



# Effect of COVID-19 on Public Health: The Latest Physical Activity and Diet Update for Counteracting New Emerging COVID-19 Strains (Omicron) and Stay Active and Do Not Lay on the Vaccine Alone: A Narrative Review

Hossein Pirani <sup>1,\*</sup>, Omid Reza Salehi <sup>2</sup>, Sarieh Shahraki <sup>3</sup>, Adeleh Khodabakhsi Fard <sup>4</sup> and Kimia Khoramipour <sup>5</sup>

<sup>1</sup>Department of Basic Sciences, Chabahar Maritime University, Chabahar, Iran

<sup>2</sup>Department of Physical Education and Sport Sciences, University of Kurdistan, Sanandaj, Iran

<sup>3</sup>Department of Physiology & Pharmacology, School of Medicine, Zabol University of Medical Sciences, Zabol, Iran

<sup>4</sup>Department of Nutrition, Faculty of Public Health, Kerman University of Medical Sciences, Kerman, Iran

<sup>5</sup>Department of Nursing, Faculty of Nursing and Midwifery, Kurdistan University of Medical Sciences, Kurdistan, Iran

\*Corresponding author: Assistant Professor, Department of Basic Sciences, Chabahar Maritime University, Chabahar, Iran. Email: hn.pirani@gmail.com

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## Abstract

**Context:** Omicron is a new type of SARS-CoV-2 that is considered the most dangerous one so far because despite emerging new variants such as XE, no more dangerous strain than omicron has been identified. On November 24, 2021, World Health Organization identified the Omicron as a global threat. High genetic mutations of Omicron makes it more dangerous than other SARS-CoV-2 variants. This manuscript conducted to systematically collect and provide the effect of COVID-19 on public health: The latest physical activity and diet update for counteracting new emerging COVID-19 strains (Omicron) and stay active and do not lay on the vaccine alone.

**EvidenceAcquisition:** We searched PubMed, Web of Science, Embase, and Scopus from January 2020 to November 2021. 3241 articles related to COVID-19 were found and based on filters such as: Physical activity, Omicron, nutrition, immune system, 36 research articles were studied.

**Results:** Studies have shown that regular exercises with low and moderate intensity can have a favorable effect by improving the function of the immune system in reducing the risks of COVID-19 disease. Also, proper nutrition, especially if it is combined with regular exercise, has favorable effects on the immune system of patients with COVID-19.

**Conclusions:** It seems that regular and long-term physical activity with low to moderate intensities (not high intensities) considering a suitable diet regime can have a favorable effect on the immune system of patients with COVID-19.

**Keywords:** COVID-19, Public Health, Physical Activity, Diet

## 1. Context

The information showed that even after the production of the SARS-CoV-2 vaccine and the decreasing trend of the disease, on November 2021, South Africa scientists have announced the worrying new variant of Omicron to the World Health Organization (WHO) (1). Then one week later, in all six WHO regions, the WHO reported Omicron in 38 countries (2). On November 13 and 18, 2021, two patients became infected with Omicron while traveling (3). The Islamic Republic of Iran reported

its first Omicron case in February 19, 2020 in the city of Qom (4). Therefore, studies and reports show that Omicron is spreading worldwide, highlighting the need for immediate action.

Omicron has 50 genetic mutations, of which about 26 to 36 are related to COVID-19 spike protein (5). These mutations increase the virus transmission, disease severity, and immune escape (5). Another reason why Omicron could be a dangerous virus is the receptor-binding domain (RBD) (5). RBD is a validated viral entity that detects Angiotensin-converting enzyme

2 (ACE2) receptors as a virus entry mediator (5). Notably, RBD is the main target for neutralizing antibodies (5). Mutations in the coronavirus at the 484 and 417 spike positions are associated with immune escape (6, 7). Since the Omicron type contains the E484A and K417N mutations, it could also resist antibodies and have a robust immune escape property (7) (Figure 1).

New findings have shown that vaccinated people are about three to four times more likely to get the virus if a family member becomes infected with Omicron (8). Studies reported that Omicron can be an indicator of SARS-CoV-2 virus (9). Mutations in the Omicron make it more infectious than previous nasopharynx and upper respiratory tract variants (10). Conversely, it is less likely to penetrate deep into the lungs (11). Protection against Omicron is less than other variants in affected and vaccinated individuals (12). Recent data suggest that re-infections are more likely to occur in the Omicron type (13). The latest COVID-19 strain, appears to be a potentially serious threat, and so far, no new and more dangerous strain than Omicron has been reported (14). Hence, developing the necessary strategies during this disease can be very effective. It has been reported that the Omicron can pass just in first line of defense in body (15); thus, T cells have been emphasized in the fight against this new variant (12). In line with this, T cell responses are associated with reduced disease symptoms (16, 17). Two primary interventions can increase T cells without side effects: regular physical activity practice and good diet (12, 18).

Based on studies, it seems that in addition to regular physical activities, a proper diet has a favorable effect on the management of COVID-19. So that a proper diet can help improve immune system by increasing the level of proteins, vitamins, and gut microbiota (19). Also, diverse and especially Mediterranean diets can lead to a reduction of free radicals. These researchers stated that diets containing antioxidants are associated with improving the function of the immune system, reducing inflammatory factors, and reducing oxidative stress (20). In another study, researchers reported that receiving a diet containing various vitamins such as C, E, D, zinc and the B family can inhibit TLR toll-like receptor, nuclear factor kappa-light-chain-enhancer of activated B cells.  $\text{NF}\kappa\text{B}$ , tumor necrosis factor (TNF) and in this way inhibit the inflammatory pathways of viruses and especially COVID-19 (21).

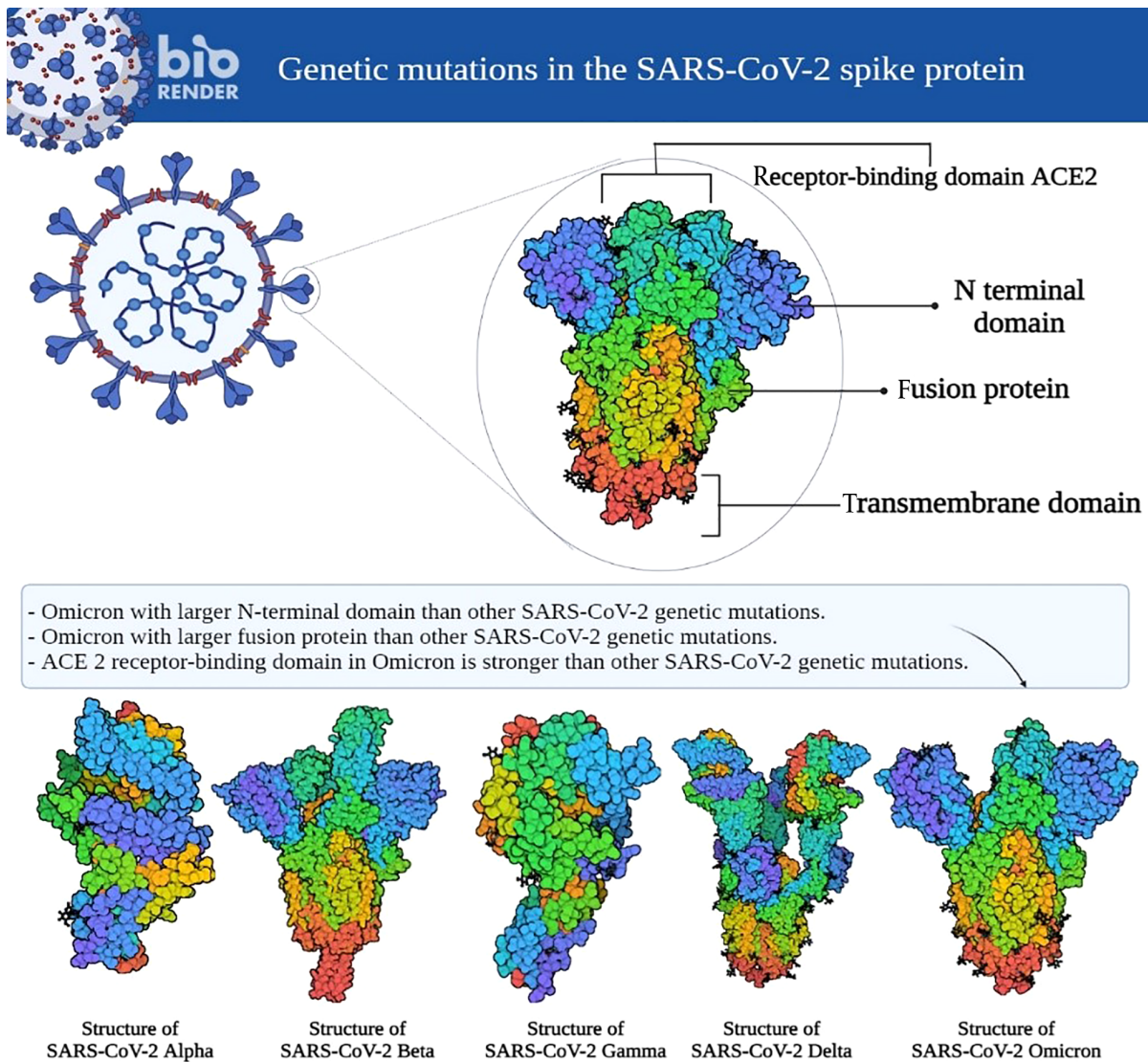
Although exercise and proper diet have favorable effects on the immune system and health; But in the conditions of the Corona pandemic, which plunged the

world into a deep dilemma. It is necessary to provide practical and non-invasive solutions for the prevention and treatment of this disease. Therefore, the current study was conducted with the aim of investigating the effect of exercise and diet on health in the conditions of the COVID-19 pandemic.

## 2. Evidence Acquisition

### 2.1. Increase Physical Activity to Counteract Omicron Dissemination

Several studies were published emphasizing staying active to improve the immune system (18, 22-24). Further studies reported low intensity training (LIT) to moderate intensity training (MIT) home-based exercise can improve the functioning of the antioxidant system and the immune system (18, 25, 26). Despite the recommendations for the population to remain physically active, the level of physical activity decreased significantly in the coronavirus outbreak (27). After the rules of social distance were relaxed, the level of physical activity did not return to pre-pandemic levels (28). However, new variants made the situation worse because they have been more resistant to immunization and can escape the immune system (29). These properties reach the highest levels in the Omicron, making it the most dangerous variant (4). Studies have shown that exercise training such as MIT home-based exercise could increase T cells, the essential part of the immune system in fighting against the Omicron (30). Doing this could bring two advantages together: First, social distancing, and second, boosting T cells (31). Physical exercise depended on type, intensity and frequency can improve the immune system in COVID-19 disease (32). It seems that low- and moderate-intensity sports activities have favorable effects on the immune system in dealing with COVID-19 by modulating the lymphocytes, pro-inflammatory and inflammatory cytokines, and regulating the expression of interferon 1 (33). So physical exercise should be commensurate with the nature of COVID-19 to prevent recurrence of infection or impaired immune function (26, 30, 34). It is recommended that children and adolescents between 5 and 17 years perform MIT (60 minutes, about 70% of heart rate maximum, three sessions per week) (35). For adults over 17 years, MIT (75 minutes of twice a week) can be effective as well. These exercises can include dancing, Zumba, stationary bike, treadmill running and rope (36). The latest update of physical activity recommendations for COVID-19 states that 3 - 5 sessions per week MIT for COVID-19 states that performing 3 - 5 sessions per week MIT for 150 minutes



**Figure 1.** Genetic mutations in the SARS-CoV-2 spike protein

is needed in the COVID-19 situation (37). Also, resistance training could bring extra advantages. Thus, we suggest doing the following: Box squat, hip bridge, push-up, handstands, tight hang, mountain climbers, split squat, floor push-up, and Bulgarian split squat (38). To maintain the intensity of the exercise with bodyweight, use the Borg Scale of 5 and the repetitions between 10 to 20 and 2 - 3 sets. With the increase in the prevalence of Omicron, the outdoor environment cannot be safe (39). Therefore, we suggest exercising at home by combining aerobic and resistance training.

Table 1 summarized our sessions for exercise training

during Omicron outbreak. Also, Table 2 provides an overview of studies related to physical activity and the immune system.

## 2.2. Can Diet Be Helpful as Well?

Several papers have highlighted the importance of a healthy diet during COVID-19 outbreak, because of its effects on the immune system (21, 63, 64), the interaction between diet and microbiota (including the gut, saliva, and lung microbiome)-which could affect CD4+ regulatory T cells (63), It has been shown that healthy gut microbiota can control the SARS-CoV-2 induced lung

**Table 1.** Recommended Physical Activity for the Middle-Aged Adults and Elderly

Exercise Type <sup>a</sup>	Age, y	Volume	Intensity
Cycling	40 - 59	2 sessions per week	45 - 55 of VO <sub>2</sub> max
Run	40 - 59	3 sessions per week	45 - 55 of VO <sub>2</sub> max
Yoga	40 - 59 and more than 60	3 sessions per week	N/A (unknown)
Elastic bands	More than 60	2 sessions per week	Borg scale 2 - 5 (scale 1 to 10)
Resistance training	40 - 59 people without heart disease	3 sessions per week	40 - 60 of 1RM
Walking	40 - 59 and more than 60	3 sessions per week	35 - 45 of VO <sub>2</sub> max

<sup>a</sup> Before exercising, make sure you do not have a cold or an infectious disease.

**Table 2.** Review the Importance of Research on the Impact of Physical Activity for Prevent the Weakening of Immune System During Pandemic of Coronavirus

Author	Year	Description	Suggested Exercise	References
Clemente-Suarez et al.	2022	MIT increased T cells and NK-cells Improvement in mental health, metabolic markers and cardiorespiratory fitness in patients Improvement of antibody responses in vaccination	Regular and MIT	(37)
Agha-Alinejad et al.	2022	Impaired immune function by high intensity training (HIT) Increase T-cells by MIT to fight COVID-19 Less improvement in immune system function by LIT	Regular and MIT	(34)
Jesus et al.	2021	Preventing viral respiratory infections (including coronavirus infection). MIT can improve immune system function (increase in T cells), nevertheless HIT can deteriorate the immune system function.	Regular and MIT	(40)
Scudiero et al.	2021	HIT can destroy immune system (by creating numerous pathologies), nevertheless MIT can help the human body to live better	Regular and MIT	(41)
Sacma and Geiger	2021	Exercise, by increase in production of immune cells from the bone marrow, the regular trainings can increase the immune system function.	Regular and MIT	(42)
Suzuki and Hayashida	2021	HIT can increase the systemic inflammation, MIT can reduce the acute upper respiratory infections and enhance immune function. Yoga and walking trainings (as LIT) can relieve stress and are not harmful for immune system.	Regular and MIT	(27)
Yoon et al.	2021	Regular trainings can improve anti-inflammatory cytokines. Decrease TNF as well as increase NK, B and T cells.	Regular and MIT	(43)
Simpson and Pawelec	2021	The mechanical load should be adjusted in such a way as to prevent suppression of the immune system, because the decrease in the function of the immune system in the elderly has a significant relationship with T cells.	Regular and MIT	(44)
Moghadam et al.	2021	Although diet can be one of the most effective and best ways to improve the functioning of the immune system, regular trainings with appropriate intensity can progress the immune system function.	Regular and MIT	(45)
Do Brito Valente et al.	2021	Trainings can decrease TNF as well as increase NK, B and T cells. Regular trainings by alteration in myokine concentrations and metabolites also modulation of the immune system can directly improve the systemic inflammation.	Regular and MIT	(46)
Papp et al.	2021	Regular training with the increasing in NKT, NK, B and T lymphocytes is a strong support to prevent viral infections.	Regular and MIT	(47)
Suzuki	2019	HIT can weaken the immune system and increase inflammation. MIT can improve the immune system. Exercise can be a drug.	Regular and MIT	(48)
Baker and Simpson	2021	MIT can prevent the spread of viral infections by increasing anti-inflammatory cytokines and T cells, as well as improving immune function.	Regular and MIT	(49)
Khoramipour et al.	2021	Exercise along with a balanced diet and proper nutrition can be essential factors to be safe in the pandemic.	Regular and MIT	(18)
Ahmadi Hekmatikar et al.	2021	The breathing trainings and low-intensity resistance training with hand-trainer can progress the strength performance and restore normal blood oxygen levels in patients with COVID-19.	Regular and MIT	(30)
Jee	2021	MIT can improve immune function, however HIT can suppress immune system, LIT could not improve immune function.	Regular and MIT	(50)
Valizadeh et al.	2021	In patients with hypertension, the submaximal endurance training lowered blood pressure and improved function of immune system	Regular and MIT	(51)
Oh et al.	2021	Vitamin D as well as regular MIT by increasing NK cells can improve the immune system function.	Regular and MIT	(52)
Córdova Martínez et al.	2021	Appropriate training programs can improve quality of life and recovery of patients with COVID-19 disease.	Regular and MIT	(53)
Rahayu et al.	2021	Regular trainings are more effective. Regarding to safe and positive effects of MIT, they are recommended in COVID-19 pandemic. It is better to increase the duration of trainings from 150 to 300 minutes to 200 to 400 minutes per week.	Regular and MIT	(54)
Domin et al.	2021	Release of the cytokines can be affected by duration and intensity of trainings so that prolonged trainings and single bout trainings have different effects on cytokines.	Regular and MIT	(55)
Fonseca et al.	2021	MIT can improve cytokines such as leptin, sTNFR1 and IL-6.	Regular LIT and MIT	(56)
Scheffer and Latini	2020	Regular and MIT have anti-inflammatory properties which decrease TNF and increase B and T cells.	Regular LIT and MIT	(57)
Scartoni et al.	2020	Performing 150 minutes MIT or 75 minutes HIT per week is recommended to reduce the sedentary lifestyle.	Regular LIT and MIT	(58)
Simpson et al.	2020	MIT have safe and positive effects in patients who are recovering from COVID-19.	Regular LIT and MIT	(59)
Da Silveira et al.	2020	regular trainings can improve NK cells, monocytes, immature B cells and lymphocytes in patients with COVID-19.	Regular LIT and MIT	(33)
Aktuğ et al.	2020	MIT can prevent viral respiratory infections and inflammation in patients with cardiovascular and T2DM diseases Long and HIT can decrease the immune system function.	Regular LIT and MIT	(60)
Wang et al.	2020	Trainings can decrease TNF as well as increase NK, B and T cells. Regular trainings can improve the immune system.	Regular LIT and MIT	(61)
Yildizgoren	2020	Combination of balance, stretching, strengthening and walking trainings can be designed as home based trainings. In safe distance situation, the MIT like brisk walking outdoors can be a good alternative. Avoid from HIT in crowded and hall places as it has less benefits than risks. Consumption of vitamin rich fluid and nutrients prior to training along with balanced diet is important.	Regular LIT and MIT	(62)

infection via a phenomenon called 'gut lung axis' (65). A high-fiber diet can affect the gut and lung microbiotas (66). In contrast, a low fiber, high fat/carbohydrate diet can lead to gut dysbiosis (67), attenuating the immune system. Studies have demonstrated that

dietary carbohydrates (68), certain probiotics (69), artificial sweeteners (70), and emulsifiers (71) could weaken immunity responses and cause inflammation in mice. Also, high-sugar diet consumption may rises the pro-inflammatory regulation of body, negatively affects

genus *Lachnobacterium*, disrupting balanced mucosal, and finally resulting in systemic inflammation (72) While a diet rich in saturated fats reduces the beneficial microbes such as *Bifidobacterium* or *Faecalibacterium* in the human gastrointestinal tract, unsaturated fats can reduce harmful microbes, including *Escherichia* and *Streptococcus* (73).

Probiotics can work with different immune cells and have important role in balance of immunogenic homeostasis of gastrointestinal tract (74). Another function of probiotics includes maintaining intestine pH, which impacts the composition of the microbial communities present in the gastrointestinal tract and lowers the invasion by the pathogens. Furthermore, probiotics act as prophylaxis and have the potential for adjunct therapy in individuals suffering from COVID-19 (75). Consumption of prebiotics such as polydextrose, inulin and maize fiber in elderly individuals can progress the immunity, digestion and gut microbiota diversity (76). It has been reported that dietary fibers and prebiotics may rise the short-chain fatty acids of butyrate, propionate and acetate which can stimulate the growth of bacterial species such as *Bifidobacteria* and *Lactobacilli* (77). Furthermore, microbiome composition and immunity are also affected by diet timing (78). Collado et al. concluded that taking meal at 17:30 instead of 14:30 (as late meal) is associated with the presence of pathobiont microbiota (79).

The foods full of probiotics, fruits, vegetables, legumes and grains as anti-inflammatory, balanced and healthy diets are the primary modulators in protecting the immune response and healthy gut microbiome (80). Beside probiotics, it has been reported that anti-inflammatory regimen can improve viral respiratory disease (80). The Mediterranean diet is well known as anti-inflammatory diet. This diet is reduced meat consumption as well as full of legumes, fruit, whole grains, vegetables, olive oil and fish. Indeed essential vitamins and minerals have immunomodulatory and anti-inflammatory property (81). The foods containing of bioactive polyphenols have anti-thrombotic, anti-inflammatory and antioxidant properties. Mediterranean diet has been recommended for treatment of COVID-19 infection (82-84). Also zinc, vitamin D, garlic, omega 3 fatty acids, vitamin C, onion, ginger, and saffron have anti-inflammatory have shown potential in their anti-inflammatory effects (85).

### 3. Conclusions

While widespread vaccination has been helping to reduce COVID-19 casualties, this new variant seems to

pass the immune system making vaccination less effective. After introducing the vaccine, people quit other helpful interventions such as diet and physical activity practice, hoping for the vaccine effectiveness. However, relying on the vaccine alone cannot guarantee immunity. To this end, we highlight the importance of staying active and having a healthy/enriched diet along with vaccination to help us fighting more effectively against Omicron.

#### 3.1. Highlights

Foods with anti-inflammatory properties can be used for treating and preventing viral respiratory disease.

The Mediterranean diet is well known as anti-inflammatory diet.

Moderate intensity training have beneficial effects on immune system in COVID-19.

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### Footnotes

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### References

- Rossler A, Riepler L, Bante D, von Laer D, Kimpel J. SARS-CoV-2 Omicron Variant Neutralization in Serum from Vaccinated and Convalescent Persons. *N Engl J Med*. 2022;**386**(7):698-700. [PubMed ID: 35021005]. [PubMed Central ID: PMC8781314]. <https://doi.org/10.1056/NEJMc2119236>.
- Ferre VM, Peiffer-Smadja N, Visseaux B, Descamps D, Ghosn J, Charpentier C. Omicron SARS-CoV-2 variant: What we know and what we don't. *Anaesth Crit Care Pain Med*. 2022;**41**(1):100998. [PubMed ID: 34902630]. [PubMed Central ID: PMC8660660]. <https://doi.org/10.1016/j.accpm.2021.100998>.

3. Gu H, Krishnan P, Ng DYM, Chang LDJ, Liu GYZ, Cheng SSM, et al. Probable Transmission of SARS-CoV-2 Omicron Variant in Quarantine Hotel, Hong Kong, China, November 2021. *Emerg Infect Dis.* 2022;**28**(2):460–2. [PubMed ID: 34860154]. [PubMed Central ID: PMC8798678]. <https://doi.org/10.3201/eid2802.212422>.
4. Khandia R, Singhal S, Alqahtani T, Kamal MA, El-Shall NA, Nainu F, et al. Emergence of SARS-CoV-2 Omicron (B.1.1.529) variant, salient features, high global health concerns and strategies to counter it amid ongoing COVID-19 pandemic. *Environ Res.* 2022;**209**:112816. [PubMed ID: 35093310]. [PubMed Central ID: PMC8798788]. <https://doi.org/10.1016/j.envres.2022.112816>.
5. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. *Nature.* 2020;**581**(7807):215–20. [PubMed ID: 3225176]. <https://doi.org/10.1038/s41586-020-2180-5>.
6. Yan R, Zhang Y, Li Y, Xia L, Guo Y, Zhou Q. Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2. *Science.* 2020;**367**(6485):1444–8. [PubMed ID: 32132184]. [PubMed Central ID: PMC7164635]. <https://doi.org/10.1126/science.abb2762>.
7. Licita BN, Millet JK, Regan AD, Hamilton BS, Rinaldi VD, Duhamel GE, et al. Mutation in spike protein cleavage site and pathogenesis of feline coronavirus. *Emerg Infect Dis.* 2013;**19**(7):1066–73. [PubMed ID: 23763835]. [PubMed Central ID: PMC3713968]. <https://doi.org/10.3201/eid1907.121094>.
8. Accorsi EK, Britton A, Fleming-Dutra KE, Smith ZR, Shang N, Derado G, et al. Association Between 3 Doses of mRNA COVID-19 Vaccine and Symptomatic Infection Caused by the SARS-CoV-2 Omicron and Delta Variants. *JAMA.* 2022;**327**(7):639–51. [PubMed ID: 35060999]. [PubMed Central ID: PMC8848203]. <https://doi.org/10.1001/jama.2022.0470>.
9. Cameron E, Bowen JE, Rosen LE, Saliba C, Zepeda SK, Culp K, et al. Broadly neutralizing antibodies overcome SARS-CoV-2 Omicron antigenic shift. *Nature.* 2022;**602**(7898):664–70. [PubMed ID: 35016195]. [PubMed Central ID: PMC9531318]. <https://doi.org/10.1038/s41586-021-04386-2>.
10. Hui KPY, Ho JCW, Cheung MC, Ng KC, Ching RHH, Lai KL, et al. SARS-CoV-2 Omicron variant replication in human bronchus and lung ex vivo. *Nature.* 2022;**603**(7902):715–20. [PubMed ID: 35104836]. <https://doi.org/10.1038/s41586-022-04479-6>.
11. Grifoni A, Sidney J, Vita R, Peters B, Crotty S, Weiskopf D, et al. SARS-CoV-2 human T cell epitopes: Adaptive immune response against COVID-19. *Cell Host Microbe.* 2021;**29**(7):1076–92. [PubMed ID: 34237248]. [PubMed Central ID: PMC8139264]. <https://doi.org/10.1016/j.chom.2021.05.010>.
12. Goldberg Y, Mandel M, Bar-On YM, Bodenheimer O, Freedman LS, Ash N, et al. Protection and Waning of Natural and Hybrid Immunity to SARS-CoV-2. *N Engl J Med.* 2022;**386**(23):2201–12. [PubMed ID: 35613036]. [PubMed Central ID: PMC9165562]. <https://doi.org/10.1056/NEJMoa2118946>.
13. Kozlov M. Waning COVID super-immunity raises questions about Omicron. *Nature.* 2021. [PubMed ID: 34907367]. <https://doi.org/10.1038/d41586-021-03674-1>.
14. Ao D, Lan T, He X, Liu J, Chen L, Baptista-Hon DT, et al. SARS-CoV-2 Omicron variant: Immune escape and vaccine development. *MedComm (2020).* 2022;**3**(1). e126. [PubMed ID: 35317190]. [PubMed Central ID: PMC8925644]. <https://doi.org/10.1002/mco2.126>.
15. Angius L, Pageaux B, Hopker J, Marcora SM, Mauger AR. Transcranial direct current stimulation improves isometric time to exhaustion of the knee extensors. *Neuroscience.* 2016;**339**:363–75. [PubMed ID: 27751960]. <https://doi.org/10.1016/j.neuroscience.2016.10.028>.
16. Rydzynski Moderbacher C, Ramirez SI, Dan JM, Grifoni A, Hastie KM, Weiskopf D, et al. Antigen-Specific Adaptive Immunity to SARS-CoV-2 in Acute COVID-19 and Associations with Age and Disease Severity. *Cell.* 2020;**183**(4):996–1012 e19. [PubMed ID: 33010815]. [PubMed Central ID: PMC7494270]. <https://doi.org/10.1016/j.cell.2020.09.038>.
17. Liao M, Liu Y, Yuan J, Wen Y, Xu G, Zhao J, et al. Single-cell landscape of bronchoalveolar immune cells in patients with COVID-19. *Nat Med.* 2020;**26**(6):842–4. [PubMed ID: 32398875]. <https://doi.org/10.1038/s41591-020-0901-9>.
18. Khoramipour K, Basereh A, Hekmatikar AA, Castell L, Ruhee RT, Suzuki K. Physical activity and nutrition guidelines to help with the fight against COVID-19. *J Sports Sci.* 2021;**39**(1):101–7. [PubMed ID: 32842905]. <https://doi.org/10.1080/02640414.2020.1807089>.
19. de Faria Coelho-Ravagnani C, Corgosinho FC, Sanches FFZ, Prado CMM, Laviano A, Mota JF. Dietary recommendations during the COVID-19 pandemic. *Nutr Rev.* 2021;**79**(4):382–93. [PubMed ID: 32653930]. [PubMed Central ID: PMC7454801]. <https://doi.org/10.1093/nutrit/nuaa067>.
20. Barrea L, Grant WB, Frias-Toral E, Vetrani C, Verde L, de Alteriis G, et al. Dietary Recommendations for Post-COVID-19 Syndrome. *Nutrients.* 2022;**14**(6). [PubMed ID: 35334962]. [PubMed Central ID: PMC8954128]. <https://doi.org/10.3390/nu14061305>.
21. Calder PC. Nutrition and immunity: lessons for COVID-19. *Nutr Diabetes.* 2021;**11**(1):19. [PubMed ID: 34168111]. [PubMed Central ID: PMC8223524]. <https://doi.org/10.1038/s41387-021-00165-0>.
22. Federighi Baisi Chagas E, Biteli P, Moreira Candeloro B, Angelo Rodrigues M, Henrique Rodrigues P. Physical exercise and COVID-19: a summary of the recommendations. *AIMS Bioeng.* 2020;**7**(4):236–41. <https://doi.org/10.3934/bioeng.2020020>.
23. Xu Z, Chen Y, Yu D, Mao D, Wang T, Feng D, et al. The effects of exercise on COVID-19 therapeutics: A protocol for systematic review and meta-analysis. *Medicine (Baltimore).* 2020;**99**(38). e22345. [PubMed ID: 32957405]. [PubMed Central ID: PMC7505377]. <https://doi.org/10.1097/MD.00000000000022345>.
24. Fallon K. Exercise in the time of COVID-19. *Aust J Gen Pract.* 2020;**49**. [PubMed ID: 32321207]. <https://doi.org/10.31128/AJGP-COVID-13>.
25. Hekmatikar AHA, Shamsi MM, Ashkazari ZSZ, Suzuki K. Exercise in an Overweight Patient with Covid-19: A Case Study. *Int J Environ Res Public Health.* 2021;**18**(11). [PubMed ID: 34070847]. [PubMed Central ID: PMC8199307]. <https://doi.org/10.3390/ijerph18115882>.
26. Molanouri Shamsi M, Vahed A, Hekmatikar AA, Suzuki K. Combined Effects of Exercise Training and Nutritional Supplementation in Cancer Patients in the Context of the COVID-19: A Perspective Study. *Front Nutr.* 2022;**9**:847215. [PubMed ID: 35356739]. [PubMed Central ID: PMC8959344]. <https://doi.org/10.3389/fnut.2022.847215>.
27. Suzuki K, Hayashida H. Effect of Exercise Intensity on Cell-Mediated Immunity. *Sports (Basel).* 2021;**9**(1). [PubMed ID: 33440732]. [PubMed Central ID: PMC7826544]. <https://doi.org/10.3390/sports9010008>.
28. Gimenes Marfori BC, Barbosa de Lira CA, Vancini RL, Nikolaidis PT, Knechtle B, Santos Andrade M. Association between lowering restriction levels during the coronavirus outbreak and physical activity among adults: a longitudinal observational study in Brazil. *Eur Rev Med Pharmacol Sci.* 2022;**26**(9):377–85. [PubMed ID: 35587092]. [https://doi.org/10.26355/eurrev\\_202205\\_28759](https://doi.org/10.26355/eurrev_202205_28759).
29. Zhang NN, Zhang RR, Zhang YF, Ji K, Xiong XC, Qin QS, et al. Rapid development of an updated mRNA vaccine against the SARS-CoV-2 Omicron variant. *Cell Res.* 2022;**32**(4):401–3. [PubMed ID: 35165421]. [PubMed Central ID: PMC8853430]. <https://doi.org/10.1038/s41422-022-00626-w>.
30. Ahmadi Hekmatikar AH, Ferreira Junior JB, Shahrbanian S, Suzuki K. Functional and Psychological Changes after Exercise Training in Post-COVID-19 Patients Discharged from the Hospital: A PRISMA-Compliant Systematic Review. *Int J Environ Res Public Health.* 2022;**19**(4). [PubMed ID: 35206483]. [PubMed Central ID: PMC8871540]. <https://doi.org/10.3390/ijerph19042290>.
31. Gleeson M, Bishop N, Walsh N. *Exercise immunology.* Routledge; 2013.
32. Improta-Caria AC, Soci UPR, Pinho CS, Aras Junior R, De

- Sousa RAL, Bessa TCB. Physical Exercise and Immune System: Perspectives on the COVID-19 pandemic. *Rev Assoc Med Bras (1992)*. 2021;**67**Suppl 1(Suppl 1):102-7. [PubMed ID: 34259761]. <https://doi.org/10.1590/j806-9282.67.Suppl1.20200673>.
33. da Silveira MP, da Silva Fagundes KK, Bizuti MR, Starck E, Rossi RC, de Resende ED. Physical exercise as a tool to help the immune system against COVID-19: an integrative review of the current literature. *Clin Exp Med*. 2021;**21**(1):15-28. [PubMed ID: 32728975]. [PubMed Central ID: PMC7387807]. <https://doi.org/10.1007/s10238-020-00650-3>.
  34. Agha-Alinejad H, Ahmadi Hekmatikar AH, Ruhee RT, Shamsi MM, Rahmati M, Khoramipour K, et al. A Guide to Different Intensities of Exercise, Vaccination, and Sports Nutrition in the Course of Preparing Elite Athletes for the Management of Upper Respiratory Infections during the COVID-19 Pandemic: A Narrative Review. *Int J Environ Res Public Health*. 2022;**19**(3). [PubMed ID: 35162910]. [PubMed Central ID: PMC8835175]. <https://doi.org/10.3390/ijerph19031888>.
  35. Cao M, Li S, Tang Y, Zou Y. A Meta-Analysis of High-Intensity Interval Training on Glycolipid Metabolism in Children With Metabolic Disorders. *Front Pediatr*. 2022;**10**:887852. [PubMed ID: 35633975]. [PubMed Central ID: PMC9133662]. <https://doi.org/10.3389/fped.2022.887852>.
  36. Hammami A, Harrabi B, Mohr M, Krustup P. Physical activity and coronavirus disease 2019 (COVID-19): specific recommendations for home-based physical training. *Manag Sport Leis*. 2020;**27**(1-2):26-31. <https://doi.org/10.1080/23750472.2020.1757494>.
  37. Clemente-Suarez VJ, Beltran-Velasco AI, Ramos-Campo DJ, Mielgo-Ayuso J, Nikolaidis PA, Belando N, et al. Physical activity and COVID-19. The basis for an efficient intervention in times of COVID-19 pandemic. *Physiol Behav*. 2022;**244**:113667. [PubMed ID: 34861297]. [PubMed Central ID: PMC8632361]. <https://doi.org/10.1016/j.physbeh.2021.113667>.
  38. Burdette J. *Weights of The World: An Examination of the Evolutionary Histories of the Atlas Stone and Gada, and the Philosophy of Resistance Training*. University of California, Irvine; 2019.
  39. Siekirk NJ. *The Effect of Treadmill vs. NuStep Recumbent Cross Trainer in Gait and Lower Extremity Electromyography after Chronic Stroke*. Wayne State University; 2018.
  40. Jesus I, Vanhee V, Deramautd TB, Bonay M. Promising effects of exercise on the cardiovascular, metabolic and immune system during COVID-19 period. *J Hum Hypertens*. 2021;**35**(1):1-3. [PubMed ID: 32943741]. [PubMed Central ID: PMC7495974]. <https://doi.org/10.1038/s41371-020-00416-0>.
  41. Scudiero O, Lombardo B, Brancaccio M, Mennitti C, Cesaro A, Fimiani F, et al. Exercise, Immune System, Nutrition, Respiratory and Cardiovascular Diseases during COVID-19: A Complex Combination. *Int J Environ Res Public Health*. 2021;**18**(3). [PubMed ID: 33494244]. [PubMed Central ID: PMC7908487]. <https://doi.org/10.3390/ijerph18030904>.
  42. Sacma M, Geiger H. Exercise generates immune cells in bone. *Nature*. 2021;**591**(7850):371-2. [PubMed ID: 33627859]. <https://doi.org/10.1038/d41586-021-00419-y>.
  43. Yoon KJ, Ahn A, Park SH, Kwak SH, Kwak SE, Lee W, et al. Exercise reduces metabolic burden while altering the immune system in aged mice. *Aging (Albany NY)*. 2021;**13**(1):1294-313. [PubMed ID: 33406502]. [PubMed Central ID: PMC7834985]. <https://doi.org/10.18632/aging.202312>.
  44. Simpson RJ, Pawelec G. Is mechanical loading essential for exercise to preserve the aging immune system? *Immun Ageing*. 2021;**18**(1):26. [PubMed ID: 34090455]. [PubMed Central ID: PMC8178824]. <https://doi.org/10.1186/s12979-021-00238-9>.
  45. Moghadam MT, Taati B, Paydar Ardakani SM, Suzuki K. Ramadan Fasting During the COVID-19 Pandemic; Observance of Health, Nutrition and Exercise Criteria for Improving the Immune System. *Front Nutr*. 2020;**7**:570235. [PubMed ID: 33521030]. [PubMed Central ID: PMC7838371]. <https://doi.org/10.3389/fnut.2020.570235>.
  46. do Brito Valente AF, Jaspers RT, Wust RC. Regular physical exercise mediates the immune response in atherosclerosis. *Exerc Immunol Rev*. 2021;**27**:42-53. [PubMed ID: 33965897].
  47. Papp G, Szabo K, Jambor I, Mile M, Berki AR, Arany AC, et al. Regular Exercise May Restore Certain Age-Related Alterations of Adaptive Immunity and Rebalance Immune Regulation. *Front Immunol*. 2021;**12**:639308. [PubMed ID: 33936054]. [PubMed Central ID: PMC8085426]. <https://doi.org/10.3389/fimmu.2021.639308>.
  48. Suzuki K. Chronic Inflammation as an Immunological Abnormality and Effectiveness of Exercise. *Biomolecules*. 2019;**9**(6). [PubMed ID: 31181700]. [PubMed Central ID: PMC6628010]. <https://doi.org/10.3390/biom9060223>.
  49. Baker FL, Simpson RJ. Exercise to support optimal immune function. *ACSMs Health Fit J*. 2021;**25**(1):5-8. <https://doi.org/10.1249/FIT.0000000000000628>.
  50. Jee YS. Acquired immunity and moderate physical exercise: 5th series of scientific evidence. *J Exerc Rehabil*. 2021;**17**(1):2-3. [PubMed ID: 33728281]. [PubMed Central ID: PMC7939985]. <https://doi.org/10.12965/jer.2142042.021>.
  51. Valizadeh R, Karampour S, Saiiari A, Sadeghi S. The effect of one bout submaximal endurance exercise on the innate and adaptive immune responses of hypertensive patients. *J Sports Med Phys Fitness*. 2022;**62**(2):244-9. [PubMed ID: 34028235]. <https://doi.org/10.23736/S0022-4707.21.11941-3>.
  52. Oh S, Chun S, Hwang S, Kim J, Cho Y, Lee J, et al. Vitamin D and Exercise Are Major Determinants of Natural Killer Cell Activity, Which Is Age- and Gender-Specific. *Front Immunol*. 2021;**12**:594356. [PubMed ID: 34248925]. [PubMed Central ID: PMC8261050]. <https://doi.org/10.3389/fimmu.2021.594356>.
  53. Córdova Martínez A, Pérez-Valdecantos D, Caballero-García A, Sarabia JM, Roche E. Effect of exercise in the recovery process after the inflammation process caused by coronavirus. *J Hum Sport Exerc*. 2023;**18**(1):83-96. <https://doi.org/10.14198/jhse.2023.181.08>.
  54. Rahayu UB, Rahman F, Setiyadi NA, Azizan A. Exercise and physical health in survivors of COVID-19: A scoping review. *J Med Chem Sci*. 2021;**4**(2):154-62. <https://doi.org/10.26655/JMCHEMSCI.2021.2.6>.
  55. Domin R, Dadej D, Pytka M, Zybek-Kocik A, Ruchala M, Guzik P. Effect of Various Exercise Regimens on Selected Exercise-Induced Cytokines in Healthy People. *Int J Environ Res Public Health*. 2021;**18**(3). [PubMed ID: 33572495]. [PubMed Central ID: PMC7908590]. <https://doi.org/10.3390/ijerph18031261>.
  56. Fonseca TR, Mendes TT, Ramos GP, Cabido CET, Morandi RE, Ferraz FO, et al. Aerobic Training Modulates the Increase in Plasma Concentrations of Cytokines in response to a Session of Exercise. *J Environ Public Health*. 2021;**2021**:1304139. [PubMed ID: 33510799]. [PubMed Central ID: PMC7826215]. <https://doi.org/10.1155/2021/1304139>.
  57. Scheffer DDL, Latini A. Exercise-induced immune system response: Anti-inflammatory status on peripheral and central organs. *Biochim Biophys Acta Mol Basis Dis*. 2020;**1866**(10):165823. [PubMed ID: 32360589]. [PubMed Central ID: PMC7188661]. <https://doi.org/10.1016/j.bbdis.2020.165823>.
  58. Scartoni FR, Sant'Ana LO, Murillo-Rodriguez E, Yamamoto T, Imperatori C, Budde H, et al. Physical Exercise and Immune System in the Elderly: Implications and Importance in COVID-19 Pandemic Period. *Front Psychol*. 2020;**11**:593903. [PubMed ID: 33329256]. [PubMed Central ID: PMC7711129]. <https://doi.org/10.3389/fpsyg.2020.593903>.
  59. Simpson RJ, Campbell JP, Gleeson M, Kruger K, Nieman DC, Pyne DB, et al. Can exercise affect immune function to increase susceptibility to infection? *Exerc Immunol Rev*. 2020;**26**:8-22. [PubMed ID: 32139352].
  60. Aktuğ ZB, İri R, Aktuğ Demir N. COVID-19 immune

- system and exercise. *J Hum Sci.* 2020;**17**(2):513–20. <https://doi.org/10.14687/jhs.v17i2.6005>.
61. Wang J, Liu S, Li G, Xiao J. Exercise Regulates the Immune System. *Adv Exp Med Biol.* 2020;**1228**:395–408. [PubMed ID: 32342473]. [https://doi.org/10.1007/978-981-15-1792-1\\_27](https://doi.org/10.1007/978-981-15-1792-1_27).
  62. Yildizgoren MT. How Exercise May Affect The Immune System Against COVID-19? *Turk J Sports Med.* 2020;**55**(2):186–7. <https://doi.org/10.5152/tjism.2020.189>.
  63. Zheng D, Liwinski T, Elinav E. Interaction between microbiota and immunity in health and disease. *Cell Res.* 2020;**30**(6):492–506. [PubMed ID: 32433595]. [PubMed Central ID: PMC7264227]. <https://doi.org/10.1038/s41422-020-0332-7>.
  64. Chaari A, Bendriss G, Zakaria D, McVeigh C. Importance of Dietary Changes During the Coronavirus Pandemic: How to Upgrade Your Immune Response. *Front Public Health.* 2020;**8**:476. [PubMed ID: 32984253]. [PubMed Central ID: PMC7481450]. <https://doi.org/10.3389/fpubh.2020.00476>.
  65. Pan L, Mu M, Yang P, Sun Y, Wang R, Yan J, et al. Clinical Characteristics of COVID-19 Patients With Digestive Symptoms in Hubei, China: A Descriptive, Cross-Sectional, Multicenter Study. *Am J Gastroenterol.* 2020;**115**(5):766–73. [PubMed ID: 32287140]. [PubMed Central ID: PMC7172492]. <https://doi.org/10.14309/ajg.0000000000000620>.
  66. Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. *BMJ.* 2018;**361**:k2179. [PubMed ID: 29899036]. [PubMed Central ID: PMC6000740]. <https://doi.org/10.1136/bmj.k2179>.
  67. Trompette A, Gollwitzer ES, Yadava K, Sichelstiel AK, Sprenger N, Ngom-Bru C, et al. Gut microbiota metabolism of dietary fiber influences allergic airway disease and hematopoiesis. *Nat Med.* 2014;**20**(2):159–66. [PubMed ID: 24390308]. <https://doi.org/10.1038/nm.3444>.
  68. Arpaia N, Campbell C, Fan X, Dikiy S, van der Veeken J, deRoos P, et al. Metabolites produced by commensal bacteria promote peripheral regulatory T-cell generation. *Nature.* 2013;**504**(7480):451–5. [PubMed ID: 24226773]. [PubMed Central ID: PMC3869884]. <https://doi.org/10.1038/nature12726>.
  69. He B, Hoang TK, Wang T, Ferris M, Taylor CM, Tian X, et al. Resetting microbiota by *Lactobacillus reuteri* inhibits T reg deficiency-induced autoimmunity via adenosine A2A receptors. *J Exp Med.* 2017;**214**(1):107–23. [PubMed ID: 27994068]. [PubMed Central ID: PMC5206500]. <https://doi.org/10.1084/jem.20160961>.
  70. Rodriguez-Palacios A, Harding A, Menghini P, Himmelman C, Retuerto M, Nickerson KP, et al. The Artificial Sweetener Splenda Promotes Gut Proteobacteria, Dysbiosis, and Myeloperoxidase Reactivity in Crohn's Disease-Like Ileitis. *Inflamm Bowel Dis.* 2018;**24**(5):1005–20. [PubMed ID: 29554272]. [PubMed Central ID: PMC5950546]. <https://doi.org/10.1093/ibd/izy060>.
  71. Viennois E, Merlin D, Gewirtz AT, Chassaing B. Dietary Emulsifier-Induced Low-Grade Inflammation Promotes Colon Carcinogenesis. *Cancer Res.* 2017;**77**(1):27–40. [PubMed ID: 27821485]. [PubMed Central ID: PMC5214513]. <https://doi.org/10.1158/0008-5472.CAN-16-1359>.
  72. Satokari R. High Intake of Sugar and the Balance between Pro- and Anti-Inflammatory Gut Bacteria. *Nutrients.* 2020;**12**(5). [PubMed ID: 32397233]. [PubMed Central ID: PMC7284805]. <https://doi.org/10.3390/nu12051348>.
  73. Yang Q, Liang Q, Balakrishnan B, Belobrajdic DP, Feng QJ, Zhang W. Role of Dietary Nutrients in the Modulation of Gut Microbiota: A Narrative Review. *Nutrients.* 2020;**12**(2). [PubMed ID: 32023943]. [PubMed Central ID: PMC7071260]. <https://doi.org/10.3390/nu12020381>.
  74. Mazziotta C, Tognon M, Martini F, Torreggiani E, Rotondo JC. Probiotics Mechanism of Action on Immune Cells and Beneficial Effects on Human Health. *Cells.* 2023;**12**(1). [PubMed ID: 3661977]. [PubMed Central ID: PMC9818925]. <https://doi.org/10.3390/cells12010184>.
  75. Rajput S, Paliwal D, Naithani M, Kothari A, Meena K, Rana S. COVID-19 and Gut Microbiota: A Potential Connection. *Indian J Clin Biochem.* 2021;**36**(3):266–77. [PubMed ID: 33495676]. [PubMed Central ID: PMC7818076]. <https://doi.org/10.1007/s12291-020-00948-9>.
  76. Dhar D, Mohanty A. Gut microbiota and Covid-19-possible link and implications. *Virus Res.* 2020;**285**:198018. [PubMed ID: 32430279]. [PubMed Central ID: PMC7217790]. <https://doi.org/10.1016/j.virusres.2020.198018>.
  77. Holscher HD. Dietary fiber and prebiotics and the gastrointestinal microbiota. *Gut Microbes.* 2017;**8**(2):172–84. [PubMed ID: 28165863]. [PubMed Central ID: PMC5390821]. <https://doi.org/10.1080/19490976.2017.1290756>.
  78. Kau AL, Ahern PP, Griffin NW, Goodman AL, Gordon JI. Human nutrition, the gut microbiome and the immune system. *Nature.* 2011;**474**(7351):327–36. [PubMed ID: 21677749]. [PubMed Central ID: PMC3298082]. <https://doi.org/10.1038/nature10213>.
  79. Collado MC, Engen PA, Bandin C, Cabrera-Rubio R, Voigt RM, Green SJ, et al. Timing of food intake impacts daily rhythms of human salivary microbiota: a randomized, crossover study. *FASEB J.* 2018;**32**(4):2060–72. [PubMed ID: 29233857]. [PubMed Central ID: PMC5893176]. <https://doi.org/10.1096/fj.201700697RR>.
  80. Das G, Heredia JB, de Lourdes Pereira M, Coy-Barrera E, Rodrigues Oliveira SM, Gutierrez-Grijalva EP, et al. Korean traditional foods as antiviral and respiratory disease prevention and treatments: A detailed review. *Trends Food Sci Technol.* 2021;**116**:415–33. [PubMed ID: 34345117]. [PubMed Central ID: PMC8321624]. <https://doi.org/10.1016/j.tifs.2021.07.037>.
  81. Razquin C, Martinez-Gonzalez MA. A Traditional Mediterranean Diet Effectively Reduces Inflammation and Improves Cardiovascular Health. *Nutrients.* 2019;**11**(8). [PubMed ID: 31395816]. [PubMed Central ID: PMC6723673]. <https://doi.org/10.3390/nu11081842>.
  82. Zabetakis I, Lordan R, Norton C, Tsoupras A. COVID-19: The Inflammation Link and the Role of Nutrition in Potential Mitigation. *Nutrients.* 2020;**12**(5). [PubMed ID: 32438620]. [PubMed Central ID: PMC7284818]. <https://doi.org/10.3390/nu12051466>.
  83. Angelidi AM, Kokkinos A, Katechaki E, Ros E, Mantzoros CS. Mediterranean diet as a nutritional approach for COVID-19. *Metabolism.* 2021;**114**:154407. [PubMed ID: 33080270]. [PubMed Central ID: PMC7833284]. <https://doi.org/10.1016/j.metabol.2020.154407>.
  84. Ling V, Zabetakis I. The Role of an Anti-Inflammatory Diet in Conjunction to COVID-19. *Diseases.* 2021;**9**(4). [PubMed ID: 34842636]. [PubMed Central ID: PMC8628803]. <https://doi.org/10.3390/diseases9040076>.
  85. Vahid F, Rahmani D. Can an anti-inflammatory diet be effective in preventing or treating viral respiratory diseases? A systematic narrative review. *Clin Nutr ESPEN.* 2021;**43**:9–15. [PubMed ID: 34024569]. [PubMed Central ID: PMC9587761]. <https://doi.org/10.1016/j.clnesp.2021.04.009>.