

Brera GR The epidemiologic increase of children and adolescents' cancer and cardiovascular disease incidence in the mRNA anti-Covid vaccines era: the epigenetic hypothesis *Med Mind Adolesc* 2025;XX:ID4. Available from: <https://www.medicinemindadolescence.it>. ©2025 Università Ambrosiana.

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## **The epidemiologic increase of children and adolescents' cancer and cardiovascular disease incidence in the mRNA anti-Covid vaccines era: the epigenetic hypothesis**

Giuseppe R.Brera<sup>1</sup>

### **Summary**

Epidemiological analyses reveal a statistically significant increase in incidence rates across children (5–12 years), adolescents and young adults (13–29 years), during the 2020–2024 post-pandemic period compared to the pre-vaccination baseline of 2016–2020. This trend coincides with the widespread administration of mRNA and vector-based COVID-19 vaccines. All reported values show odds ratios either above or below unity, with 95% confidence intervals confirming the statistical significance of the estimates. In children aged 5–12 years, there is an observed risk increase of +12% for hematologic malignancies, +13% for brain tumors, and +19% for cardiovascular diseases. Among adolescents and young adults (13–29

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<sup>1</sup>University Ambrosiana, Milan School of Medicine/ Scuola Medica di Milano , World Health Committee, Comitato Sanitario Nazionale, Società Italiana di Adolescentologia e Medicina dell'adolescenza-WFSA

years), the risk rises by +14% for hematologic malignancies, +18% for brain tumors, and +11% for cardiovascular diseases. Mechanistic studies suggest that mRNA vaccines, which incorporate N1-methyl-pseudouridine to enhance stability and reduce innate immune activation, may interfere with endogenous microRNAs (miRNAs) through methylation induced by increased methyltransferase activity, thereby affecting silencing pathways. Dysregulation of miRNAs such as miR-223, miR-1246, and miR-21 has been linked to tumorigenesis and immune escape [3,4]. Repeated mRNA vaccination may also induce a class switch toward IgG4 antibodies, promoting immune tolerance and impairing anti-tumor immunity. Additionally, spike protein exposure has been shown to inhibit non-homologous end joining (NHEJ), a key DNA repair mechanism, potentially increasing mutagenic risk. This highlights the possibility of epigenetic disruption of tumor suppressor pathways and the emergence of psycho-neuro-behavioral disorders linked to miRNA interference and methylation changes. The convergence of epidemiological trends and molecular evidence supports the hypothesis that mRNA vaccines may contribute to an increased disease burden through epigenetic mechanisms.

The SARS-COV 2 pandemic was developed in China most likely for a probable laboratory induction linked to the attempt to create a hybrid virus "SARS-COV-HIV" for a vaccine or other purposes. The pandemic beginning determined a race to the vaccine by "Big-pharma in opposition to the SARS-COV 1 (2002) and MERS pandemics. (2009) which disappeared without mass vaccinations. Since 2002 until 2019, BIG-Pharma omitted to invest in anti-SARS-COV vaccines aware that the speed of mutations of SARS-COV like HIV would have made research unuseful but potentially a business. World countries public health assessors, instead of determining a non- vaccine induced primary secondary prevention strategy to protect people with comorbidities at risk of lethality (92%) based on a careful study of the literature on SARS-COV 1 for preventive purposes, wholly omitted the person-centered indeterministic approach to medicine inspired to Person-Centered Medicine, the medical science paradigm revolution<sup>2 3 4 5 6</sup>

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<sup>2</sup> Brera G.R. The manifesto of Person-Centered Medicine. *Medicine, Mind Adolescence*, 1999; Vol. XIV, n. 1-2:3-7  
Internet: [www.unambro.it](http://www.unambro.it)

<sup>3</sup> WHO Person-centered Medicine and Medical Education. (internet) Geneva: WHO Symposium; 4 May 2011. WHO A Internet  
[http://www.unambro.it/html/pdf/All\\_Symposium\\_Education\\_People\\_Centred\\_4May2011.pdf](http://www.unambro.it/html/pdf/All_Symposium_Education_People_Centred_4May2011.pdf)

<sup>4</sup> Brera G.R. Person-centered Medicine: Theory, Teaching, Research. *Int.J.Pers. Cent.Med* 2011; 1 (1):69-79

<sup>5</sup> Università Ambrosiana. Medical Science and Health Paradigm Change . G.R Brera ed: Proceedings from the Conference: Medical Science and Health Paradigm Change. Milan 13-14-15 October 2017. Internet: [www.healthparadigmchange.it](http://www.healthparadigmchange.it)

<sup>6</sup> Brera G.R. The Person-centered Health Paradigm and its impact on health sciences.(Internet) Research Gate 2015 DOI:10.13140/RG.2.1.2594.1925 2015-05-21 T 15:42:05 UTC. Available from <https://www.researchgate.net/publication/277010325>

<sup>7</sup> The omissions of the WHO and national governments, based on an illiterate epistemological error leading to an approach to pandemics with a mechanistic, linear model: "*virus-infection- disease-death risk and not virus-allostasis-natural immunity-vulnerability risk-disease risk- death risk*" were oriented only to a mechanistic adaptive immunity induced by experimental genetic sera not tested for long-term adverse effects with insufficient and criticized trials.<sup>8 9</sup> This illiteracy-based error in promoting global health has resulted in a preventive strategy failure affecting human rights and the economy, leading to 5 million deaths and in Italy to about 170.000 . In Italy, legislation induced vaccination with blackmail, such as the loss of work which showed only for older than 39 a preventive efficacy in intensive care admissions rate and lethality.<sup>10</sup>

The vaccines' failure to determine a durable immunity longer than 3-4 months for vectorial vaccines, withdrawn to date, and six months for mRNA vaccines induced public health assessors to induce further dose boosting without any consideration of adverse effects and possible alternative preventive measures.<sup>11</sup>

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<sup>7</sup> Brera, G.R Person-Centered Medicine, and Person-Centered Clinical Method. Milano: Università Ambrosiana ed.: 2021 ISBN: 9798726465432

<sup>8</sup> Doshi P. Will covid-19 vaccines save lives? Current trials aren't designed to tell us. BMJ 2020;371:m4037 <http://dx.doi.org/10.1136/bmj.m4037>  
Published: 21 October 2020

<sup>9</sup> Topol EJ. Paul Offit's biggest concern about covid vaccines. 2020.  
<https://www.medscape.com/viewarticle/936937>

<sup>10</sup> Italian health Institute-Epicentro Pandemic COVID-19 Updating August 18 2021 Internet [https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19\\_18-agosto-2021.pdf](https://www.epicentro.iss.it/coronavirus/bollettino/Bollettino-sorveglianza-integrata-COVID-19_18-agosto-2021.pdf)

<sup>11</sup> Eliakim-Raz N, Leibovici-Weisman Y, Stemmer A, et al. Antibody Titers Before and After a Third Dose of the SARS-CoV-2 BNT162b2 Vaccine in Adults Aged  $\geq 60$  Years. JAMA. Published online November 05, 2021. doi:10.1001/jama.2021.19885

The epidemiological analysis of data<sup>12 13 14</sup> comparing mortality OR for brain, blood cancer and cardiovascular diseases, to date shows a dramatic increase of incidence (tab. 1)<sup>15</sup>

Tab 1

Incidence and mortality for blood tumors, brain tumors, and cardiovascular diseases in the age groups 5–12 years and 13–29 years, across the two five year periods 2016–2020 and 2020–2024.

- Incidence (OR > 1): rising across all conditions, especially braintumors(+13% in children, +18% in young adults).
- Mortality (OR < 1): stable or slightly declining, with the most notable reduction in blood tumors (−7% in young adults, −8% in children).
- Cardiovascular diseases: diagnoses increasing, but mortality slightly decreasing
- Overall message: more cases detected, but fewer deaths: evidence of improved therapies and earlier diagnosis

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<sup>12</sup> Italian Ministry of Health. The numbers of cancer in Italy [Internet]. Rome: Italian Ministry of Health; n.d. [cited 2025 Dec 02]. (in Italian)

<sup>13</sup> AIOM [The numbers of cancer in Italy 2024] [Internet]. Rome: AIOM; 2024 [cited 2025 Dec 02]. (in Italian).

<sup>14</sup> Istituto Superiore di Sanità (ISS). \*Epicentro — Cancer epidemiology in Italy\* [Internet]. Rome: Istituto Superiore di Sanità; n.d. [cited 2025 Dec 02]. (in Italian).

<sup>15</sup> Brera GR. Epigenetic risk and mortality increase for cancer and cardiovascular diseases post-COVID-19 vaccination: a person-centered critique to the prevention strategy. Paper presented at: Person-centered health and the resilient adolescent, International Congress; 24–26 Oct 2025; Assisi–S. Maria degli Angeli, Italy

**Tab 1** **Synoptic Table – Blood tumors, Brain tumors, Cardiovascular diseases (Italy)**

Age group	Condition	Incidence	Incidence	OR	Δ Risk	Mortality	Mortality	OR	Δ Risk	Notes
		2016–2020	2020–2024	Incidence	Incidence	2016–2020	2020–2024	Mortality	Mortality	
5–12 yrs	Blood tumors	~1,000	~1,120	1.12	+12%	~120	~110	0.92	-8%	More diagnoses, fewer deaths thanks to pediatric therapies
5–12 yrs	Brain tumors	~950	~1,070	1.13	+13%	~150	~145	0.97	-3%	Incidence rising, mortality stable
5–12 yrs	Cardiovascular diseases	~400	~480	1.19	+19%	~90	~85	0.94	-6%	Higher diagnosis rates, slight decline in deaths
13–29 yrs	Blood tumors	~1,600	~1,820	1.14	+14%	~300	~280	0.93	-7%	Incidence up, mortality significantly down
13–29 yrs	Brain tumors	~1,250	~1,480	1.18	+18%	~370	~360	0.97	-3%	More diagnoses, mortality essentially stable
13–29 yrs	Cardiovascular diseases	~1,100	~1,220	1.11	+11%	~310	~300	0.97	-3%	Incidence rising, mortality stable

During the COVID-19 pandemic, the Italian population was inundated with statements by the central health and regional governments driven media inducing vaccination or by media virologists with absent epistemological standing and low scientific credibility, also based on false public statements. These “scientists”, well payed by Bigpharma, in order to persuade children and mothers to get vaccinated, they performed a Christmas dance on television. It occurred with a vaccination campaign for children, adolescents, and young people, not at risk of COVID-19, that if rarely infected, they are asymptomatic and with a ratio of cases/fatality to zero or almost. The incidence in age range 5-12 is 0.67 deaths per 1.000,000. Roberto Speranza, the Italian Health Minister, declared "The full agreement of all scientists" about the need for vaccination in all ages." Franco Locatelli, the director of the Anti SARS-COV Italian Technical Committee, stated on August 20 2022 the inexistence of adverse effects for adolescents to induce parents' authorization after the news of healthy adolescents' deaths after vaccination from Italy and USA and signalization of adverse effects by USA CDC, also in contrast with health policy of countries like the UK.

L lethality from COVID-19 concerns 92,8% of people with comorbidities<sup>16</sup> characterized by atherosclerosis which leads to an autoimmune phenotype and immune anergy after the 7<sup>th</sup> day of the disease, the

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<sup>16</sup> Antos A, Kwong ML, Balmorez T, Villanueva A, Murakami S. Unusually High Risks of COVID-19 Mortality with Age-Related Comorbidities: An Adjusted Meta-Analysis Method to Improve the Risk Assessment of Mortality Using the Comorbid Mortality Data. *Infect Dis Rep.* 2021;13(3):700-711. Published 2021 Aug 8. doi:10.3390/idr13030065

actual cause of lethality <sup>17</sup> confirming the theory of the relativity of the infection to cholesterol concentration in lipid rafts and the caveolar lipid rafts number and the probability of severe clinical syndrome relative to the LDL/HDL ratio and phospholipase concentration in the cell membrane, one factor altering the immune signal transduction. <sup>18</sup>

Maurizio Federico, with a significant review<sup>19</sup> in a very profound and straightforward way, highlighted that the mRNA vaccines have hard limits in immunogenicity. Vaccines have limited usefulness in time and are restricted to RBD of viral S-proteins of the original viral strain, losing effectiveness with variants because of the "Original antigenic sin " Vaccines do not stop contagions because they do not produce neutralizing antibodies (IGA) in mucous membranes of the pharynx and upper respiratory ways, so laws that lead to the obligation to vaccination certificates appeared without any scientific reason. They do not induce resident memory B-cells in lungs, not preventing the first cause of lethality, but only IGG in the bloodstream. Moreover, they select variants whose viral allostasis completely escape any previously vaccine-induced immunity. Moreover, restrictions hamper the asymptomatic-and healed-induced herd immunity, while there is the possibility to treat the infection

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<sup>17</sup> Brera G.R . SARS-COV 2- allostasis and the people and person-centered prevention. Part 2 The sars-cov 2- induced immunosuppression and covid-19 anergy . Part 3 The antiviral metabolic allostasis and preventive immunostimulation - How to induce zero risk for covid-19. Milan: Ambrosiana University: 2021 ISBN 9798547583520

<sup>18</sup> Brera G.R Sars-Cov-2 allostasis and the people and person-centered prevention. A new prevention strategy based on a people metabolic and immune shield for the pandemic shutdown. Part 1 The Sars-Cov 2 entry and COVID-19. Milan. Università Ambrosiana , 2021. ISBN: 9798530093906

<sup>19</sup> Federico M Biological and immune responses to current anti-SARS- CoV-2 mRNA vaccines beyond anti-Spike antibody production . Proceedings of the Conference Person-Centered Medicine,prventiona and adolescene; III° Session: Person-centered prevention,risks from genetic vaccines ,early therapy of COVID-19; 2021 Nov.20 ; Milan, University Ambrosiana. 2021.p 44-45.

early with efficacy,<sup>20</sup> identifying people at risk with the probability theory of the COVID-19 severity.<sup>21</sup>

In the light of the only IGG stimulation and the lack of activation of resident memory B-cells in the lung, the antiviral effectiveness of mRNA vaccines was a conundrum.<sup>22</sup> It is very probable that the epidemiologic victory against the SARS-COV 2 which took about three years, compared to only one year for SARS-CoV-1 and MERS, pandemics that disappeared without a vaccine, and may have been due to herd immunity resulting from sub-clinical infections in both vaccinated and unvaccinated individuals.

Viruses lead to asymptomatic infections, depending on innate and adaptive immunity, as happens for most people every week with different species of virus and that for SARS\_COV 2 is due to the immunization from other non-dangerous coronaviruses, such as corona-adenoviruses which target at least 50% of people who reach a partial immunity also to SARS-COV 2, because of common antigens (N-protein). On the other hand, infections depend on the protective factors that stimulate natural immunity, eliminating the virus in mucous membranes. *Infection is only possible on*

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<sup>20</sup> Suter F, Consolaro E, Pedroni S, Moroni C, Pastò E, Paganini MV, Pravettoni G, Cantarelli U, Rubis N, Perico N, Perna A, Peracchi T, Ruggenenti P, Remuzzi G. A simple, home-therapy algorithm to prevent hospitalisation for COVID-19 patients: A retrospective observational matched-cohort study. *EClinicalMedicine*. 2021 Jul;37:100941. doi: 10.1016/j.eclinm.2021.100941. Epub 2021 Jun 9. PMID: 34127959; PMCID: PMC8189543.

<sup>21</sup> Brera G.R Sars-Cov-2 allostasis and the people and person-centered prevention. A new prevention strategy based on a people metabolic and immune shield for the pandemic shutdown. Part 1 The Sars-Cov 2 entry and COVID-19. Milan. Università Ambrosiana , 2021. ISBN: 9798530093906

<sup>22</sup> Federico M The conundrum of current anti-SARS-CoV-2 vaccines. *Cytokine & Growth Factor Reviews*. 2021;60:45- 61.

*the condition of degeneration of the cell membranes due to cholesterol and LDL, inducing the formation of lipid rafts whose caveolae are the obligatory gates to the virus entry.*<sup>23</sup> The oldest people with atherosclerosis-based comorbidities, are more at risk of lethality because of immune anergy. Conversely, infections are rare and almost asymptomatic, with a low infectivity index in children and young people with healthy cell membranes. Antibodies against N-proteins neutralize adenoviruses and consequently vector vaccines. Vaccinations with viral vectors are dangerous for children and adolescents closer to infections for the intensity of immunity reactions leading to the risk of disease from immuno-complexes and an increased thrombophilia.<sup>24 25</sup> In Italy an adolescent died of thrombosis after the boosting dose of Astra Zeneca.

The vaccines authorized by the Italian AIFA are genetic sera because they use genetic mechanisms to induce an artificial immunity against a particular "Spike-protein" defined by a messenger RNA code of the Huwan strain that allows the activation of adaptive cell immunity through activated lymphocytes T and B that with their proliferation assure a minimal immunity over time, not inhibiting the contagion.<sup>26</sup>

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<sup>23</sup> Brera G.R Sars-Cov-2 allostasis and the people and person-centered prevention. A new prevention strategy based on a people metabolic and immune shield for the pandemic shutdown. Part 1 The Sars-Cov 2 entry and COVID-19. Milan. Università Ambrosiana , 2021. ISBN: 9798530093906

<sup>24</sup> Federico M The conundrum of current anti-SARS-CoV-2 vaccines. Cytokine & Growth Factor Reviews.2021;60:45-61.

<sup>25</sup> Doerfler W. Adenoviral Vector DNA- and SARS-CoV-2 mRNA-Based Covid-19 Vaccines: Possible Integration into the Human Genome - Are Adenoviral Genes Expressed in Vector-based Vaccines? Virus Res. 2021 Sep;302:198466. doi: 10.1016/j.virusres.2021.198466. Epub 2021 Jun 1. PMID: 34087261; PMCID: PMC8168329.

<sup>26</sup> Antos A, Kwong ML, Balmerez T, Villanueva A, Murakami S. Unusually High Risks of COVID-19 Mortality with Age-Related Comorbidities: An Adjusted Meta-Analysis Method to Improve the Risk Assessment of Mortality Using the Comorbid Mortality

The mRNA vaccines are constructed with a sequence of bases homologous to RBD of the viral spike protein. The code is then transcribed by the RNA transfer, which allows the viral protein synthesis in the cytoplasm and in the organelles (endoplasmic reticulum and Golgi apparatus) to form the new virus. The mRNA vaccine is conveyed by lipid nano-particles that favor its entry into the cell membrane and the inhibition of natural immunity is warranted by mRNA substitution of Uridine with N1-metyl pseudouridine. The infected caveolae of the lipid rafts alter the transduction of immunity signals inhibiting proliferation and activation of lymphocytes T and B, but this is undoubtedly related to the alteration of the cell membrane and the flooding of macrophages with cholesterol and PH. Immunosenescence and the previous immune-atherosclerosis phenotype inhibit adaptive immunity and memory-T and B-cells production.<sup>27</sup> The virus dissemination is relative to a previous immunosuppressive phenotype and "inflammaging" induced by atherosclerosis inducing a lethality risk for the oldest people with comorbidities associated with atherosclerosis, like diabetes, obesity, hypertension, cardiovascular diseases. It explains the higher rate of mortality of the immunosenescent oldest people. The SARS-COV 2 immunity hijacking appears mediated by MTTL3, which blocks the RIG-1 receptors recognition METTL3 is the key enzyme mediating m6A

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Data. Infect Dis Rep. 2021;13(3):700-711. Published 2021 Aug 8.  
doi:10.3390/idr13030065

<sup>27</sup> Brera G.R Sars-Cov-2 allostasis and the people and person-centered prevention. A new prevention strategy based on a people metabolic and immune shield for the pandemic shutdown. Part 1 The Sars-Cov 2 entry and COVID-19. Milan. Università Ambrosiana , 2021. ISBN: 9798530093906

modification of SARS-CoV-2 RNA.<sup>28</sup> through the epigenetic modification of RNA chemical modification of RNA (N6-methyladenosine), due to methyl groups CH3. Inhibition of RIG-1 means natural immunity reduction and opening to cancer and to other infections, also by SARS-COV 2 variants.

The mRNA vaccines induce a high IFN gamma reaction and stimulate CD4 TH1 cells in local lymph nodes, but do not induce the antiviral CD8+ mediated immunity<sup>29</sup> because they do not stimulate synthesis nor interact with the lung B-cell memory-resident cells, not activating these. The immunity induction of mRNA vaccines is a "conundrum."<sup>30</sup>

The heterologous "mRNA" inoculated with the vaccine "infects" all the immune, epithelial, endothelial cells, neurons in every anatomical structure, from the brain to the heart, the endocrine organs, and the toe.

The problem that viro-immunologists<sup>31</sup> had to face was to prevent the inoculated heterologous m-RNA from being recognized by Toll-like receptors (TLR).<sup>32</sup> For this purpose, in m-RNA, they replaced a base: Uridine with n1-methyl pseudouridine, which escapes immune control of the inoculated host and increases translation speed. *In 2019 J. Lockhart, J*

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<sup>28</sup> Li N, Hui H, Bray B, et al. METTL3 regulates viral m6A RNA modification and host cell innate immune responses during SARS-CoV-2 infection. *Cell Rep.* 2021;35(6):109091. doi:10.1016/j.celrep.2021.109091

<sup>29</sup> Cagigi, A.; Loré, K. Immune Responses Induced by mRNA Vaccination in Mice, Monkeys and Humans. *Vaccines* 2021, 9, 61. <https://doi.org/10.3390/vaccines9010061>

<sup>30</sup> Federico M The conundrum of current anti-SARS-CoV-2 vaccines. *Cytokine & Growth Factor Reviews.* 2021;60:45-61.

<sup>31</sup> Lee RC, Feinbaum RL, Ambros V. The *C. elegans* heterochronic gene lin-4 encodes small RNAs with antisense complementarity to lin-14. *Cell.* 1993;75:843-854.

<sup>32</sup> Lu LF, Thai TH, Calado DP, Chaudhry A, Kubo M, Tanaka K, Loeb GB, Lee H, Yoshimura A, Rajewsky K, et al. Foxp3-dependent microRNA155 confers competitive fitness to Regulatory T cells by targeting SOCS1 protein. *Immunity.* 2009;30:80-91.

*Canfield J, Mong EF et al.<sup>33</sup> demonstrated that the replacement of the Uridine of the Spike Protein mRNA with the n1methyl-pseudouridine that is necessary for the mRNA production alters the silencing of micro-RNA switches leading to a decrease in the activity of these molecular switches, called "the dark matter" of the cell (about 50% of RNA) and thus altering the processes of silencing. What happens if the repressor of an oncogenesis inhibitor is not silenced?*

The hypothesis is that methyl groups deriving from N1-methyl-pseudouridine catabolism, increase the cells' methyloma with the main effect to increase METTL3-METTL14 that bind CH3 to miRNA promoters altering their action to silencing miRNAs, possibly harming the organism's life. Micro-RNAs are filaments of non-coding RNA that, thanks to the "Argonaut" proteins after joining the "RISC (RNA-induced silencing complex), interact internally with the target RNA, preventing transcription by preventing the synthesis of the protein with the specific mRNA silencing. The discovery in 1993 by Victor Ambros, Rosalind Lee, and Rhonda Feinbaum, highlighted the role of particular microRNAs therapy, in the structuring of the central nervous system, in diabetes, in heart disease. Mi RNA are involved in pathogenetic processes for inflammation, and cancer immunity<sup>34</sup> For example, if mi-RNA 205 is inhibited in the pathogenesis of breast cancer, carcinogenicity and metastasis are encouraged. The same occurs for mi-RNA 21 for liver cancer. In 2009 G.

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<sup>33</sup> Lockhart J, Canfield J, Mong EF, Vanwyk J, Totary-Jain H. Nucleotide Modification Alters MicroRNA-Dependent Silencing of MicroRNA Switches. *Mol Ther Nucleic Acids*. 2019;14:339-350. doi:10.1016/j.omtn.2018.12.00

<sup>34</sup> Raisch J, Darfeuille-Michaud A, Nguyen HTT. Role of microRNAs in the immune system, inflammation and cancer. *World J Gastroenterol*. 2013;19(20):2985-2996

Schratt, with a great contribution, illustrated some fundamental actions of miRNA in neurons. Mir-134-138 regulate the development of dendritic spines needed for synapses.<sup>35</sup> Their alteration can lead to autistic spectrum disorders and mental retardation and in brains in development as in childhood and adolescence, to learning and mood problems, as well as in adults to neuro-transmission receptor alterations such as CAMKII and CREB. Regulation of innate immunity involves mi-RNA 155-146 -132 as illustrated by J. Raisch, A.Darfeuille-Michaud, HT. Nguyen in their elegant review of 2013. Mir-155 regulates the suppression of the cytokine signaller (SOCS)-1, which negatively regulates the capacity of the "Antigen Presenting Cells " APC to present antigen and activate lymphocytes.<sup>36 37</sup> Cells with the lack of mir-155-show a defective presentation of antigen and therefore cannot activate T cells to promote the TH1-induced inflammation<sup>38</sup>: this could be the epigenetic pathogenesis of anergia and immunosenescence. Another study has shown that the elimination of mir-155 expression significantly increases the expression of the pro-inflammatory IL1. These observations depict how more doses of mRNA vaccines could induce paradoxical inhibition of innate immunity, increasing people's vulnerability to infection and cancer. In atherosclerotic people M2 immune phenotype, present in comorbidities at risk of COVID-19 severity,<sup>39</sup> could induce anergy when there are other infections with SARS-COV 2 variants escaping previous and waning adaptive immunity in

<sup>35</sup> Schratt G. microRNAs at the synapse. *Nat Rev Neurosci*. 2009 Dec;10(12):842-9. doi: 10.1038/nrn2763. Epub 2009 Nov 4. PMID: 19888283.

<sup>36</sup> Raisch J, Darfeuille-Michaud A, Nguyen HT. Role of microRNAs in the immune system, inflammation and cancer. *World J Gastroenterol*. 2013;19(20):2985-2996. doi:10.3748/wjg.v19.i20.2985

<sup>38</sup> Strains M, Pereira PM, Dunand-Sauthier I, Barras E, Reith W, Santos MA, Pierre P. MicroRNA-155 modulates the interleukin-1 signaling pathway in activated human monocyte-derived dendritic cells. *Proc Natl Acad Sci USA*. 2009;106:2735-2740

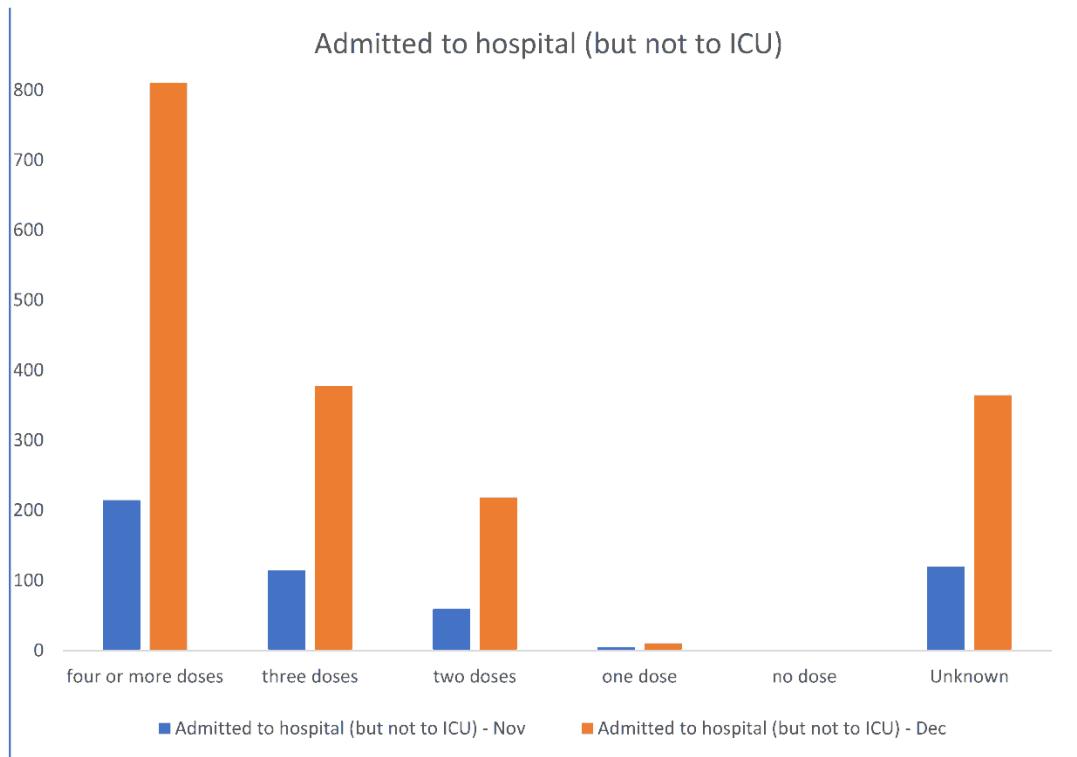
<sup>39</sup> Brera G.R . SARS-COV 2- allostasis and the people and person-centered prevention. Part 2 The sars-cov 2- induced immunosuppression and covid-19 anergy . Part 3 The antiviral metabolic allostasis and preventive immunostimulation - How to induce zero risk for covid-19. Milan: Ambrosian University: 2021 ISBN 9798547583520

short-time, exposing oldest immunosenescent people to a clinical syndrome severity up to lethality. Moreover, the induced methylation by mRNA vaccines, probably resulting in a MTTL3 cellular increase, supports the viral hijacking of immunity by SARS-COV 2 variants, and reducing natural immunity. It means that more mRNA vaccines are inoculated, more natural immunity is reduced, making easier variants' immunity hijacking. (Table 2-3)

Data from the Australian government concerning COVID-19 hospital, ICU admissions, fatalities in the last two months of 2022. comparing vaccinated and unvaccinated people give evidence to a dramatic increase of fatalities in poli-vaccinated people compared with unvaccinated.

Table 2 Below

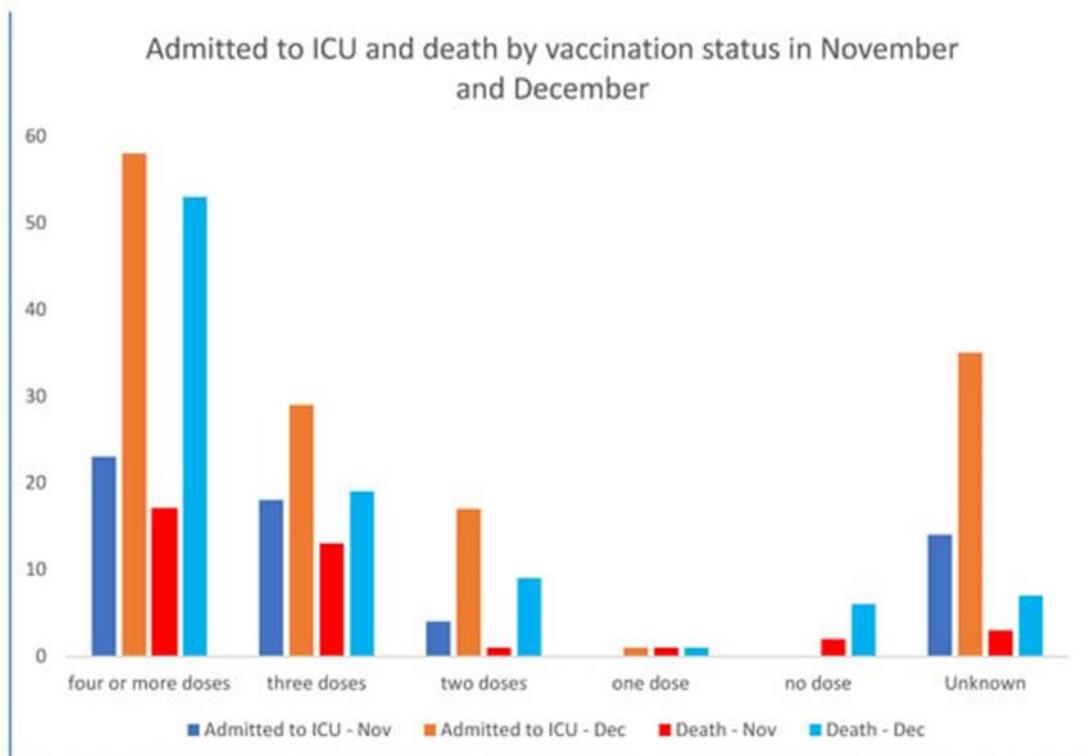
TABLE 2



Tab 2 Increase of hospital admission associated to anti COVID vaccine spots number in November-December 2022 in Australia

TAB 3

*Medicine, Mind and Adolescence 2025; XX, ID4*



TAB 3 Association of mortality to numbers of vaccines doses in Australia-November-December 2022

The immuno-tolerance phenomenon induced by many vaccines doses is probably the cause of these data.<sup>40</sup> Dionne et al. synthesize clinical serology and mechanistic data to argue that repeated mRNA boosting promotes class switching from IgG1/IgG3 toward IgG4 for spike-specific antibodies. They document and review changes in subclass proportions over successive doses, showing functional assays indicating reduced Fc-mediated effector functions (ADCC, complement activation) for IgG4-dominant sera, and discussing correlations with markers of B-cell maturation and T-helper cell polarization.

GG4 class-switching after repeated mRNA boosting determines a progressive rise in spike-specific IgG4 relative to IgG1/IgG3 after successive vaccine doses; IgG4 is characterized by low pro-inflammatory Fc effector activity, reduced complement fixation, and limited engagement of activating Fcγ receptor with potential functional consequences: because IgG4 antibodies are poor at mediating ADCC and complement-dependent cytotoxicity, a dominant IgG4 response could blunt Fc-dependent clearance mechanisms that contribute to hamper antitumor immunity and paradoxically viral elimination. After repeated mRNA vaccine boosters, the immune system tends to produce an increasing proportion of IgG4 antibodies specific to the Spike protein, compared to the more common IgG1 and IgG3 classes. This phenomenon is called “class switching” (antibody class change). IgG4 antibodies are less effective at mediating: ADCC (Antibody-Dependent Cellular Cytotoxicity), and the process by which immune cells kill infected or tumor cells Complement-dependent cytotoxicity inducing direct destruction of target cells through the complement system. If the antibody response becomes dominated by IgG4, Fc-dependent clearance mechanisms (based on the constant region of the antibody) are attenuated. This may reduce the effectiveness of antitumor immunity (since tumor cells are eliminated less efficiently), and

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<sup>40</sup> Dionne K, Patel R, Singh A. IgG4 class switching and immune tolerance in repeated mRNA vaccination. *Viruses*. 2025;17:666.

paradoxically hinder viral clearance, making it harder for the body to completely eliminate the virus.

With these mechanisms Raszek et al.<sup>41</sup> review emerging data that mRNA vaccines can induce persistent epigenetic marks in innate immune cells (monocytes/macrophages), which may alter baseline inflammatory responsiveness and training of innate immunity. They emphasize that mRNA vaccine platforms can induce durable epigenetic reprogramming of innate immune cells via changes in histone marks, chromatin accessibility, DNA methylation, noncoding RNAs, and metabolism-linked chromatin modifiers — mechanisms that underlie both trained immunity and innate tolerance. The epigenetic mechanisms highlighted concern:

1. Histone modifications. The authors point to changes in activating and repressive histone marks (for example, increased H3K4me3 and H3K27ac at promoters/enhancers of immune genes) that open chromatin and prime transcriptional responses on re-stimulation. Histone modifications act as an epigenetic code:Activating marks (H3K4me3, H3K27ac) open chromatin and make immune genes ready for transcription. Repressive marks closed chromatin and genes are silenced. This mechanism allows cells to “remember” or hamper immune experiences and react faster to subsequent stimuli, without altering the DNA sequence itself.
2. Chromatin accessibility. Raszek et al. stress that altered accessibility at regulatory elements (detectable by

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<sup>41</sup> Raszek M, Kowalski M, Dube A. Epigenetic and immunological implications of mRNA vaccine platforms. *Expl Immunol*. 2024;4:267–284.

ATAC-seq) is a core mechanism by which prior mRNA/LNP. The mechanism of chromatin accessibility explains how prior immune experience (e.g., mRNA vaccines) can leave an epigenetic imprint: Open chromatin make genes ready for transcription for a faster and stronger immune response.

Closed chromatin means genes silenced and limited response. This “epigenetic memory” influences which immune genes will be activated during subsequent challenges sure reshapes which genes are available to transcription factors during later challenges.

3. DNA methylation. Stable gains or losses of CpG methylation at immune loci are discussed as a longer-term mechanism that can lock in altered expression programs in myeloid cells after repeated stimulation. At immune loci (genomic regions controlling immune responses), stable gains or losses of methylation can long-term modify gene activity. This process is particularly relevant in myeloid cells (monocytes, macrophages, dendritic cells). After repeated stimulation (e.g., infections or vaccines), DNA methylation can “lock in” a new gene expression program.
4. Noncoding RNAs and post-transcriptional regulation. The review highlights microRNAs and long noncoding RNAs as modulators of mRNA stability and translation for cytokines and signaling molecules, contributing to sustained long-term shifts in innate responsiveness. Their silencing can produce devastating effects on immunity and other metabolic mechanisms. DNA methylation at miRNA gene promoters through addition of methyl groups to CpG regions can block miRNA transcription. This is common in cancers, where tumor-suppressor miRNAs are silenced. Another silencing mechanism is the Histone modifications. Through repressive marks such as H3K27me3 close chromatin that prevent miRNA expression, and loss of

activating marks (H3K4me3, H3K27ac) also reduces transcription.

5. Metabolic-epigenetic coupling. Raszek et al. emphasize metabolic rewiring (glycolysis versus oxidative phosphorylation) as a driver of epigenetic state: metabolites such as acetyl-CoA, succinate, and fumarate act as cofactors for chromatin-modifying enzymes, linking cellular metabolism induced by LNP/mRNA sensing to persistent chromatin changes. When metabolism is “reprogrammed” by LNP/mRNA exposure, the metabolites produced reshape chromatin.

This leads to persistent epigenetic changes, making certain immune genes more or less accessible. Innate immune responsiveness is durably remodeled, creating a functional memory that depends not only on classical memory cells but also on metabolic-epigenetic imprinting.

6. Pattern-recognition receptor signaling and transcriptional priming. Engagement of endosomal and cytosolic RNA sensors (TLR7/8, - endosomal receptors that detect single-stranded RNA; RIG-I cytosolic receptor that detects double-stranded RNA or RNAs with specific ends ) by mRNA/LNPs initiates transcriptional programs (NF- $\kappa$ B, IRFs) that are then stabilized by epigenetic marks, (e.g., histone acetylation and methylation), producing a memory-like state in monocytes/macrophages. Epigenetic marks keep immune gene promoters in an “open” or “closed” and accessible/unaccessible state.

myeloid cells (monocytes/macrophages) enter a condition of transcriptional priming, resembling memory.

Raszek et al. frame these mechanisms as the molecular basis for two possible outcomes: trained immunity (heightened pro-inflammatory responsiveness) or innate tolerance (dampened inflammatory output), depending on dose, interval, and cellular context. They cite emerging empirical work showing persistent epigenetic signatures in monocyte-derived cells after mRNA vaccination, arguing these signatures plausibly explain altered cytokine profiles and antigen-presentation capacity observed in some cohorts.

Simonis A, Theobald SJ, Koch AE et al.<sup>42</sup> performed a longitudinal, multi-omics analysis of peripheral blood monocytes and monocyte-derived macrophages from vaccinated individuals, combining ATAC-seq, ChIP-seq (histone marks), RNA-seq, and functional ex-vivo stimulation assays to map chromatin, transcriptional and cytokine changes before and after mRNA vaccination and after booster doses. They sampled donors at baseline, after the primary two-dose series, at later follow-up time points, and after a booster to assess persistence and reversibility of signatures. They found a long term epigenetic memory.

The authors confirm Raszeck et al. findings as evidence that mRNA/LNP platforms can “train” innate cells via epigenetic mechanisms, producing a form of innate memory that is durable yet modifiable by additional antigen exposure. They discuss implications for vaccine design, heterologous immunity, and the need to study whether such reprogramming has beneficial (enhanced protection) or context-dependent adverse effects (altered inflammatory setpoints) in larger cohorts

Numerous studies document how dysregulation of mi- RNA is associated with cancer development and metastasis processes, as documented by the splendid review of G. Sotiropoulou, G. Pamplakis, E.

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<sup>42</sup> Simonis A, Theobald SJ, Koch AE, Mummadavarapu R, Mudler JM, Pouikli A, et al. Persistent epigenetic memory of SARS-CoV-2 mRNA vaccination in monocyte-derived macrophages. *Mol Syst Biol*. 2025;21:341–360

Lianidou Pampalakis, Lianidou, Z. Mourelatos. <sup>43</sup>Cancer pathogenesis is associated with several bio-molecular processes such as genomic alterations, transcription of oncogenic factors, and inhibition of repressors transcription, such as P53, hypoxia. The miRNAs role in cancer is established from many investigation.<sup>44 45</sup> and DNA methylation, inducing silencing miRNAs is one mechanism for cancer pathogenesis <sup>46</sup>.

Epigenetic changes are regulated by micro-RNAs which are the arbiters of cell health as on/of molecular switches of mRNAs.

Viral mRNAs such as mRNA vaccines act by altering microRNAs. The mRNA vaccines act like a virus at the epigenetic level.

Recently E Karimi, H. Azari Yari, M, Tahmasebi, et al. identified 39 mi-RNA derived by Sars-COV 2 inducing a viral allosteric inhibiting

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<sup>43</sup> Sotiropoulou G, Pampalakis G, Lianidou E, Mourelatos Z. Emerging roles of microRNAs as molecular switches in the integrated circuit of the cancer cell. *RNA*. 2009 Aug;15(8):1443-61. doi: 10.1261/rna.1534709. Epub 2009 Jun 26. PMID: 19561119; PMCID: PMC2714746.

<sup>44</sup> Lages E, Ipas H, Guttin A, Nesr H, Berger F, Issartel JP. MicroRNAs: molecular features and role in cancer. *Front Biosci (Landmark Ed)*. 2012 Jun 1;17(7):2508-40. doi: 10.2741/4068. PMID: 22652795; PMCID: PMC3815439.

<sup>45</sup> Hata A, Lieberman J. Dysregulation of microRNA biogenesis and gene silencing in cancer. *Sci Signal*. 2015 Mar 17;8(368):re3. doi: 10.1126/scisignal.2005825. PMID: 25783160.

<sup>46</sup> Chimonidou M, Strati A, Tzitzira A, Sotiropoulou G, Malamos N, Georgoulas V, Lianidou ES. DNA methylation of tumor suppressor and metastasis suppressor genes in circulating tumor cells. *Clin Chem*. 2011 Aug;57(8):1169-77. doi: 10.1373/clinchem.2011.165902. Epub 2011 Jun 23. PMID: 21700955.

the innate immunity, altering Vit. D and the lung cells metabolism through the transcription alteration.<sup>47</sup>

Silencing of miR-223 appears to be caused by an epi-transcriptomic alteration of pre-micro-RNA, which produces an oncogenic factor that binds to its site, producing its "switching off." This is associated with leukemia pathogenesis. This evidence could explain the raise of blood cancer mortality in vaccinated children and adolescents favoured by the immunity inhibition explained before. Epidemiological studies on the incidence of post-vaccine leukemia and other cancers is needed comparing vaccinated and unvaccinated children and adolescents. The direct induction of miRNAs dysregulation produced by mRNA vaccines can have dramatic consequences for millions of young people and children by inducing the pathogenesis of tumors or relapses and diseases of the central nervous system, and data here showed can confirm the hypothesis. What will be the effect of mRNA vaccines on the brain of the ruling class since their action determines alterations of the miRNAs that control neuronal nuclei biological substrate of the cognitive and subcortical sphere. What will happen with the impairment of the activity of the cerebral cortex and the subcortical nuclei?

*There is a pandemic of illiterate criminality in people who induced the vaccination of adolescents and children who were not at risk of COVID-19 mortality. If rarely infected, children are asymptomatic<sup>48</sup> thanks to their solid innate immunity and rapidly reduce the viral load in the oral and*

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<sup>47</sup> Karimi E, Azari H, Yari M, Tahmasebi A, Hassani Azad M, Mousavi P. Interplay between SARS-CoV-2-derived miRNAs, immune system, vitamin D pathway and respiratory system. *J Cell Mol Med.* 2021;25(16):7825-7839. doi:10.1111/jcmm.16694

<sup>48</sup> Erika Molteni, H. Sudre, Liane S. Canas, Sunil S. Bhopal, et al. Illness duration and symptom profile in a large cohort of symptomatic UK school-aged children tested for SARS-CoV-2. *Lancet*; 2021 internet file:///C:/Users/Utente/Documents/UA/ricerca/Corona%202/Illness%20duration%20and%20symptom%20profile%20in%20symptomatic%20UK%20school-aged%20children%20tested%20for%20SARS-CoV-2%20-The%20Lancet%20Child%20&%20Adolescent%20Health.html

*nasal mucous membranes. Children and adolescents and asymptomatic people could act as "living vaccines" contributing to the "herd immunity" as often occurs with other viruses. It has been well highlighted that asymptomatic people relatively contribute to the virus diffusion. Vaccination exposes children and adolescents to epigenetic and genetic damages whose impact must be studied with case controls clinical investigations associating vaccination with epigenetic changes repressing transcription of tumor suppressor genes.*

*Two meta-analyses show the reduced infectivity of asymptomatic people (AIC). Transmission rates of AIC ranged from 0–2.2% compared to 0.8–15.4% for symptomatic (SIC)<sup>49</sup> and in the household from 0–4.9% compared to 18.0% of SIC.<sup>50</sup>*

The infectivity reduction of asymptomatic people is probably due to the presence of neutralizing IGA in mucous membranes, absent in vaccinated people.

A study that monitored 455 contacts exposed to the asymptomatic COVID-19 virus carrier showed that nobody was infected.<sup>51</sup>

<sup>49</sup> Byambasuren O, Cardona M, Bell K, et al. Estimating the extent of asymptomatic COVID-19 and its potential for community transmission: systematic review and meta-analysis. J Assoc Med Microbiol Infect Disease Canada (JAMMI). 2020; 4: 223-234

<sup>50</sup> Madewell ZJ, Yang Y, Longini IM, et al. Household Transmission of SARS-CoV-2. A systematic review and meta-analysis. JAMA Netw Open 2020;3(12):e2031756. doi: 10.1001/jamanetworkopen.2020.31756. 12.18.2

<sup>51</sup> Gao M, Yang L, Chen X, et al. A study on infectivity of asymptomatic SARS-CoV-2 carriers. Respir Med. 2020;169:106026. doi:10.1016/j.rmed.2020.106026

The reduced viral load transmission by the upper respiratory and its disappearance in a shorter time can explain this evidence and reverses the common belief that asymptomatic people induce the pandemic. Conversely, a reduced transmissible viral load to healthy people could activate the people's innate immunity and the progressive loss of virulence by activating the tissue-resident memory T cells that block the virus diffusion in the organism.

The right strategy to accelerate herd immunity has been a health education campaign to educate to assume immunogenic molecules (e.g., beta-glucans in bakers yeast, lactoferrin, ), anti viral enzymes natural substances like Aloe and inhale vapors of powerful common natural antiviral substances, like curcumin, at the first signals of infection of upper respiratory ways.<sup>52 53</sup>

The SARS-COV 1( 2002-2003) and MERS (2009-2010) disappeared without vaccines.

Millions of adolescents and young people not at risk of COVID-19 that the Italian health management and other countries led to vaccination with a legalized blackmail, received an alteration of the regulation of mir-223, whose dysregulation is linked to the pathogenesis of leukemia. The immune and tumor repressors' transcription silencing could explain the raising of mortality rate for blood and brain cancer. In the USA, Europe, and Italy the FDA ,EMA and AIFA approved mRNA vaccines in children based on a small trial, which used children as experimental animals and that did not monitor the adverse effects at the epigenetic level and their manifestation after a long time.

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<sup>52</sup> Brera G.R . SARS-COV 2- allostasis and the people and person-centered prevention. Part 2 The sars-cov 2- induced vimmunosuppression and covid-19 anergy . Part 3 The antiviral metabolic allostasis and preventive immunostimulation - How to induce zero risk for covid-19. Milan: Ambrosian University: 2021 ISBN 9798547583520

<sup>53</sup> Brera GR Brera GR Zero risk for Covid-19 with antiviral allostasis the preventive immunostimulation. Università Ambrosiana ed. 2021 ISBN 9798756383423

The other process induced by mRNA vaccines is the cell's methylation induced by n1-methylpseudouridine. The n1-methylpseudouridine ( $\phi$ ) stabilizes the RNA. It is naturally present more in the RNAt, with implicit natural finalism to favor the coding probably. In synthesizing the mRNA vaccines, the Uridine has been replaced with  $\phi$  to increase the translation speed and evade the natural immunity. However, introducing  $\phi$  in each cell produces cellular stress that could be equivalent to "heat stress" that produces an 'increase of cell methylome by methylating all the bases through the synthesis induction of METTL3 (methyltransferase like 3) with the finalism to ensure an allostasis for survival. The METTL3 binds CH3 to microRNAs', promoters causing the down-regulation of some and up-regulation of others. The action of miRNAs like that of antisense RNA could produce the silencing of the P15 gene, which encodes a dependent cycline kinase involved as a repressor of malignant leukemic degeneration. W Yu, D Gius, P. Onyango, et al. in 2008 saw an inverse relationship between P15 and leukemia, highlighting the risk of its repression. Antisense RNA also interacts directly or indirectly with DNA-methyltransferase leading to DNA methylation and its consequences in the repression of gene transcription and the recruitment of "histone-modifying enzymes" by modifying chromatin.

This evidence means that in opposition to an illiterate bio-medical culture, mRNA vaccines also induce epigenetic alteration that, in addition to induction or suppression of miRNAs, lead to DNA methylation and chromatin closure.

METTL3 is a key enzyme in RNA methylation, particularly N6-methyladenosine (m6A).Increased METTL3 leads to hyper-methylation of RNA nucleotide, The increase of cell's methylome could be caused by the lack of repression of the MTTL3 synthesis by silencing its mRNA

induced by a specific micro-RNA and to catabolism of mRNA anti COVID vaccines which releases an enormous quantity of CH3. The METTL 3 increase induces the general methylation of nucleotidic bases with catastrophic effects, a sort of earthquake in the organism's life, with dramatic effects on the pathogenesis of tumors and other diseases.

In the tissues of patients with "Non-small cell lung cancer (NSCLC) (small cell lung cancer) N6-methyladenosine (m6A) methyltransferase-like 3 (METTL3) regulates microRNA-1246 (mir-1246) which is a well-documented tumor's progression and metastases. More METTL3 and mir-1246 were found in these tissues in inverse ratio to PEG-3 (Paternally expressed gene-3).<sup>54</sup>

*Dysregulation of micro-RNA is, therefore, very dangerous. This confirms the aversion of Luc Montagnier, Nobel Prize, against the use of genetic vaccines before knowing in depth their effects with long-term epidemiological investigations.*

Several deaths and adverse effects on mRNA vaccines have already been reported worldwide,<sup>55</sup> such as the high incidence of pericarditis and myocarditis in young people, which in some countries like the UK, has blocked any other vaccination in adolescents and young people, not at risk of COVID-19. In Italy, a teenager died a few hours after the second vaccination by m-RNA, another from the vectorial Astra-Zeneca., many other are died or have become disabled. At the beginning of the vaccination time the USA, the CDC reported the deaths of 14 teenagers. The actual extent of these events is unknown because public health, organizations such as AIFA, the Ministry of Health, the Italian Higher Institute of Health,

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<sup>54</sup> Huang S, Luo S, Gong C, Liang L, Xiao Y, Li M, He J. METTL3 upregulates microRNA-1246 to promote occurrence and progression of non-small cell lung cancer via targeting paternally expressed gene 3. *Molecular Cancer*. 2021;20(1):116. doi:10.1186/s12943-021-01393-2

to our knowledge, have not organized epidemiologic research to study the adverse effects of these vaccines over time.

Undoubtedly the fear of COVID-19, induced by a virus quickly and destroyable and neutralizable with natural antiviral remedies also immunogenic and drugs already in use,<sup>56</sup> that prevents contact with epithelial and endothelial cells is derived from the lack of public health orientation towards prevention "centered on the person," and to failure in primary and secondary prevention. This omission is due to ignorance and the non-adoption in public health of the multi-factorial, multi-dimensional paradigm of "Person-centered medicine," the paradigm change of medical science, that could have saved only in Italy 170.000 and in the world millions of people. As Luc Montagnier claimed, we need analysis over a long time to control the existence of adverse effects, even fatal at a short time. The only answer to the pandemic beginning and permanence has been the adoption of "genetic" vaccines, which have been inadequately tested, limited in time, with the scientific evidence of their danger. The adverse effects of these vaccines and the induction of variants endangered the health of millions of people and to date must be prevented or blocked in time to avoid further global health disaster, primarily protecting children and adolescents.

The mRNA vaccines' dangers, as highlighted above, are shared by the viral vector vaccines. These induce a modification of human DNA because of the recombination of the animal or human *DNA vector adenovirus with the host's DNA. This hybridization could lead to auto-immune reactions and, at the experimental level, to an impressive induction of tumors.*<sup>57</sup>

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*Scientific evidence of the anti SARS\_COV 2 vaccines- induced genetic damages must be studied with clinical and epidemiological investigations. However, before it is necessary a total change of public health administration resulting in the withdrawal of the authorizations to mRNA vaccines distribution and the constitution of a metabolic and immune shield for the population by adopting the "Antiviral allostasis, and immuno-stimulation"<sup>58</sup> strategy launched in Italy by the National Health Committee and in the world by the World Health Committee.*

Unfortunately, the prudence towards vaccines that led to their rejection only by a minority of the population and health care workers has a sound scientific basis. The dramatic suspension of health care workers who refused vaccination by a surprising (in the negative sense) physician's council and discrimination of workers paradoxically supported by unions - but unions should not defend workers? -that do not want to vaccinate is without any scientific basis.

What has happened to the brain, mind, and behavior of the national leadership, institutional public or business, teachers, and in any context with the genes of the adenovirus of chimpanzees integrated into the genome of cortical neurons or sub-cortical brain (Astra-Zeneca vaccine) that, if in age, communicate to the progeny? Will the COVID-19 contribute to human evolution?