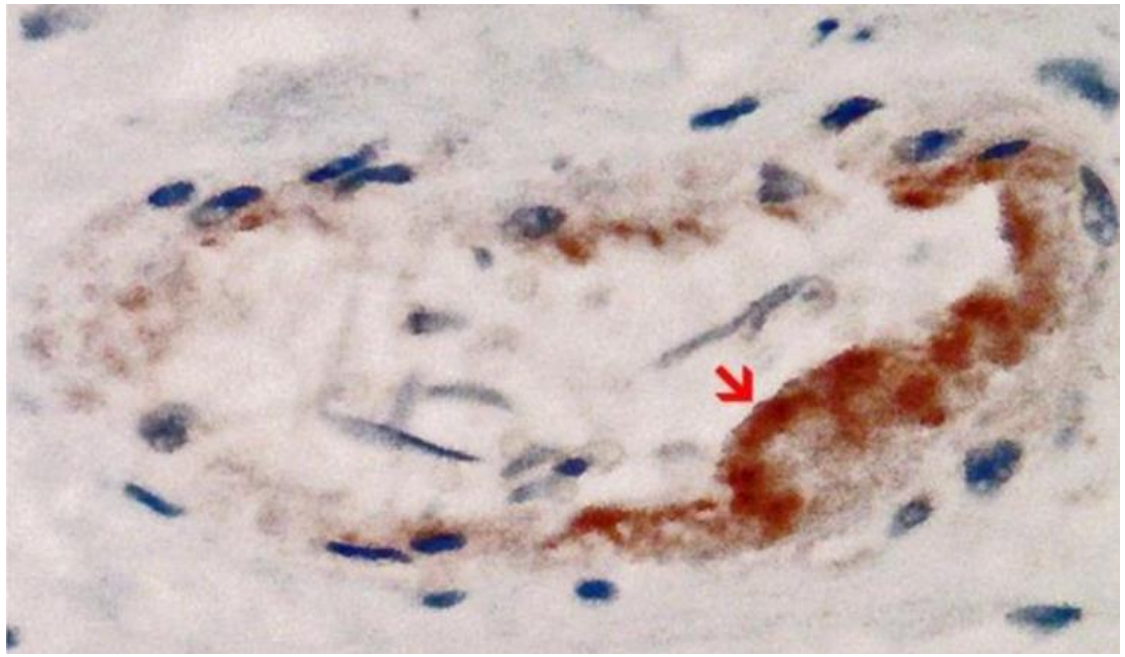
Case Report

A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against COVID-19

Michael Mörz

Nota: **Mörz** ha utilizzato sia l'Ab anti-spike, sia quello anti-nucleocapside.





Reazione immunoistochimica contro la proteina spike del SARS-CoV-2 nell'encefalo (**sinistra**), visibile come granuli marroni, e nel ventricolo sinistro del cuore (**destra**) [immagini tratte e modificate da **Mörz**, Int J Mol Sci, 2022].

Referti istopatologici da biopsie

International Journal of *Molecular Sciences*

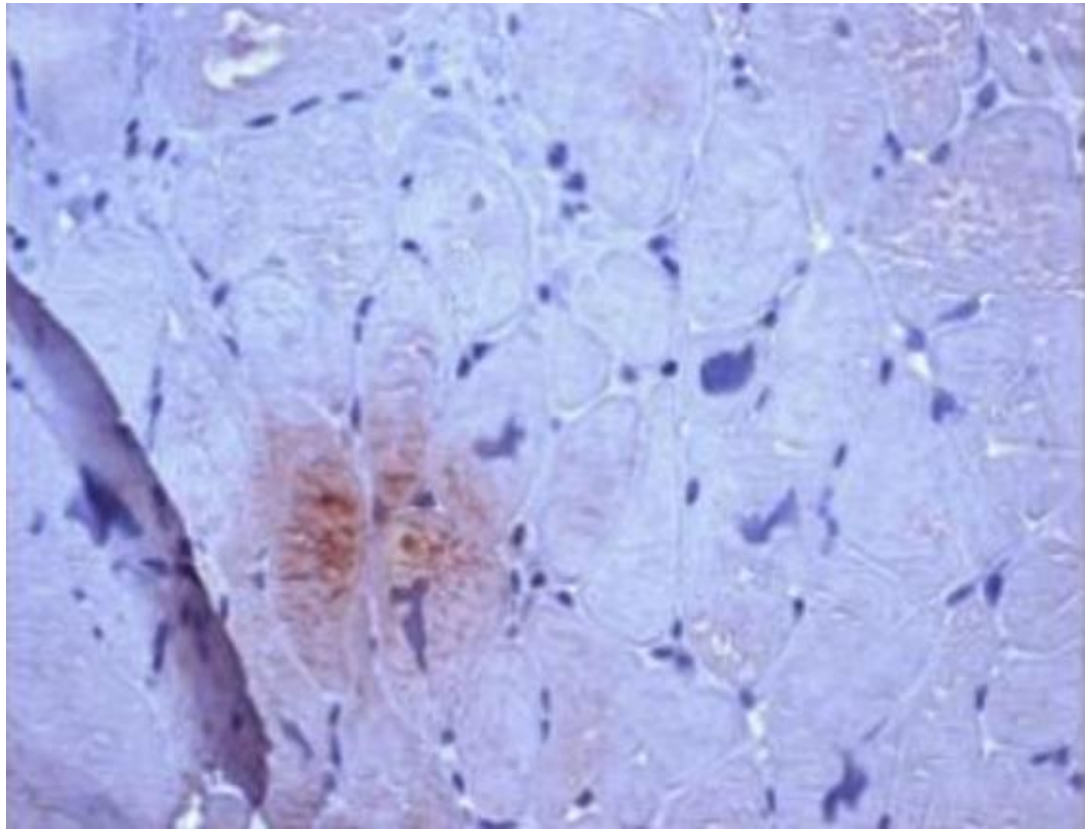
MDPI

Article

Intramyocardial Inflammation after COVID-19 Vaccination: An Endomyocardial Biopsy-Proven Case Series

Christian Baumeier [1,*], Ganna Aleshcheva [1], Dominik Harms [1], Ulrich Gross [1], Christian Hamm [2,3], Birgit Assmus [3], Ralf Westenfeld [4], Malte Kelm [4], Spyros Rammos [5], Philip Wenzel [6], Thomas Münzel [6], Albrecht Elsässer [7], Mudather Gailani [8], Christian Perings [9], Alae Bourakkadi [10], Markus Flesch [11], Tibor Kempf [12], Johann Bauersachs [12], Felicitas Escher [1,13,14] and Heinz-Peter Schultheiss [1]

Nota: **Baumeier** et al. hanno utilizzato solo Ab anti-spike. Tuttavia, a sostegno del fatto che la proteina spike era derivata dal vaccino, riportano: “Tutti le biopsie endomiocardiche sono state testate negativamente per SARS-CoV-2 utilizzando sequenze specifiche del gene E”.



Colorazione immunoistochimica che rileva la proteina spike SARS-CoV-2 nella biopsia endomiocardica del paziente 5 con diagnosi di cardiomiopatia infiammatoria, dopo aver ricevuto Comirnaty® [immagine tratta e modificata da: **Baumeier** et al., Int J Mol Sci, 2022].

Referti istopatologici da autopsie

Clinical Research in Cardiology
https://doi.org/10.1007/s00392-022-02129-5

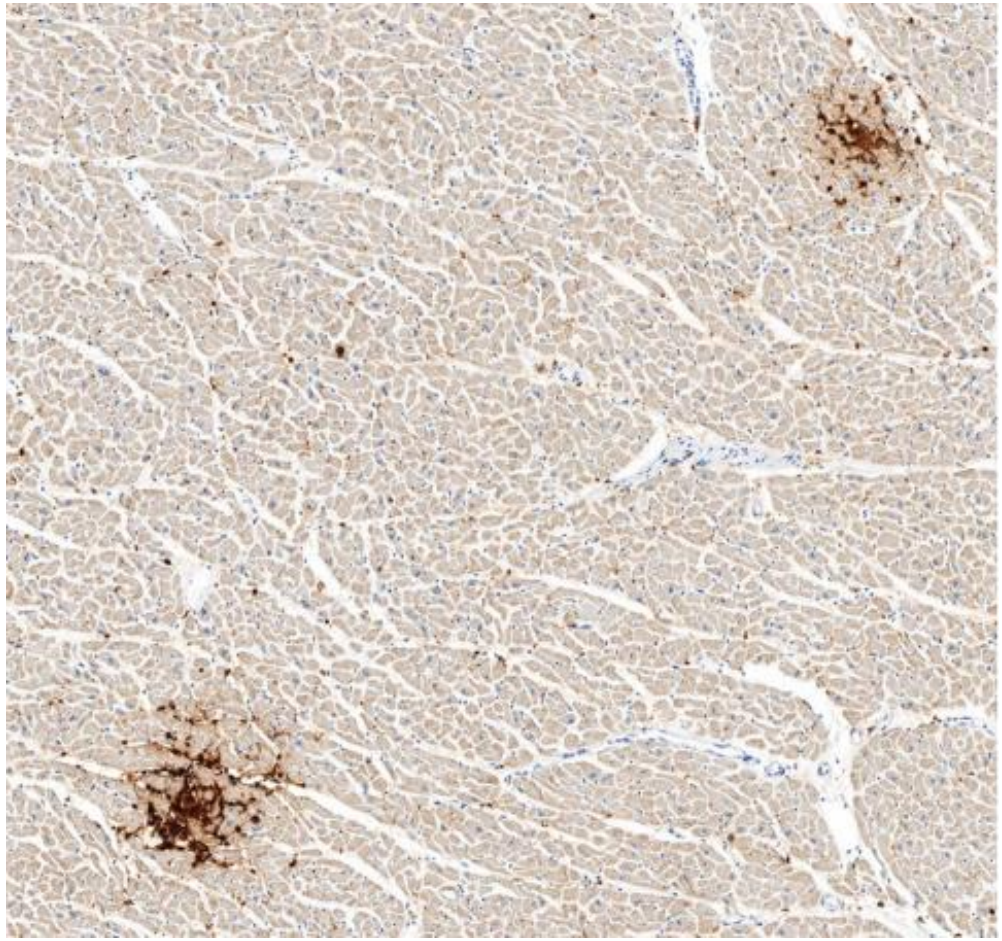
ORIGINAL PAPER

Check for updates

Autopsy-based histopathological characterization of myocarditis after anti-SARS-CoV-2-vaccination

Constantin Schwab[1] · Lisa Maria Domke[1,2] · Laura Hartmann[1,2] · Albrecht Stenzinger[1] · Thomas Longerich[1] · Peter Schirmacher[1]

Received: 22 July 2022 / Accepted: 17 November 2022



Nota: **Schwab** et al., non hanno utilizzato un Ab anti-spike. Tuttavia, un nesso causale tra miocardite e vaccinazione è supportato da: (**a**) una stretta relazione temporale (tutti i pazienti sono deceduti entro una settimana dalla vaccinazione); (**b**) assenza di qualsiasi altra significativa malattia cardiaca preesistente; (**c**) test negativi per potenziali agenti infettivi che causano miocardite; (**d**) presenza di un peculiare infiltrato di cellule T $CD4^+$, suggerendo un meccanismo autoinfiammatorio immunomediato.

Aggregati linfocitari ($CD4^+$) nel setto interventricolare con associata distruzione dei cardiomiociti [immagine tratta e modificata da: **Schwab** et al., Clin Res Cardiol, 2022].

Referti istopatologici da autopsie

Contents lists available at ScienceDirect

Legal Medicine

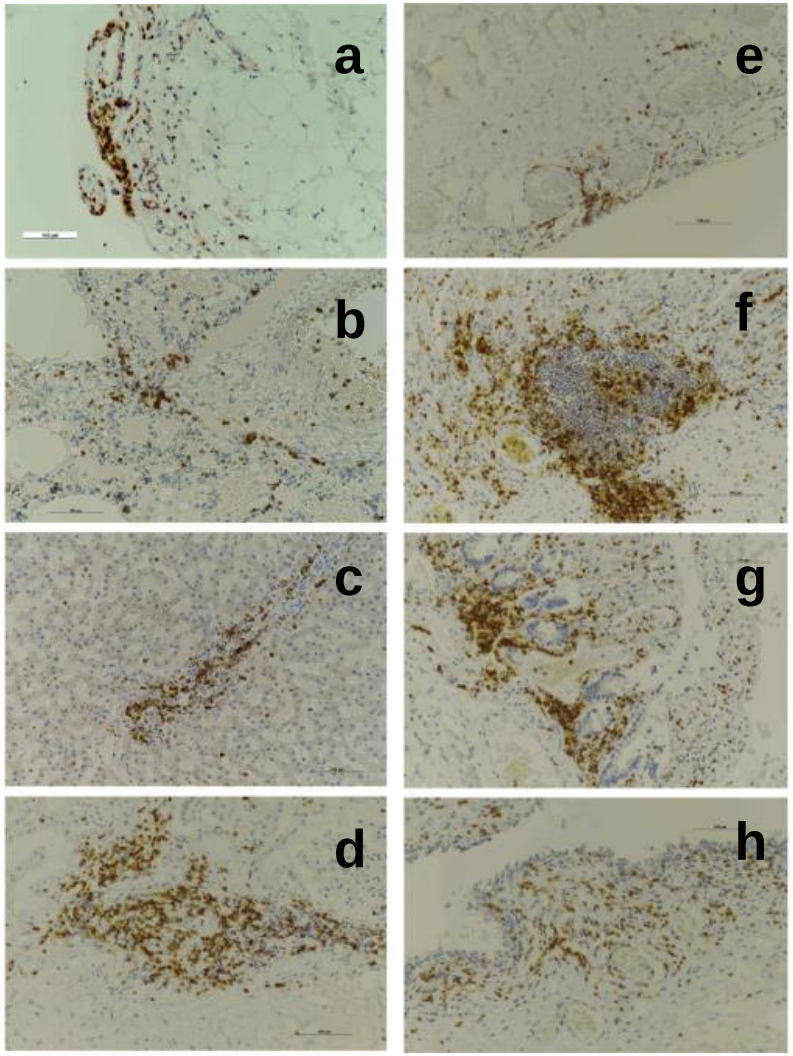
journal homepage: www.elsevier.com/locate/legalmed

Case Report

A case of fatal multi-organ inflammation following COVID-19 vaccination

Hideyuki Nushida [a,*], Asuka Ito [a], Hiromitsu Kurata [a,b], Hitomi Umemoto [a,c], Itsuo Tokunaga [a], Hirofumi Iseki [a,b], Akiyoshi Nishimura [a]

[a] Department of Forensic Medicine, Institute of Biomedical Sciences, Tokushima University Graduate School, Tokushima, Japan
[b] Department of Physical Medicine, Nakazu-Yagi Hospital, Tokushima, Japan
[c] Division of Anatomical Education Support, Tokushima University Graduate School, Tokushima, Japan



Nota: **Nushida** et al., non hanno utilizzato un Ab anti-spike. Una Tuttavia la bambina giapponese di 14 anni è morta due giorni dopo aver ricevuto la terza dose del vaccino Pfizer/BioNTech e. Non vi era alcuna precedente esposizione a infezioni, allergie o tossicità da farmaci, al paziente è stata diagnosticata un'infiammazione multiorgano post-vaccinazione.

Referti istopatologici del (**a**) cuore, (**b**) polmone, (**c**) fegato, (**d**) rene, (**e**) diaframma, (**f**) stomaco, (**g**) duodeno e (**h**) vescica, che mostrano infiltrazione linfocitaria [imagine tratta e modificata da: **Nushida** et al., Legal Medicine, 2023].

Reazioni infiammatorie autoimmuni indotte dai vaccini genetici

AUTOIMMUNITY
2023, VOL. 56, NO. 1, 2259123
https://doi.org/10.1080/08916934.2023.2259123

Taylor & Francis
Taylor & Francis Group

REVIEW ARTICLE

OPEN ACCESS Check for updates

Autoimmune inflammatory reactions triggered by the COVID-19 genetic vaccines in terminally differentiated tissues

Panagis Polykretis[a,b], Alberto Donzelli[a,b], Janci C. Lindsay[c], David Wiseman[d], Anthony M. Kyriakopoulos[e], Michael Mörz[f], Paolo Bellavite[g], Masanori Fukushima[h], Stephanie Seneff[i] and Peter A. McCullough[j]

[a]"Allineare Sanità e Salute" Foundation, Milano, Italy; [b]Independent Medical Scientific Commission (CMSi), Milano, Italy; [c]Toxicology & Molecular Biology, Toxicology Support Services, LLC, Sealy, TX, USA; [d]Synechion, Inc, Dallas, TX, USA; [e]Infectious Disease, Nasco AD Biotechnology Laboratory, Piraeus, Greece; [f]Independent researcher, Dresden, Germany; [g]Independent medical researcher, Verona, Italy; [h]Foundation of Learning Health Society Institute, Nagoya, Japan; [i]Computer Science and Artificial Intelligence Laboratory, MIT, Cambridge, MA, USA; [j]Cardiology, Truth for Health Foundation, Tucson, AZ, USA

age groups, has been widely recognised [23,80–83]. In a growing number of studies, it has been determined upon autopsy that vaccine-induced conditions were the cause of death [39,41,84,85]. In general, the potential risks of a genetic vaccine that induces human cells to become targets for autoimmune attack cannot be fully assessed, without knowing the exact distribution and kinetics of LNPs and mRNA, as well as the production of spike protein. Since the human body is not a strictly compartmentalised system, this is a matter of serious concern for every genetic vaccine (current or to be developed in the future) which induces human cells to synthesise non-self antigens. In fact, for some tissues, such as those terminally differentiated, the loss of cells results in irreversible damage with a potentially fatal prognosis. In conclusion, in light of the undeniable evidence of off-target distribution, the administration of genetic vaccines against COVID-19 should be halted until accurate pharmacokinetic, pharmacodynamic and genotoxicity studies are performed, or they should only be delivered in circumstances when the benefits greatly outweigh the risks.

Tratto da: **Polykretis** et al., *Autoimmunity*, 2023.

Niente autopsie, un'occasione mancata e il lockdown della scienza

Journal of *Clinical Medicine*

MDPI

Review

No Autopsies on COVID-19 Deaths: A Missed Opportunity and the Lockdown of Science

Monica Salerno [1,†], Francesco Sessa [2,†], Amalia Piscopo [3], Angelo Montana [1], Marco Torrisi [1], Federico Patanè [1], Paolo Murabito [4], Giovanni Li Volti [5,*] and Cristoforo Pomara [1,*]

and septic shock. Only 7 papers reported histological investigations. Nevertheless, only two complete autopsies are described and the cause of death was listed as COVID-19 in only one of them. The lack of postmortem investigation did not allow a definition of the exact cause of death to determine the pathways of this infection. Based on the few histopathological findings reported in the analyzed studies, it seems to be a clear alteration of the coagulation system: frequently prothrombotic activity with consequent thromboembolism was described in COVID-19 patients. As a scientific community, we are called on to face this global threat, and to defeat it with all the available tools necessary. Despite the improvement and reinforcement of any method of study in every field of medicine and science,

We firmly believe that the answer to Edward's question in the 1970s is "yes, we still need the autopsy in 2020!" and we need it more nowadays, to answer a plethora of questions related to COVID-19 deaths.

As a scientific community, we are called on to face this global threat, and to defeat it with all available tools necessary, the new and the old ones, as the new and the old represent a proper union for continued progress in medicine.

This lesson, inherited from pioneers of medicine, should never be forgotten.

The time is now to shout out against this terrible lockdown of science: autopsy, autopsy, autopsy!

Tratto da: **Salerno** et al., *J Clin Med*, 2020.

Incidenza di miocardite e pericardite nei pazienti non vaccinati

Journal of *Clinical Medicine*

MDPI

Article

The Incidence of Myocarditis and Pericarditis in Post COVID-19 Unvaccinated Patients—A Large Population-Based Study

Ortal Tuvali [1,†], Sagi Tshori [2,†], Estela Derazne [3], Rebecca Regina Hannuna [2], Arnon Afek [3,4], Dan Haberman [1], Gal Sella [1] and Jacob George [1,*]

Abstract: Myocarditis and pericarditis are potential post-acute cardiac sequelae of COVID-19 infection, arising from adaptive immune responses. We aimed to study the incidence of post-acute COVID-19 myocarditis and pericarditis. Retrospective cohort study of 196,992 adults after COVID-19 infection in Clalit Health Services members in Israel between March 2020 and January 2021. Inpatient myocarditis and pericarditis diagnoses were retrieved from day 10 after positive PCR. Follow-up was censored on 28 February 2021, with minimum observation of 18 days. The control cohort of 590,976 adults with at least one negative PCR and no positive PCR were age- and sex-matched. Since the Israeli vaccination program was initiated on 20 December 2020, the time-period matching of the control cohort was calculated backward from 15 December 2020. Nine post-COVID-19 patients developed myocarditis (0.0046%), and eleven patients were diagnosed with pericarditis (0.0056%). In the control cohort, 27 patients had myocarditis (0.0046%) and 52 had pericarditis (0.0088%). Age (adjusted hazard ratio [aHR] 0.96, 95% confidence interval [CI]; 0.93 to 1.00) and male sex (aHR 4.42; 95% CI, 1.64 to 11.96) were associated with myocarditis. Male sex (aHR 1.93; 95% CI 1.09 to 3.41) and peripheral vascular disease (aHR 4.20; 95% CI 1.50 to 11.72) were associated with pericarditis. Post COVID-19 infection was not associated with either myocarditis (aHR 1.08; 95% CI 0.45 to 2.56) or pericarditis (aHR 0.53; 95% CI 0.25 to 1.13). We did not observe an increased incidence of neither pericarditis nor myocarditis in adult patients recovering from COVID-19 infection.

Tratto da: **Tuvali** et al., *J Clin Med*, 2022.

Incidenza dei danni al miocardio dopo la vaccinazione

Tropical Medicine and Infectious Disease

MDPI

Article

Cardiovascular Manifestation of the BNT162b2 mRNA COVID-19 Vaccine in Adolescents

Suyanee Mansanguan [1], Prakaykaew Charunwatthana [2], Watcharapong Piyaphanee [2], Wilanee Dechkhajorn [3], Akkapon Poolcharoen [4] and Chayasin Mansanguan [2,*]

Abstract: This study focuses on cardiovascular manifestation, particularly myocarditis and pericarditis events, after BNT162b2 mRNA COVID-19 vaccine injection in Thai adolescents. This prospective cohort study enrolled students aged 13–18 years from two schools, who received the second dose of the BNT162b2 mRNA COVID-19 vaccine. Data including demographics, symptoms, vital signs, ECG, echocardiography, and cardiac enzymes were collected at baseline, Day 3, Day 7, and Day 14 (optional) using case record forms. We enrolled 314 participants; of these, 13 participants were lost to follow-up, leaving 301 participants for analysis. The most common cardiovascular signs and symptoms were tachycardia (7.64%), shortness of breath (6.64%), palpitation (4.32%), chest pain (4.32%), and hypertension (3.99%). One participant could have more than one sign and/or symptom. Seven participants (2.33%) exhibited at least one elevated cardiac biomarker or positive lab assessments. Cardiovascular manifestations were found in 29.24% of patients, ranging from tachycardia or palpitation to myopericarditis. Myopericarditis was confirmed in one patient after vaccination. Two patients had suspected pericarditis and four patients had suspected subclinical myocarditis. In conclusion, Cardiovascular manifestation in adolescents after BNT162b2 mRNA COVID-19 vaccination included tachycardia, palpitation, and myopericarditis. The clinical presentation of myopericarditis after vaccination was usually mild and temporary, with all cases fully recovering within 14 days. Hence, adolescents receiving mRNA vaccines should be monitored for cardiovascular side effects. Clinical Trial Registration: NCT05288231.

Tratto da: **Mansanguan** et al., *Trop Med Infect Dis*, 2022.

Incidenza dei danni al miocardio dopo la vaccinazione

ESC European Society of Cardiology

European Journal of Heart Failure (2023)
doi:10.1002/ejhf.2978

RESEARCH ARTICLE

Sex-specific differences in myocardial injury incidence after COVID-19 mRNA-1273 booster vaccination

Natacha Buergin[1], Pedro Lopez-Ayala[1], Julia R. Hirsiger[2], Philip Mueller[1], Daniela Median[1], Noemi Glarner[1], Klara Rumora[1], Timon Herrmann[1], Luca Koechlin[1], Philip Haaf[1], Katharina Rentsch[3], Manuel Battegay[4], Florian Banderet[5,6], Christoph T. Berger[2,7], and Christian Mueller[1]*

[1]Department of Cardiology and Cardiovascular Research Institute Basel (CRIB), University Hospital Basel, University of Basel, Basel, Switzerland; [2]Department of Biomedicine, Translational Immunology, University of Basel, Basel, Switzerland; [3]Department of Laboratory Medicine, University Hospital Basel, University of Basel, Basel, Switzerland; [4]Department of Infectious Diseases and Hospital Epidemiology, University Hospital Basel, University of Basel, Basel, Switzerland; [5]Department of Internal Medicine, Medical Outpatient Unit, University Hospital Basel, Basel, Switzerland; [6]Health Service, University Hospital Basel, Basel, Switzerland; and [7]University Center for Immunology, University Hospital Basel, Basel, Switzerland

Received 13 March 2023; revised 4 July 2023; accepted 5 July 2023

Aims To explore the incidence and potential mechanisms of oligosymptomatic myocardial injury following COVID-19 mRNA booster vaccination.

Methods and results Hospital employees scheduled to undergo mRNA-1273 booster vaccination were assessed for mRNA-1273 vaccination-associated myocardial injury, defined as acute dynamic increase in high-sensitivity cardiac troponin T (hs-cTnT) concentration above the sex-specific upper limit of normal on day 3 (48–96 h) after vaccination without evidence of an alternative cause. To explore possible mechanisms, antibodies against interleukin-1 receptor antagonist (IL-1RA), the SARS-CoV-2-nucleoprotein (NP) and -spike (S1) proteins and an array of 14 inflammatory cytokines were quantified. Among 777 participants (median age 37 years, 69.5% women), 40 participants (5.1%; 95% confidence interval [CI] 3.7–7.0%) had elevated hs-cTnT concentration on day 3 and mRNA-1273 vaccine-associated myocardial injury was adjudicated in 22 participants (2.8% [95% CI 1.7–4.3%]). Twenty cases occurred in women (3.7% [95% CI 2.3–5.7%]), two in men (0.8% [95% CI 0.1–3.0%]). Hs-cTnT elevations were mild and only temporary. No patient had electrocardiographic changes, and none developed major adverse cardiac events within 30 days (0% [95% CI 0–0.4%]). In the overall booster cohort, hs-cTnT concentrations (day 3; median 5, interquartile range [IQR] 4–6 ng/L) were significantly higher compared to matched controls ($n = 777$, median 3 [IQR 3–5] ng/L, $p < 0.001$). Cases had comparable systemic reactogenicity, concentrations of anti-IL-1RA, anti-NP, anti-S1, and markers quantifying systemic inflammation, but lower concentrations of interferon (IFN)-λ1 (IL-29) and granulocyte-macrophage colony-stimulating factor (GM-CSF) versus persons without vaccine-associated myocardial injury.

Conclusion mRNA-1273 vaccine-associated myocardial injury was more common than previously thought, being mild and transient, and more frequent in women versus men. The possible protective role of IFN-λ1 (IL-29) and GM-CSF warrant further studies.

Tratto da: **Buergin** et al., *Eur. J Heart Fail,* 2023.

Conclusioni

I dati clinici indicano che in caso di grave infezione naturale, l'iperattività immunitaria può provocare una tempesta di citochine che può innescare reazioni autoinfiammatorie, molto probabilmente dovute a cloni di cellule B naturali preesistenti o al mimetismo molecolare.

Per quanto riguarda i vaccini genetici contro il COVID-19:
- Qualsiasi cellula umana che produce antigeni estranei è destinata ad essere eliminata dal sistema immunitario.

- Il corpo umano non è un sistema strettamente compartimentalizzato e gli LNP contenenti l'mRNA del vaccino hanno dimostrato di essere in grado di diffondersi a livello sistemico.

- I risultati istopatologici, provenienti da biopsie e autopsie, confermano che la proteina spike derivata dal vaccino può essere sintetizzata in tessuti terminali differenziati ed essenziali per la vita, causando gravi reazioni infiammatorie autoimmuni.

- Gli studi prospettici di sorveglianza attiva hanno mostrato un'incidenza spaventosa di danni cardiaci correlati alla vaccinazione (uno su 35 vaccinati, nello studio di **Buergin** et al., Eur. J Heart Fail, 2023).

- Sono necessari studi accurati di farmacocinetica, farmacodinamica e genotossicità, nonché valutazioni razionali del rapporto rischio-beneficio per fascia di età, al fine di prevenire la perdita di ulteriori vite umane.

- Bansal S, Perincheri S, Fleming T, Poulson C, Tiffany B, Bremner RM, Mohanakumar T. 2021. Cutting Edge: Circulating Exosomes with COVID Spike Protein Are Induced by BNT162b2 (Pfizer-BioNTech) Vaccination prior to Development of Antibodies: A Novel Mechanism for Immune Activation by mRNA Vaccines. Journal of Immunology (Baltimore, Md.: 1950) 207:2405–2410. DOI: 10.4049/jimmunol.2100637.- Baumeier C, Aleshcheva G, Harms D, Gross U, Hamm C, Assmus B, Westenfeld R, Kelm M, Rammos S, Wenzel P, Münzel T, Elsässer A, Gailani M, Perings C, Bourakkadi A, Flesch M, Kempf T, Bauersachs J, Escher F, Schultheiss H-P. 2022. Intramyocardial Inflammation after COVID-19 Vaccination: An Endomyocardial Biopsy-Proven Case Series. International Journal of Molecular Sciences 23:6940. DOI: 10.3390/ijms23136940.
- Bonometti R, Sacchi MC, Stobbione P, Lauritano EC, Tamiazzo S, Marchegiani A, Novara E, Molinaro E, Benedetti I, Massone L, Bellora A, Boverio R. 2020. The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. European Review for Medical and Pharmacological Sciences 24:9695–9697. DOI: 10.26355/eurrev_202009_23060.
- Buergin N, Lopez-Ayala P, Hirsiger JR, Mueller P, Median D, Glarner N, Rumora K, Herrmann T, Koechlin L, Haaf P, Rentsch K, Battegay M, Banderet F, Berger CT, Mueller C. 2023. Sex-specific differences in myocardial injury incidence after COVID-19 mRNA-1273 booster vaccination. European Journal of Heart Failure. DOI: 10.1002/ejhf.2978.
- EMA, 2020a. Assessment report Comirnaty Common name: COVID-19 mRNA vaccine (nucleosidemodified) [WWW Document]. accessed 3.14.21. https://www.ema.eu ropa.eu/en/documents/assessment-report/comirnaty-epar-public-assessment-repo rt_en.pdf. 2021.
- Fertig TE, Chitoiu L, Marta DS, Ionescu V-S, Cismasiu VB, Radu E, Angheluta G, Dobre M, Serbanescu A, Hinescu ME, Gherghiceanu M. 2022. Vaccine mRNA Can Be Detected in Blood at 15 Days Post-Vaccination. Biomedicines 10:1538. DOI: 10.3390/biomedicines10071538.
- Hanna N, Mejia CMD, Heffes-Doon A, Lin X, Botros B, Gurzenda E, Clauss-Pascarelli C, Nayak A. 2023. Biodistribution of mRNA COVID-19 vaccines in human breast milk. eBioMedicine 96. DOI: 10.1016/j.ebiom.2023.104800.
- https://phmpt.org/wp-content/uploads/2022/03/125742_S1_M4_4223_185350.pdf.
- Hussein HM, Rahal EA. 2019. The role of viral infections in the development of autoimmune diseases. Critical Reviews in Microbiology 45:394–412. DOI: 10.1080/1040841X.2019.1614904.
- Mansanguan S, Charunwatthana P, Piyaphanee W, Dechkhajorn W, Poolcharoen A, Mansanguan C. 2022. Cardiovascular Manifestation of the BNT162b2 mRNA COVID-19 Vaccine in Adolescents. Tropical Medicine and Infectious Disease 7:196. DOI: 10.3390/tropicalmed7080196.
- Krauson AJ, Casimero FVC, Siddiquee Z, Stone JR. 2023. Duration of SARS-CoV-2 mRNA vaccine persistence and factors associated with cardiac involvement in recently vaccinated patients. *npj Vaccines* 8:1–8. DOI: 10.1038/s41541-023-00742-7.
- Mörz M. 2022. A Case Report: Multifocal Necrotizing Encephalitis and Myocarditis after BNT162b2 mRNA Vaccination against COVID-19. Vaccines 10:1651. DOI: 10.3390/vaccines10101651.
- Nushida H, Ito A, Kurata H, Umemoto H, Tokunaga I, Iseki H, Nishimura A. 2023. A case of fatal multi-organ inflammation following COVID-19 vaccination. Legal Medicine 63:102244. DOI: 10.1016/j.legalmed.2023.102244.
- Polykretis P. 2022. Role of the antigen presentation process in the immunization mechanism of the genetic vaccines against COVID-19 and the need for biodistribution evaluations. Scandinavian Journal of Immunology 96:e13160. DOI: 10.1111/sji.13160.
- Polykretis P, Donzelli A, Lindsay JC, Wiseman D, Kyriakopoulos AM, Mörz M, Bellavite P, Fukushima M, Seneff S, McCullough PA. 2023. Autoimmune inflammatory reactions triggered by the COVID-19 genetic vaccines in terminally differentiated tissues. Autoimmunity 56:2259123. DOI: 10.1080/08916934.2023.2259123.
- Reutlinger Autopsie-/Histologie-Studie: Nebenwirkungen und Todesfälle durch die Corona Impfungen. 2022. Available at https://corona-blog.net/2022/03/10/reutlinger-autopsie-histologie-studie-nebenwirkungen-und-todesfaelle-durch-die-corona-impfungen/ (accessed September 12, 2023).
- Sacchi MC, Tamiazzo S, Stobbione P, Agatea L, De Gaspari P, Stecca A, Lauritano EC, Roveta A, Tozzoli R, Guaschino R, Bonometti R. 2021. SARS-CoV-2 infection as a trigger of autoimmune response. Clinical and Translational Science 14:898–907. DOI: 10.1111/cts.12953.
- Röltgen K, Nielsen SCA, Silva O, Younes SF, Zaslavsky M, Costales C, Yang F, Wirz OF, Solis D, Hoh RA, Wang A, Arunachalam PS, Colburg D, Zhao S, Haraguchi E, Lee AS, Shah MM, Manohar M, Chang I, Gao F, Mallajosyula V, Li C, Liu J, Shoura MJ, Sindher SB, Parsons E, Dashdorj NJ, Dashdorj ND, Monroe R, Serrano GE, Beach TG, Chinthrajah RS, Charville GW, Wilbur JL, Wohlstadter JN, Davis MM, Pulendran B, Troxell ML, Sigal GB, Natkunam Y, Pinsky BA, Nadeau - KC, Boyd SD. 2022. Immune imprinting, breadth of variant recognition, and germinal center response in human SARS-CoV-2 infection and vaccination. *Cell* 185:1025-1040.e14. DOI: 10.1016/j.cell.2022.01.018.
- Salerno M, Sessa F, Piscopo A, et al. No autopsies on COVID-19 deaths: a missed opportunity and the lockdown of science. J Clin Med. 2020;9(5):1472.
- Schwab C, Domke LM, Hartmann L, Stenzinger A, Longerich T, Schirmacher P. 2022. Autopsy-based histopathological characterization of myocarditis after anti-SARS-CoV-2-vaccination. Clinical Research in Cardiology. DOI: 10.1007/s00392-022-02129-5.
- Tuvali O, Tshori S, Derazne E, Hannuna RR, Afek A, Haberman D, Sella G, George J. 2022. The Incidence of Myocarditis and Pericarditis in Post COVID-19 Unvaccinated Patients-A Large Population-Based Study. *Journal of Clinical Medicine* 11:2219. DOI: 10.3390/jcm11082219.
- Vlachoyiannopoulos PG, Magira E, Alexopoulos H, Jahaj E, Theophilopoulou K, Kotanidou A, Tzioufas AG. 2020. Autoantibodies related to systemic autoimmune rheumatic diseases in severely ill patients with COVID-19. Annals of the Rheumatic Diseases 79:1661–1663. DOI: 10.1136/annrheumdis-2020-218009.
- Yamamoto M, Kase M, Sano H, et al. Persistent varicella zoster virus infection following mRNA COVID-19 vaccination was associated with the presence of encoded spike protein in the lesion. J Cutaneous Imm Allergy. 2023;6(1):18–23.
- Zhou Y, Han T, Chen J, Hou C, Hua L, He S, Guo Y, Zhang S, Wang Y, Yuan J, Zhao C, Zhang J, Jia Q, Zuo X, Li J, Wang L, Cao Q, Jia E. 2020. Clinical and Autoimmune Characteristics of Severe and Critical Cases of COVID-19.

Ringraziamenti

Coautori:

Dr. Peter A. McCullough
Dr. Alberto Donzelli
Dr. Janci C. Lindsay
Dr. David Wiseman
Dr. Anthony M. Kyriakopoulos
Dr. Michael Mörz
Prof. Paolo Bellavite
Prof. Masanori Fukushima
Prof. Sephanie Seneff

Allineare Sanità & Salute
Fondazione

COMMISSIONE MEDICO
SCIENTIFICA INDIPENDENTE

Grazie per l'attenzione