Original Article

Study of the Antitumor Activity of Selenium Nanoparticles

Arina Romanovna Maslyakova[1], Sabina Arturovna Magomedova[1], Islam Nazirovich Romantsov[1], Sharip Magomedrasulovich Nurbagandov[1]*, Mikhail Nikolaevich Bulovin[1], Oleg Rodionovich Podobin[1]

[1]*Department of Therapy, Faculty of Medicine, Stavropol State Medical University, Stavropol, Russia.*

Abstract

In the scientific literature, studies on the feasibility of using selenium nanoparticles in the development of pharmaceuticals are widely presented. The positive effects of selenium in the treatment of cancer, hepatitis C, thyroid disease, cardiovascular disease, asthma, and other diseases have been studied. This scientific paper presents the results of studies on the effect of selenium nanoparticles on the development of a cancerous tumor. The experiment was carried out on five groups of white laboratory mice, with group 1 (positive control) being healthy individuals; group 2 (negative control) - individuals infected with EPNT-5 cancer cells; group 3 (experiment) - infected individuals that received an injection of selenium nanoparticles; group 4 (experiment) - infected individuals that received an injection of selenium nanoparticles and immunoglobulin imG; group 5 (experiment) - infected individuals who received an injection of immunoglobulin imG. During the experiment, the development of the disease and the behavior of laboratory animals were monitored. After 4 weeks, blood was taken for a general and biochemical test, and the masses of the internal organs of laboratory mice were also examined.

Keywords: *Selenium nanoparticles, Cancer, EPNT-5, Immunoglobulin ImG*

Introduction

Selenium deficiency causes a large number of diseases in humans, animals, and birds [1]. In animals and birds - white muscle disease, toxic liver dystrophy, encephalomalacia, exudative diathesis, depression, retained placenta, and pancreatic fibrosis [2-4].

Selenium provides activity, redox enzymes, and vitamins; immunological resistance, but in addition, antioxidant protection of the body [5-8].

Selenium is considered an essential trace element in the life of animals and humans. The positive effect of selenium in the treatment of cancer, hepatitis C, diabetes, cerebrovascular insufficiency, Alzheimer's disease, poisoning with salts of heavy metals, thyroid diseases, cardiovascular diseases, asthma, and other diseases has been more studied [9-13]. The use of selenium compounds as growth stimulants, antioxidants, and restorers of the enzymatic functions of the liver and brain is also being studied [14, 15]. It was confirmed that selenium nanoparticles are capable of exerting their action permanently, unlike antibiotics [16-18].

Selenium nanoparticles affect biological objects at the cellular level, introducing their excess energy, which increases the effectiveness of the processes taking place in plants, i.e. are considered bioactive substances [19-21].

It is known that with a low concentration of selenium in the body, the chance of developing oncological diseases increases [22-24]. It has been established that in areas with a higher content of selenium in the soil, the data on the incidence of cancer of the rectum, lungs, and cervix are significantly lower [25]. Moderate intake of selenium is one of the main values in maintaining the balance of expression of most selenium-dependent and selenium-independent microsomal enzymes that ensure the biotransformation of xenobiotics. Basically, selenium is the most important gene protector that blocks DNA damage by peroxidation products and metals and regulates the processes of their systemic elimination in a living organism [26]. The possibilities of using nanoparticles in the development of pharmaceutical preparations are widely discussed in the literature.

It has been studied that selenium nanoparticles show high antitumor activity,

How to cite this article: Maslyakova AR, Magomedova SA, Romantsov IN, Nurbagandov SM, Bulovin MN, Podobin OR. Study of the Antitumor Activity of Selenium Nanoparticles. Clin Cancer Investig J. 2023;12(1):43-7. https://doi.org/10.51847/yt84akUBr0

Address for correspondence:
Sharip Magomedrasulovich Nurbagandov,
Department of Therapy, Faculty of Medicine, Stavropol State Medical University, Stavropol, Russia.
E-mail:
ruslankalmykov777@yandex.ru

Access this article online

Website: www.ccij-online.org

DOI: 10.51847/yt84akUBr0

Quick Response Code:

and they can act in combination with other agents for cancer chemotherapy [27]. Some mechanisms of antitumor activity have been confirmed. It has been shown that the antitumor effects of selenium nanoparticles are explained by their ability to inhibit the growth of cancer cells by inducing cell cycle arrest, inducing apoptosis, and activating autophagy [28, 29]. In addition to the original anticancer efficacy, selenium nanoparticles provide the best selectivity between normal and cancer cells.

Materials and Methods

The studies were carried out on five groups of laboratory animals (white mice). Each group included five clinically healthy individuals with standard weight and size, aged from 1.5 to 2 months.

The object of the study was laboratory animals (mice) inoculated with cancer cells (EPNT-5).

Group 1 - positive control, clinically healthy animals;
Group 2 - Negative control, cancer cells (EPNT-5) were injected subcutaneously into the withers;
Group 3 - experimental group, which received an injection with a solution of nano-selenium (0.75 mg/ml) intraperitoneally, 1 time immediately after the injection of cancer cells (EPNT-5);
Group 4 - experimental group, which received an injection with a solution of nano-selenium (0.75 mg/ml) and immunoglobulin imG intraperitoneally, 1 time immediately after the introduction of the cell line (EPNT-5);
Group 5 - experimental group, which received an injection of immunoglobulin imG intraperitoneally, 1 time immediately after the injection of cancer cells (EPNT-5).

The studies were carried out following the "Rules of Laboratory Practice in the Russian Federation" (Order of the Ministry of Health of the Russian Federation No. 708n dated August 23, 2010). Animal experiments were carried out in accordance with the rules adopted by the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.

The subject of the study was selenium nanoparticles, which were introduced to assess their antitumor activity. ImG immunoglobulin was also additionally used.

All animals were subjected to examination, which included clinical, microbiological, and laboratory studies.

Preparation and injection of cancer cells (EPNT-5)

Observing safety precautions, we centrifuge the tube with the cell line for 5 minutes at 2500 rpm, then, observing sterility, remove the supernatant to 2 ml, and resuspend the sediment without bubbles. Cell suspension with a concentration of 10^{-7} is taken into a syringe and injected subcutaneously. Groups without administration of immunoglobulin imG are administered 100 µl per animal in accordance with [30]. Groups with immunoglobulin imG are injected with 200 µl per animal.

Premedication

Before the introduction of immunoglobulin imG, premedication is carried out (Dimedrol, Analgin, and Prednisolone).

We introduce prednisolone intramuscularly 10 µl for 1 laboratory mouse, solutions of dipyrone and diphenhydramine are collected in one insulin syringe and injected 20 µl each. per animal intramuscularly, observing safety precautions.

Introduction of immunoglobulin imG

ImG immunoglobulin is administered intraperitoneally, the dose in solution at a concentration (50 mg/ml) is 100 µl. per animal at the rate of 400 mcg/kg of body weight.

Synthesis of selenium nanoparticles from dichlorodiacetophenonyl selenide

Pour 500 ml of isopropyl alcohol into a glass flask, then add 57.72 g of polyvinylpyrrolidone. We put it in the mixer at a temperature of 50 degrees. After complete mixing, 28.86 g of dichlorodiacetophenonyl selenide is added, the mixture is stirred at 1000 rpm [31]. After 40 minutes, and the resulting solution is brought to 2000 ml with distilled water.

Next, the resulting solution is put to freeze in the freezer and then sent to freeze-drying. The size of Se nanoparticles was 1-2 nm.

Preparation and introduction of a solution of selenium nanoparticles

To prepare the solution, we take 0.0175 grams of selenium nanoparticles and 10 ml of distilled water. We inject 100 µl of nano-selenium solution per mouse (intraperitoneally), which corresponds to 7 mg/kg of body weight [32].

Equipment

During the research, the following modern equipment was used: magnetic stirrer, freeze-drying, pipette dispenser, laboratory centrifuge Sigma-202MK Refrigerated, Sigma (USA); MicroCC-20 Plus (veterinary) - automatic hematology analyzer for 20 parameters with differentiation of leukocytes into 3 populations and construction of 3 histograms; analytical balance Explorer Pro EP214C, Ohaus Europe (Switzerland); laboratory electronic scales VK-300, manufactured by CJSC Massa-K (Russia) and other devices.

Results and Discussion

During the administration of the drugs, the mice showed no visible reaction or anxiety [33]. No changes were observed within 14 days. On the 15th day of the study, formations were found in groups 2, 3, 4. In group 5, no obvious changes were observed.

Group 2 had the most pronounced formations. The dimension ranged from 0.4 to 1.6 cm in diameter. The shape is round, the borders are even and clear **(Figure 1)**.

Figure 1. Neoplasms in group 2 mice. Day 15.

In group 3, the percentage of formations was significantly less compared to the control group 2. Formations of a round shape with decorated edges. Their dimension varied from 4 to 8 mm.

Group 4 had a slightly higher percentage of education than group 3. Neoplasms had a different shapes, mostly they had a size in the range of 7-10 mm. In special cases, they reached up to 2 cm in diameter. However, the formations stood out against the background of other groups in a heterogeneous form. On day 18, education studies progressed proportionally, and evenly.

Also, one mouse from group 5 developed a neoplasm.

By the end of the experiment, it was necessary to evaluate changes in the blood and internal organs of the animals. Mice were bled by decapitation of the animal's head. After dissection, the organs were weighed, and their percentage of the total mass of animals was also compiled **(Table 1)**. Visually, in animals of group 4, the liver was paler than in other groups. A general and biochemical blood test was performed **(Tables 2 and 3)**.

Table 1. Mass of organs of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
Mouse weight	29.04±1.47	25.07±9.92	28.78±2.95	26.87±1.86	**27.77±2.82**
Heart weight	0.134±0.03	0.103±0.03	0.128±0.03	0.113±0.03	**0.113±0.03**
% heart	0.459±0.1	0.427±0.08	0.445±0.09	0.421±0.08	**0.406±0.05**
Liver weight	1.16±0.21	1.44±0.51	1.28±0.16	1.38±0.05	**1.3±0.2**
% liver	4±0.62	5.8±0.46	4.45±0.35	5.15±0.52	**4.66±0.34**
Kidney weight	0.284±0.07	0.307±0.11	0.328±0.1	0.347±0.04	**0.347±0.12**
% of kidneys	0.974±0.23	1.241±0.11	1.13±0.29	1.295±0.19	**1.233±0.3**
Spleen weight	0.084±0.02	0.217±0.12	0.106±0.05	0.187±0.08	**0.11±0.02**
% spleen	**0.289±0.05**	**1.05±0.88**	**0.367±0.15**	**0.7±0.31**	**0.4±0.06**

Table 2. General blood test of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
White blood cells, x10^9/L	1.26±0.61	4.37±3.53	1.02±0.35	2.17±0.8	**11.9±9.73**
Lymphocytes, x10^9/L	0.96±0.52	2.37±1.46	0.78±0.29	1.23±0.46	**11.63±9.45**
Content of monocytes, basophils, and eosinophils (MID), x10^9/L	0.28±0.11	1.6±1.58	0.2±0.11	0.57±0.17	**0.23±0.24**
Granulocytes, x10^9/L	0.02±0.04	0.37±0.52	0.04±0.05	0.1±0.01	**0.03±0.06**
Lymphocytes %	0.71±0.08	0.58±0.1	0.75±0.1	0.66±0.05	**0.98±0.01**
Content of monocytes, basophils, and eosinophils (MID), %	0.23±0.08	0.34±0.06	0.17±0.07	0.28±0.04	**0.02±0.01**
Granulocytes %	0.05±0.02	0.08±0.04	0.09±0.05	0.06±0.01	**0±0**
Red blood cells, x10^{12}/L	6.17±1.36	7.72±2.27	5.62±0.93	5.18±0.74	**4.97±0.86**
Hemoglobin, g/L	92.6±20.49	120±32.74	87.2±14.51	87±7.92	**75±15.9**
Mean corpuscular hemoglobin concentration, g/L	361.2±12.93	369±25.74	385.2±20.38	378±4.28	**383±10.45**
Mean concentration hemoglobin, pg	15.04±0.51	15.7±0.88	15.52±0.63	16.1±0.97	**15.1±0.69**
Mean corpuscular volume, fl	41.66±1.48	42.53±1.01	40.36±1.23	43.5±2.75	**39.5±1.42**
Red cell distribution width (RDW-CV), %	0.16±0.01	0.15±0.01	0.18±0.02	0.15±0.01	**0.14±0.01**
Red cell distribution width (RDW-SD), fl	33.06±3.54	31.77±2.73	35.44±2.7	32±4.02	**27.43±0.94**
Hematocrit, %	0.26±0.02	0.33±0.1	0.23±0.04	0.23±0.02	**0.2±0.04**

Platelets, x10^9/L	371.2±166.4	403.67±86.8	580±344.92	308.33±70.8	**378±88.23**
Mean platelet volume, fl	7.18±2.67	6.3±1.13	7±2.89	5.83±0.35	**5.2±0.2**
Relative width of platelet distribution by volume (PDW),fl	7.96±5.47	6.5±3.53	4.14±0.52	4.03±0.24	**4±0.49**
Thrombocrit, %	0.216±0.05	0.0025±0	0.01±0.01	0.0017±0	**0.002±0**
Percentage of large platelets (P-LCR), %	**0.15±0.2**	**0.112±0.11**	**0.14±0.21**	**0.047±0.03**	**0.008±0.01**

Table 3. Biochemical blood test of laboratory mice

Indicator	Group 1	Group 2	Group 3	Group 4	Group 5
Alanine Aminotransferase	34.52±4.09	44.07±29.72	49.64±8.5	49.27±33.08	**42.83±19.97**
Aspartate Aminotransferase	104.92±16.02	192.24±26.71	128.5±10.74	332.33±155.06	**160.03±39.91**
Creatinine	58.62±2.92	133.67±17.02	110.72±14.99	49.67±12.76	**89±55.57**
Urea	6.1±0.2	5.5±1.7	6.38±0.84	5.47±0.69	**6.67±0.33**
Phosphorus	**1.62±0.07**	**2.8±0.57**	**1.84±0.54**	**2.83±0.46**	**2.23±0.24**

Based on the data of **Tables 1-3** and observations, we can conclude that the most severe cases of the course of the disease are observed in groups 2 and 4. This indicates the depressing consequences of tumor development in animals of these groups.

At the same time, the use of selenium nanoparticles (group 3) reduces the likelihood of a cancerous tumor by 60%. The same trends were declared by Tian *et al*. [34], Stolzoff and Webster [35], and Spyridopoulou *et al*. [36]. In addition, the use of Immunoglobulin imG significantly reduces the likelihood of a tumor, which was also confirmed by Cervia *et al*. [37]

Conclusion

Over the past two decades, the direction of the use of nanoparticles in various fields has been actively developed, in particular, nanoparticles of various compositions can be used as medicinal substances. In various studies, it was found that selenium nanoparticles, unlike crystalline or amorphous selenium, can be absorbed by cells. Oncological diseases are currently one of the most important directions in the development of pharmaceuticals due to the widespread of these diseases and the lack of effective and safe therapy. We have established on laboratory animals that selenium nanoparticles 1-2 nm in size can be used as substances preventing the development of oncological diseases. As a result of the study, the following conclusions were drawn:

1. Selenium nanoparticles at a dosage of 7 mg/kg reduced the likelihood of developing an EPNT5 tumor by 60%.
2. ImG immunoglobulin reduces the likelihood of tumor development.
3. The combined use of selenium nanoparticles with immunoglobulin imG does not prevent tumor development.

Acknowledgments

The authors are thankful to the rector of North Ossetian State Medical Academy for providing a vivarium for the experiment.

Conflict of interest

None.

Financial support

None.

Ethics statement

The protocol for experiments with laboratory animals complied with the requirements of the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes.

References

1. Rayman MP. Selenium intake, status, and health: a complex relationship. Hormones (Athens). 2020;19(1):9-14. doi:10.1007/s42000-019-00125-5
2. Mehdi Y, Hornick JL, Istasse L, Dufrasne I. Selenium in the environment, metabolism, and involvement in body functions. Molecules. 2013;18(3):3292-311. doi:10.3390/molecules18033292
3. Zhao L, Liu M, Sun H, Yang JC, Huang YX, Huang JQ, et al. Selenium deficiency-induced multiple tissue damage with dysregulation of immune and redox homeostasis in broiler chicks under heat stress. Sci China Life Sci. 2023:1-4. doi:10.1007/s11427-022-2226-1
4. Abbas AO, Alaqil AA, Mehaisen GMK, El Sabry MI. Effect of Organic Selenium-Enriched Yeast on Relieving the Deterioration of Layer Performance, Immune Function, and Physiological Indicators Induced by Heat Stress. Front Vet Sci. 2022;9:880790. doi:10.3389/fvets.2022.880790
5. Kieliszek M. Selenium. Adv Food Nutr Res. 2021;96:417-29. doi:10.1016/bs.afnr.2021.02.019
6. Wesolowski LT, Semanchik PL, White-Springer SH. Beyond antioxidants: Selenium and skeletal muscle mitochondria. Front Vet Sci. 2022;9:1011159. doi:10.3389/fvets.2022.1011159
7. Blinov AV, Nagdalian AA, Siddiqui SA, Maglakelidze DG, Gvozdenko AA, Blinova AA, et al. Synthesis and characterization of selenium nanoparticles stabilized with cocamidopropyl betaine. Sci Rep. 2022;12(1):21975. doi:10.1038/s41598-022-25884-x
8. Shakoor H, Feehan J, Al Dhaheri AS, Ali HI, Platat C, Ismail LC, et al. Immune-boosting role of vitamins D, C, E, zinc, selenium and omega-3 fatty acids: Could they help against COVID-19? Maturitas. 2021;143:1-9. doi:10.1016/j.maturitas.2020.08.003
9. Mojadadi A, Au A, Salah W, Witting P, Ahmad G. Role for Selenium in Metabolic Homeostasis and Human Reproduction. Nutrients. 2021;13(9):3256. doi:10.3390/nu13093256
10. Khandia R, Ali Khan A, Alexiou A, Povetkin SN, Verevkina MN. Codon Usage Analysis of Pro-Apoptotic Bim Gene Isoforms. J

Alzheimers Dis. 2022;86(4):1711-25. doi:10.3233/JAD-215691
11. Méplan C, Hughes DJ. The Role of Selenium in Health and Disease: Emerging and Recurring Trends. Nutrients. 2020;12(4):1049. doi:10.3390/nu12041049
12. Ibrahim SAZ, Kerkadi A, Agouni A. Selenium and Health: An Update on the Situation in the Middle East and North Africa. Nutrients. 2019;11(7):1457. doi:10.3390/nu11071457
13. Barchielli G, Capperucci A, Tanini D. The Role of Selenium in Pathologies: An Updated Review. Antioxidants. 2022;11(2):251. doi:10.3390/antiox11020251
14. Golmohammadi R, Najar-Peerayeh S, Tohidi Moghadam T, Hosseini SM. Synergistic antibacterial activity and wound healing properties of selenium-chitosan-mupirocin nanohybrid system: an in vivo study on rat diabetic staphylococcus aureus wound infection model. Sci Rep. 2020;10(1):1-0. doi:10.1038/s41598-020-59510-5
15. Sahebari M, Rezaieyazdi Z, Khodashahi M. Selenium and Autoimmune Diseases: A Review Article. Curr Rheumatol Rev. 2019;15(2):123-34. doi:10.2174/1573397114666181016112342
16. Vahdati M, Tohidi Moghadam T. Synthesis and characterization of selenium nanoparticles-lysozyme nanohybrid system with synergistic antibacterial properties. Sci Rep. 2020;10(1):510. doi:10.1038/s41598-019-57333-7
17. Huang Z, Rose AH, Hoffmann PR. The role of selenium in inflammation and immunity: from molecular mechanisms to therapeutic opportunities. Antioxid Redox Signal. 2012;16(7):705-43. doi:10.1089/ars.2011.4145
18. Bachinina KN, Povetkin SN, Simonov AN, Pushkin SV, Blinova AA, Sukhanova ED, et al. Effects of Selenium Preparation on Morphological and Biochemical Parameters of Quail Meat. ITJEMAST. 2021;12(13):1213.
19. Mirlean N, Seus-Arrache ER, Vlasova O. Selenium deficiency in subtropical littoral pampas: environmental and dietary aspects. Environ Geochem Health. 2018;40(1):543-56. doi:10.1007/s10653-017-9951-4
20. Siddiqui SA, Blinov AV, Serov AV, Gvozdenko AA, Kravtsov AA, Nagdalian AA, et al. Effect of Selenium Nanoparticles on Germination of Hordéum Vulgáre Barley Seeds. Coatings. 2021;11(7):862. doi:10.3390/coatings11070862
21. Adhikary S, Biswas B, Chakraborty D, Timsina J, Pal S, Chandra Tarafdar J, et al. Seed priming with selenium and zinc nanoparticles modifies germination, growth, and yield of direct-seeded rice (Oryza sativa L.). Sci Rep. 2022;12(1):7103. doi:10.1038/s41598-022-11307-4
22. Vinceti M, Filippini T, Cilloni S, Crespi CM. The Epidemiology of Selenium and Human Cancer. Adv Cancer Res. 2017;136:1-48. doi:10.1016/bs.acr.2017.07.001
23. Narod SA, Huzarski T, Jakubowska A, Gronwald J, Cybulski C, Oszurek O, et al. Serum selenium level and cancer risk: a nested case-control study. Hered Cancer Clin Pract. 2019;17(1):1-7. doi:10.1186/s13053-019-0131-7
24. Sayehmiri K, Azami M, Mohammadi Y, Soleymani A, Tardeh Z. The association between Selenium and Prostate Cancer: a Systematic Review and Meta-Analysis. Asian Pac J Cancer Prev. 2018;19(6):1431-17. doi:10.22034/APJCP.2018.19.6.1431
25. Méplan C, Hesketh J. Selenium and cancer: a story that should not be forgotten-insights from genomics. Cancer Treat Res. 2014;159:145-66. doi:10.1007/978-3-642-38007-5_9
26. Rataan AO, Geary SM, Zakharia Y, Rustum YM, Salem AK. Potential Role of Selenium in the Treatment of Cancer and Viral Infections. Int J Mol Sci. 2022;23(4):2215. doi:10.3390/ijms23042215
27. Maiyo F, Singh M. Selenium nanoparticles: potential in cancer gene and drug delivery. Nanomedicine (Lond). 2017;12(9):1075-89. doi:10.2217/nnm-2017-0024
28. Fouda A, Hassan SE, Eid AM, Abdel-Rahman MA, Hamza MF. Light enhanced the antimicrobial, anticancer, and catalytic activities of selenium nanoparticles fabricated by endophytic fungal strain, Penicillium crustosum EP-1. Sci Rep. 2022;12(1):11834. doi:10.1038/s41598-022-15903-2
29. Al-Shukri AF, Al-Marzook FA, Al-Hammadi NA, Mutlag IH. Antitumor activity of alkaloid extracts from opuntia polyacantha plant using high content screening technique (Hcs). Pharmacophore. 2020;11(1):129-35.
30. Ma Z, Li J, Lin K, Ramachandran M, Zhang D, Showalter M, et al. Pharmacophore hybridisation and nanoscale assembly to discover self-delivering lysosomotropic new-chemical entities for cancer therapy. Nat commun. 2020;11(1):4615.
31. Blinov AV, Maglakelidze DG, Rekhman ZA, Yasnaya MA, Gvozdenko AA, Golik AB, et al. Investigation of the Effect of Dispersion Medium Parameters on the Aggregative Stability of Selenium Nanoparticles Stabilized with Catamine AB. Micromachines. 2023;14(2):433. doi:10.3390/mi14020433
32. O'Connell J, Porter J, Kroeplien B, Norman T, Rapecki S, Davis R, et al. Small molecules that inhibit TNF signalling by stabilising an asymmetric form of the trimer. Nat Commun. 2019;10(1):5795. doi:10.1038/s41467-019-13616-1
33. Eltokhi A, Kurpiers B, Pitzer C. Behavioral tests assessing neuropsychiatric phenotypes in adolescent mice reveal strain-and sex-specific effects. Sci Rep. 2020;10(1):1-5. doi:10.1038/s41598-020-67758-0
34. Tian J, Wei X, Zhang W, Xu A. Effects of selenium nanoparticles combined with radiotherapy on lung cancer cells. Front Bioeng Biotechnol. 2020;8:598997. doi:10.3389/fbioe.2020.59899
35. Stolzoff M, Webster TJ. Reducing bone cancer cell functions using selenium nanocomposites. J Biomed Mater Res A. 2016;104(2):476-82. doi:10.1002/jbm.a.35583
36. Spyridopoulou K, Aindelis G, Pappa A, Chlichlia K. Anticancer Activity of Biogenic Selenium Nanoparticles: Apoptotic and Immunogenic Cell Death Markers in Colon Cancer Cells. Cancers. 2021;13(21):5335. doi:10.3390/cancers13215335
37. Cervia C, Zurbuchen Y, Taeschler P, Ballouz T, Menges D, Hasler S, et al. Immunoglobulin signature predicts risk of post-acute COVID-19 syndrome. Nat Commun. 2022;13(1):446. doi:10.1038/s41467-021-27797-1