ACS NANOSCIENCE Au
AN OPEN ACCESS JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

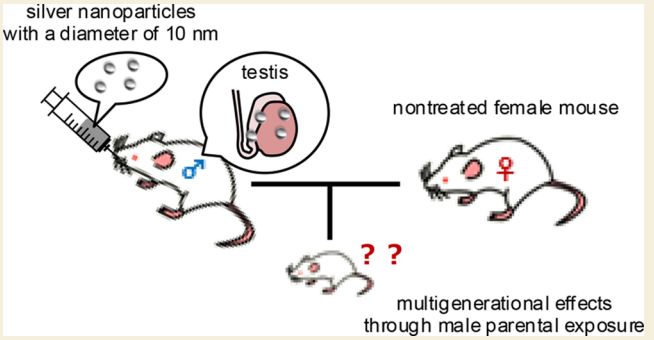
pubs.acs.org/nanoau
Letter

Orally Administered Silver Nanoparticles Are Absorbed and Migrate to Testes in Mice

Yuma Saeki,[‡] Kazuma Higashisaka,*[,‡] Rina Izutani, Jiwon Seo, Kazuki Miyaji, Yuya Haga, and Yasuo Tsutsumi*

Cite This: *ACS Nanosci. Au* 2024, 4, 317–321
Read Online

ABSTRACT: Given that daily exposure to nanoparticles is now unavoidable, there are concerns that nanoparticles have unexpected biological effects due to their small size. Here, we examined the biodistribution of silver nanoparticles, which are the most frequently used nanoparticles owing to their antibacterial activity, with a diameter of 10 nm (nAg10) to the male genital tract, and the effects of paternal treatment with nAg10 on fetal development. Male Slc:ICR male mice were orally treated with nAg10 for 14 consecutive days. Inductively coupled plasma mass spectrometry analysis detected silver in the blood and testis of male mice, but no general toxicological effects were induced. Moreover, there were no significant changes in fetal development when these treated male mice were mated with nontreated female mice. This implies that although orally ingested nAg10 is distributed to the male genital tract, it does not affect fetal development under the present treatment conditions.



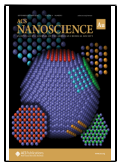
KEYWORDS: *fetal development, nanosafety, male parental exposure, silver nanoparticle, testis*

Nanoparticles are particles that measure less than 100 nm in at least one dimension. Their large specific surface area affords nanoparticles with many useful properties, and their use is currently expanding in many areas, including the cosmetics, food, and medical industries.[1,2] For example, due to their enhanced antimicrobial activity compared with conventionally sized particles, silver nanoparticles are being incorporated into food handling tools, clothing, and cosmetics, and their use in hundreds of other daily use products is being considered.[3] Given this marked increase of daily exposure, there is concern that nanoparticles may induce unexpected biological effects as a result of their small size altering their pharmacokinetics compared with those of conventionally sized particles.[4] Indeed, specific provisions for nanomaterials are now included within the European regulation on the Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH).[5] Thus, the safety of nanoparticles is of growing interest.

Fetuses and pregnant women are particularly vulnerable to exposure to chemicals and other foreign substances, and the effects of these chemicals may be passed on for several generations.[6] Our group has been conducting studies in the field of nanoparticle safety, including an analysis of the correlations among the pharmacokinetics, toxicity, physicochemical properties, and safety of nanoparticles.[7] Through our studies, we have shown that exposure to silver nanoparticles inhibits placental syncytialization in the human choriocarcinoma cell line BeWo[8] and that exposure to silica nanoparticles in mice during late pregnancy causes fetal growth restriction (i.e., decreased fetal weight).[9] Despite recent advances in the field of nanosafety, the majority of safety evaluations conducted on the fetotoxicity of nanoparticles have focused mainly on exposure of the female parent during pregnancy.

However, in recent years, the Paternal Origins of Health and Disease concept, which relates to the study of how factors such as exposure to environmental pollutants affect the generations through the male parent, has begun to attract attention as an extension of the Developmental Origin of Health and Disease concept.[10] For instance, there are reports that exposure of the male parent to nicotine causes significant increases in spontaneous locomotor activity and significant deficits in reversal learning in their F1 generation,[11] and that exposure to lead acetate adversely affects the fertility of both the male parent and their offspring.[12] In the field of nanosafety, the effects of nanoparticles on the reproductive system of the F0

Received: May 27, 2024
Revised: August 21, 2024
Accepted: August 22, 2024
Published: August 29, 2024



https://doi.org/10.1021/acsnanoscienceau.4c00021
ACS Nanosci. Au 2024, 4, 317–321

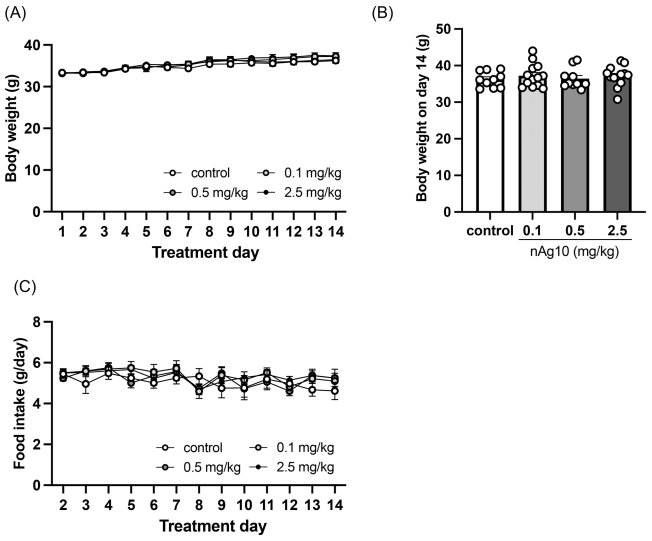


Figure 1. Effects of nAg10 on body weight and food intake. Male Slc:ICR (6−8 weeks) mice were treated with glucose or nAg10 (0.1, 0.5, or 2.5 mg/kg mouse) by oral gavage for 14 consecutive days. (A) Body weight was determined each day during the treatment period. (B) Body weight on day 14 was determined. (C) Daily food intake was determined each day during the treatment period. Data were pooled from two experiments and are presented as means ± SEM; n = 10−13.

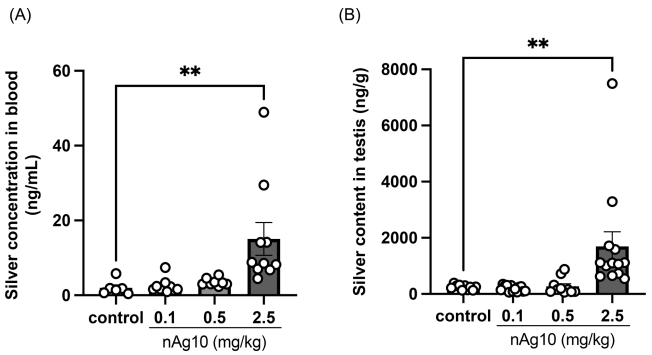


Figure 2. Silver concentration in blood and testis in nAg10-treated mice. Male Slc:ICR (6−8 weeks) mice were treated with glucose or nAg10 (0.1, 0.5, or 2.5 mg/kg mouse) by oral gavage for 14 consecutive days. After the mating period, the mice were euthanized, and testes and blood were collected. (A) Silver concentration in blood (n = 6−10) and (B) silver content in testes (n = 10−13) were measured by inductively coupled plasma mass spectrometry. Data were pooled from two experiments and are presented as individual plots together with mean ± SEM; $^{**}P < 0.01$.

generation have already been reported. For example, silver nanoparticles showed a decrease in sperm count and their motility in male mice[13] or in serum gonadotropins and testosterone production in male rat.[14] However, it remains unclear whether nanoparticles have multigenerational effects through parental male parental exposure.

Here, using Slc:ICR mice, we examined the biodistribution of a model nanoparticle, in this case silver nanoparticles with a diameter of 10 nm (nAg10), to the male genital tract and the effects of this biodistribution on pregnancy outcomes. These nanoparticles were chosen based on the particle size of silver nanoparticles currently used as food additives, which is around 11 ± 4 nm.[15]

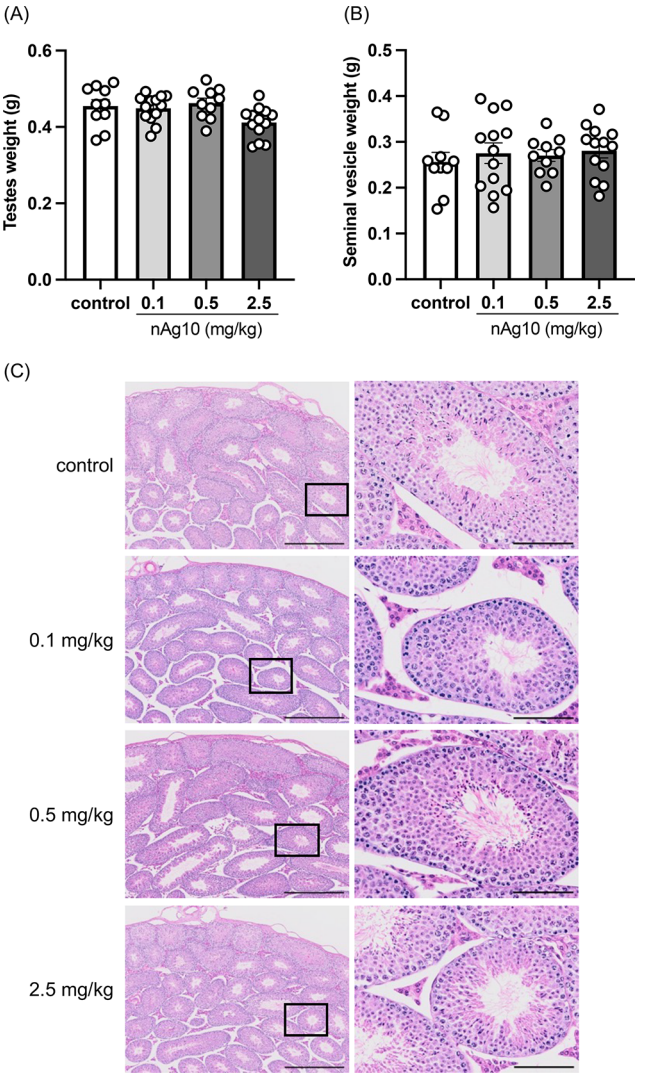


Figure 3. Effect of nAg10 nanoparticles on testes. Male Slc:ICR (6−8 weeks) mice were treated with glucose or nAg10 (0.1, 0.5, or 2.5 mg/kg mouse) by oral gavage for 14 consecutive days. After the mating period, the mice were euthanized, and the weight of (A) both the testes and (B) seminal vesicles was measured. Independent experiments were performed two times. n = 10−13. Data are presented as means ± SEM (C) Sections of the testes were stained with hematoxylin and eosin for histological analysis. Images to the right show higher magnification views of the black area in the images to the left (left images: ×4, right images: ×20). Scale bars, 500 or 100 μm.

Testicular Biodistribution and Toxicity after Oral Treatment with nAg10

An aqueous suspension of silver nanoparticles with a diameter of 10 nm (nAg10) was used in this study. We previously confirmed by transmission electron microscopy that the nanoparticles were smooth-surfaced spheres.[16] Male Slc:ICR male mice were treated with glucose (control) or nAg10 (0.1, 0.5, and 2.5 mg/kg mouse) by oral gavage for 14 consecutive days. During the treatment period, there were no significant changes in body weight (Figure 1A), the average weight on day 14 (Figure 1B) or daily food intake between the four groups (Figure 1C).

Moreover, we evaluated the effects of nAg10 on general hematology. Hematologic analysis revealed that the numbers of total leukocytes, erythrocytes, platelets, monocytes,

https://doi.org/10.1021/acsnanoscienceau.4c00021
ACS Nanosci. Au 2024, 4, 317−321

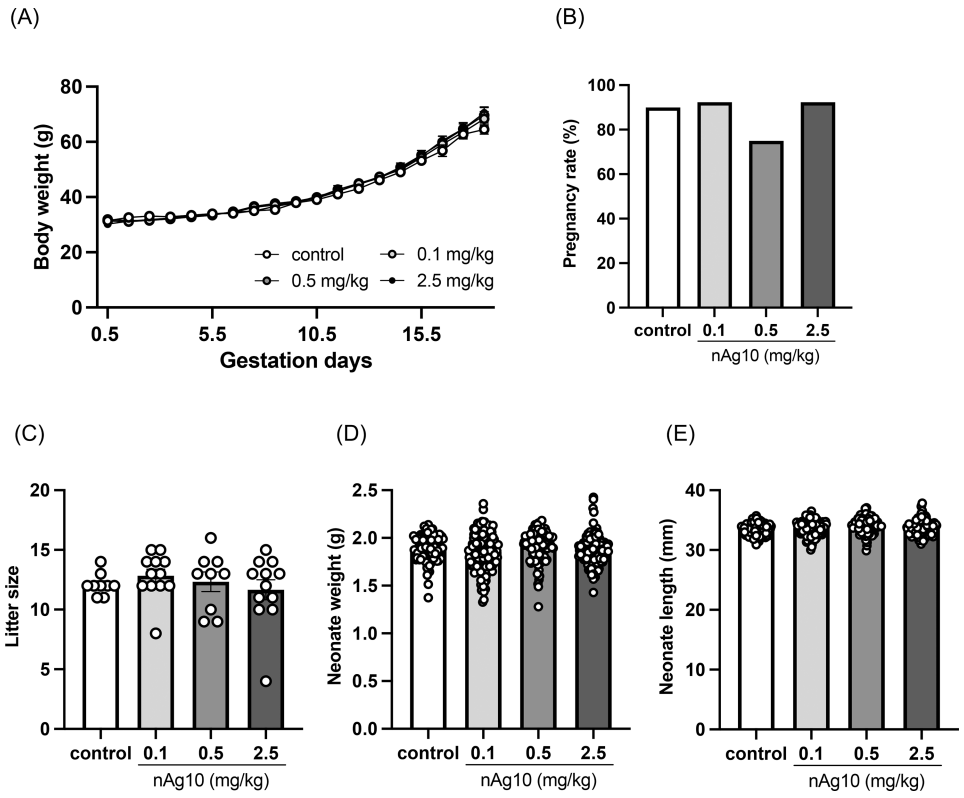


Figure 4. Effects of silver nanoparticles on mouse pups. Male Slc:ICR (6−8 weeks) mice were treated with glucose or nAg10 (0.1, 0.5, or 2.5 mg/kg mouse) by oral gavage for 14 consecutive days. After the final treatment, the male mice were mated with female mice for 4 days. (A) Maternal body weight was measured every day during pregnancy; n = 3−6. (B) Pregnancy rate was calculated. After birth, (C) litter size, (D) neonate weight, and (E) neonate length was measured. Data were pooled from two experiments (B, n = 10−13; B, n = 9−12; C, D, n = 109−154) and are presented as individual plots together with means ± SEM.

lymphocytes, and granulocytes also did not differ among the four groups (Supplementary Methods and Supplementary Figure S1). The plasma levels of alanine aminotransferase and aspartate aminotransferase also did not differ among the four groups (Supplementary Methods and Supporting Information Figure S2). ICP-MS analysis revealed significantly higher concentrations of silver in the blood (Figure 2A) and testis (Figure 2B) of the mice treated with 2.5 mg/kg of nAg10 compared with those of the control group.

However, no significant changes were observed in the weights of the testes with epididymis or the seminal vesicle (Figure 3) or in the weights of the liver, kidneys, or spleen (Supplementary Figure S3) between the treated and untreated groups. Moreover, pathological analysis revealed no evidence of damage in the testes from mice treated with nAg10 at any dose (Figure 3C). Taken together, these results indicate that although orally administered nAg10 was absorbed into the blood and biodistributed to the testes, no general toxicological effects were induced under the present treatment conditions.

To maintain a safe and isolated environment for germ cell maturation after meiosis, the testes have one of the strictest blood−tissue barriers that restricts the migration of foreign substances into the lumen of the seminiferous tubules.[17] However, there are reports that silver nanoparticles decrease the expression of zonula occludens-1 at tight junctions, which increases the permeability of the blood−brain barrier,[18] and that silver nanoparticles increase mitochondrial-mediated apoptosis of Sertoli cells in the testis.[19] Given that silver was detected in the testes after treatment with nAg10, silver nanoparticles likely have the potential to also break through the blood−testis barrier. Thus, studies to determine the mechanisms of migration and accumulation of silver nanoparticles in the testes are needed.

We showed that nAg10 was distributed to the testes through continuous oral treatment for 14 days, suggesting that nAg10 may have a chronic effect on the testes. The testes are an organ that produce hormones and sperm.[20] Although there were no significant effects on the pathology of testes in the nAg10-treated mice in the present study, that does not negate the possibility that the silver nanoparticles may affect hormone production and sperm motility. Given that nanosized-plastics downregulate the expression of testosterone secretion-related genes in Leydig cells in the testes,[21] the chronic effects of silver nanoparticles on male reproductive system should be assessed. Moreover, this study was conducted using Slc:ICR mice, and to extrapolate to humans, it is necessary to calculate the threshold value and set the Acceptable Daily Intake in the future.

Understanding the mechanisms of barrier permeation of nAg10 is an important goal for the future. Generally, transcellular and paracellular pathways have been reported to be involved in the mechanisms of biological barrier permeation by nanoparticles.[22] For example, it has been reported that nanoparticles modulate the expression of tight junction and adhesion-binding proteins, inducing abnormal placement of Sertoli cells,[23,24] and *in vitro* studies have shown that Sertoli cells and spermatogonial cells take up nanoparticles,[25,26] suggesting that nanoparticles may be able to cross the blood-testis barrier. On the other hand, present study showed that no abnormalities in pathological analyses of the testes in nAg10-

https://doi.org/10.1021/acsnanoscienceau.4c00021
ACS Nanosci. Au 2024, 4, 317−321

treated mice, which suggests that the transcytotic pathway may be involved, but further analyses are required in this area.

Effect of Daily Oral Administration of nAg10 on Mouse Pups

To evaluate the effect of male parental exposure to nAg10 on pregnancy outcomes, male Slc:ICR mice were treated with glucose or nAg10 (0.1, 0.5, and 2.5 mg/kg mouse) by oral gavage for 14 consecutive days and then mated with nontreated female Slc:ICR mice for 4 days. Maternal body weight was measured daily during pregnancy, and there was no significant difference between the mice that had mated with the treated or untreated males (Figure 4A). There was no significant change in the pregnancy rate (Figure 4B) and all pregnant female mice gave birth on GD 18.5. Moreover, litter size, neonate weight, and neonate length showed no significant changes between the groups (Figure 4C–E). These results indicate that paternal treatment with nAg10 did not affect fetal development under these treatment conditions.

We are already exposed to nanoparticles on a daily basis. For the general population, the human use level of silver has been described as 0.4–27 μg per day for the general population. And orally administered silver has been described to be absorbed in a range of 0.4–18% in mammals with a human value of 18%.[27] Thus, it is assumed that 0.072–4.86 μg per day of silver is absorbed in human (1.2–81 mg/kg). Assuming that all the absorbed silver was nanosized, the amount (2.5 mg/kg) which mice were treated in the present study might be about the same. Since it is unknown how much nanosized silver is contained in the products, there is room for consideration about this assumption, but our results indicate the need to accelerate assessments of the multigenerational effects of nanoparticles.

Although there have been reports on assessing the effects of nanoparticles on the male reproductive system,[13,14] there is little knowledge about their effects on the next generation in terms of the Paternal Origins of Health and Disease concept. This is a strength of this paper; however, we only assessed fetal development as an indicator of impact of nAg10 on the next generation in the present study. However, it has been reported that cadmium causes abnormal glucose tolerance, decreased insulin sensitivity, and abnormal accumulation of hepatic glycogen in the daughters of male mice exposed to cadmium.[28] Therefore, from the Developmental Origin of Health and Disease and Paternal Origins of Health and Disease perspectives, future studies should also consider the effects of paternal nanoparticle exposure on the health of their offspring such as the reproductive system, emotional cognition, and metabolic functions.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsnanoscienceau.4c00021.

Experimental section, hematology, biochemical analysis, tissue weights (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

Kazuma Higashisaka − *School of Pharmaceutical Sciences, Graduate School of Pharmaceutical Sciences, and Institute for Advanced Co-Creation Studies, Osaka University, Osaka 565-0871, Japan;* orcid.org/0000-0001-9473-8302; Email: higashisaka@phs.osaka-u.ac.jp

Yasuo Tsutsumi − *School of Pharmaceutical Sciences and Graduate School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan; Global Center for Medical Engineering and Informatics and Institute for Open and Transdisciplinary Research Initiatives, Osaka University, Osaka 565-0871, Japan*; Email: ytsutsumi@phs.osaka-u.ac.jp

Authors

Yuma Saeki − *School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan*

Rina Izutani − *School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan*

Jiwon Seo − *School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan*

Kazuki Miyaji − *School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan*

Yuya Haga − *School of Pharmaceutical Sciences and Graduate School of Pharmaceutical Sciences, Osaka University, Osaka 565-0871, Japan;* orcid.org/0000-0003-4148-2256

Complete contact information is available at: https://pubs.acs.org/10.1021/acsnanoscienceau.4c00021

Author Contributions

‡Y.S. and K.H. contributed equally. CRediT: **Yuma Saeki** data curation, formal analysis, investigation, visualization, writing - original draft; **Kazuma Higashisaka** conceptualization, data curation, funding acquisition, project administration, supervision, writing - original draft, writing - review & editing; **Rina Izutani** investigation, writing - review & editing; **Jiwon Seo** investigation, writing - review & editing; **Kazuki Miyaji** investigation, writing - review & editing; **Yuya Haga** supervision, writing - review & editing; **Yasuo Tsutsumi** funding acquisition, supervision, writing - review & editing.

Funding

This study was supported by a Grant-in-Aid for Scientific Research from the Japan Society for the Promotion of Science (no. 22H03749 to K.H. and no. 23H02651 to Y.T.) and by a grant from the Ministry of Health, Labour and Welfare of Japan (no. 21KD1002 to Y.T.).

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This research was partially supported by the Platform Project for Supporting Drug Discovery and Life Science Research (Basis for Supporting Innovative Drug Discovery and Life Science Research (BINDS)) from the Japan Agency for Medical Research and Development under grant numbers JP24ama121052 and JP24ama121054.

■ REFERENCES

(1) Gupta, V.; Mohapatra, S.; Mishra, H.; Farooq, U.; Kumar, K.; Ansari, M. J.; Aldawsari, M. F.; Alalaiwe, A. S.; Mirza, M. A.; Iqbal, Z. Nanotechnology in Cosmetics and Cosmeceuticals-A Review of Latest Advancements. *Gels* **2022**, *8*, 173.

(2) Joshi, N. C.; Negi, P. B.; Gururani, P. A review on metal/metal oxide nanoparticles in food processing and packaging. *Food Sci Biotechnol* **2024**, *33*, 1307–1322.

(3) Bruna, T.; Maldonado-Bravo, F.; Jara, P.; Caro, N. Silver Nanoparticles and Their Antibacterial Applications. *Int J Mol Sci* **2021**, *22*, 7202.
(4) Malakar, A.; Kanel, S. R.; Ray, C.; Snow, D. D.; Nadagouda, M. N. Nanomaterials in the environment, human exposure pathway, and health effects: A review. *Sci. Total Environ.* **2021**, *759*, 143470.
(5) Schwirn, K.; Voelker, D.; Galert, W.; Quik, J.; Tietjen, L. Environmental Risk Assessment of Nanomaterials in the Light of New Obligations Under the REACH Regulation: Which Challenges Remain and How to Approach Them? *Integr Environ Assess Manag* **2020**, *16*, 706−717.
(6) Plotka-Wasylka, J.; Mulkiewicz, E.; Lis, H.; Godlewska, K.; Kurowska-Susdorf, A.; Sajid, M.; Lambropoulou, D.; Jatkowska, N. Endocrine disrupting compounds in the baby's world - A harmful environment to the health of babies. *Sci. Total Environ.* **2023**, *881*, 163350.
(7) Higashisaka, K. Health Effects and Safety Assurance of Nanoparticles in Vulnerable Generations. *Biol. Pharm. Bull.* **2022**, *45*, 806−812.
(8) Sakahashi, Y.; Higashisaka, K.; Isaka, R.; Izutani, R.; Seo, J.; Furuta, A.; Yamaki-Ushijima, A.; Tsujino, H.; Haga, Y.; Nakashima, A.; Tsutsumi, Y. Silver nanoparticles suppress forskolin-induced syncytialization in BeWo cells. *Nanotoxicology* **2022**, *16*, 883−894.
(9) Yamashita, K.; Yoshioka, Y.; Higashisaka, K.; Mimura, K.; Morishita, Y.; Nozaki, M.; Yoshida, T.; Ogura, T.; Nabeshi, H.; Nagano, K.; Abe, Y.; Kamada, H.; Monobe, Y.; Imazawa, T.; Aoshima, H.; Shishido, K.; Kawai, Y.; Mayumi, T.; Tsunoda, S.; Itoh, N.; Yoshikawa, T.; Yanagihara, I.; Saito, S.; Tsutsumi, Y. Silica and titanium dioxide nanoparticles cause pregnancy complications in mice. *Nat Nanotechnol* **2011**, *6*, 321−8.
(10) Soubry, A. POHaD: why we should study future fathers. *Environ Epigenet* **2018**, *4*, No. dvy007.
(11) McCarthy, D. M.; Morgan, T. J., Jr; Lowe, S. E.; Williamson, M. J.; Spencer, T. J.; Biederman, J.; Bhide, P. G. Nicotine exposure of male mice produces behavioral impairment in multiple generations of descendants. *PLoS Biol* **2018**, *16*, No. e2006497.
(12) Dolati, P.; Zamiri, M. J.; Akhlaghi, A.; Khodabandeh, Z.; Mehrabani, D.; Atashi, H.; Jamhiri, I. Reproductive and embryological toxicity of lead acetate in male mice and their offspring and mitigation effects of quercetin. *J Trace Elem Med Biol* **2021**, *67*, 126793.
(13) Abu-Taweel, G. M.; Albetran, H. M.; Al-Mutary, M. G.; Ahmad, M.; Low, I. M. Alleviation of silver nanoparticle-induced sexual behavior and testicular parameters dysfunction in male mice by yttrium oxide nanoparticles. *Toxicol Rep* **2021**, *8*, 1121−1130.
(14) Shehata, A. M.; Salem, F. M. S.; El-Saied, E. M.; Abd El-Rahman, S. S.; Mahmoud, M. Y.; Noshy, P. A. Zinc Nanoparticles Ameliorate the Reproductive Toxicity Induced by Silver Nanoparticles in Male Rats. *Int J Nanomedicine* **2021**, *16*, 2555−2568.
(15) De Vos, S.; Waegeneers, N.; Verleysen, E.; Smeets, K.; Mast, J. Physico-chemical characterisation of the fraction of silver (nano)-particles in pristine food additive E174 and in E174-containing confectionery. *Food Addit Contam Part A Chem Anal Control Expo Risk Assess* **2020**, *37*, 1831−1846.
(16) Morishita, Y.; Yoshioka, Y.; Takimura, Y.; Shimizu, Y.; Namba, Y.; Nojiri, N.; Ishizaka, T.; Takao, K.; Yamashita, F.; Takuma, K.; Ago, Y.; Nagano, K.; Mukai, Y.; Kamada, H.; Tsunoda, S.; Saito, S.; Matsuda, T.; Hashida, M.; Miyakawa, T.; Higashisaka, K.; Tsutsumi, Y. Distribution of Silver Nanoparticles to Breast Milk and Their Biological Effects on Breast-Fed Offspring Mice. *ACS Nano* **2016**, *10*, 8180−91.
(17) Luaces, J. P.; Toro-Urrego, N.; Otero-Losada, M.; Capani, F. What do we know about blood-testis barrier? current understanding of its structure and physiology. *Front Cell Dev Biol* **2023**, *11*, 1114769.
(18) Xu, L.; Dan, M.; Shao, A.; Cheng, X.; Zhang, C.; Yokel, R. A.; Takemura, T.; Hanagata, N.; Niwa, M.; Watanabe, D. Silver nanoparticles induce tight junction disruption and astrocyte neurotoxicity in a rat blood-brain barrier primary triple coculture model. *Int J Nanomedicine* **2015**, *10*, 6105−18.
(19) Han, J. W.; Jeong, J. K.; Gurunathan, S.; Choi, Y. J.; Das, J.; Kwon, D. N.; Cho, S. G.; Park, C.; Seo, H. G.; Park, J. K.; Kim, J. H. Male- and female-derived somatic and germ cell-specific toxicity of silver nanoparticles in mouse. *Nanotoxicology* **2016**, *10*, 361−73.
(20) Suede, S. H.; Malik, A.; Sapra, A. *Histology, Spermatogenesis*; StatPearls Publishing: Treasure Island, FL, 2024.
(21) Sun, Z.; Wen, Y.; Zhang, F.; Fu, Z.; Yuan, Y.; Kuang, H.; Kuang, X.; Huang, J.; Zheng, L.; Zhang, D. Exposure to nanoplastics induces mitochondrial impairment and cytomembrane destruction in Leydig cells. *Ecotoxicol Environ Saf* **2023**, *255*, 114796.
(22) Cary, C.; Stapleton, P. Determinants and mechanisms of inorganic nanoparticle translocation across mammalian biological barriers. *Arch. Toxicol.* **2023**, *97*, 2111−2131.
(23) Gao, G.; Ze, Y.; Zhao, X.; Sang, X.; Zheng, L.; Ze, X.; Gui, S.; Sheng, L.; Sun, Q.; Hong, J.; Yu, X.; Wang, L.; Hong, F.; Zhang, X. Titanium dioxide nanoparticle-induced testicular damage, spermatogenesis suppression, and gene expression alterations in male mice. *J Hazard Mater* **2013**, *258*−*259*, 133−43.
(24) Ni, D. Q.; Ma, D. D.; Hao, S. L.; Yang, W. X.; Kovacs, T.; Tan, F. Q. Titanium dioxide nanoparticles perturb the blood-testis barrier via disruption of actin-based cell adhesive function. *Aging (Albany NY)* **2021**, *13*, 25440−25452.
(25) Habas, K.; Brinkworth, M. H.; Anderson, D. Silver nanoparticle-mediated cellular responses in isolated primary Sertoli cells in vitro. *Food Chem. Toxicol.* **2018**, *116*, 182−188.
(26) Mancuso, F.; Arato, I.; Di Michele, A.; Antognelli, C.; Angelini, L.; Bellucci, C.; Lilli, C.; Boncompagni, S.; Fusella, A.; Bartolini, D.; Russo, C.; Moretti, M.; Nocchetti, M.; Gambelunghe, A.; Muzi, G.; Baroni, T.; Giovagnoli, S.; Luca, G. Effects of Titanium Dioxide Nanoparticles on Porcine Prepubertal Sertoli Cells: An "In Vitro" Study. *Front Endocrinol (Lausanne)* **2022**, *12*, 751915.
(27) Hadrup, N.; Lam, H. R. Oral toxicity of silver ions, silver nanoparticles and colloidal silver–a review. *Regul. Toxicol. Pharmacol.* **2014**, *68*, 1−7.
(28) Tan, L. L.; Xiong, Y. W.; Zhang, J.; Li, D. X.; Huang, Y.; Wang, H. Like father, like daughter:Paternal cadmium exposure causes hepatic glucose metabolic disorder and phospholipids accumulation in adult female offspring. *Chemosphere* **2023**, *338*, 139437.

https://doi.org/10.1021/acsnanoscienceau.4c00021
ACS Nanosci. Au 2024, 4, 317−321