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Author Correction: Safety evaluation of extracellular vesicles derived from hypoxia primed mesenchymal stem cells of umbilical cord and adipose tissue

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Correction to: *Scientific Reports* https://doi.org/10.1038/s41598-026-36511-4, published online 16 October 2025

The original version of this Article contained errors.

The Authors performed two sets of experiments described in this and another study, which shared a control group. These experiments were performed under similar conditions, and the control group was re-used to minimise the use of animals, in line with 3R principles (Replacement, Reduction, Refinement). This was, however, not stated in the Article. This disclosure is now added in the "Methods" section and in the legends of Figures 2, 6, and 7, and the other paper is cited as Reference 27. All subsequent references were renumbered. As a result,

In the "Method" section, under subheading "In vivo vascular and muscle stimulation tests",

"New Zealand white rabbits (1,8 – 2,3 kg, 4-4.5 month old, total 21 animals) were randomly distributed into 3 groups ($n = 7$). The rabbits were subjected to vascular stimulation test, which refers to the local response of blood vessels at the injection site and muscle stimulation refers to tissue reactivity following intramuscular injection. For the vascular stimulation test, the rabbits were intravenously injected with 50 µg of AD-MSC-EVs, 50 µg of UC-MSC-EVs, or Ringer Lactate as a control via the marginal ear vein. For the muscle stimulation test, the rabbits were intramuscularly injected with the same amount of Ringer Lactate, AD-MSC-EVs, or UC-MSC-EVs via the right quadriceps muscle. The temperature at the site of injection was measured daily. Four days after the treatment, the rabbits were sacrificed. The injection sites were collected and fixed in 4% paraformaldehyde, embedded in paraffin and cut into serial 5-µm sections, which were then subjected to hematoxylin and eosin (HE) staining. The degree of vascular stimulation and muscle stimulation was assessed via macroscopic observation and histopathological examination. A positive response was defined as a ≥ 1.5 °C temperature increase or evidence of local inflammation. Images were captured using a microscope (Olympus, Japan)."

now reads:

"New Zealand white rabbits (1,8 – 2,3 kg, 4-4.5 month old, total 21 animals) were randomly distributed into 3 groups ($n = 7$). The rabbits were subjected to vascular stimulation test, which refers to the local response of blood vessels at the injection site and muscle stimulation refers to tissue reactivity following intramuscular injection. For the vascular stimulation test, the rabbits were intravenously injected with 50 µg of AD-MSC-EVs, 50 µg of UC-MSC-EVs, or Ringer Lactate as a control via the marginal ear vein. For the muscle stimulation test, the rabbits were intramuscularly injected with the same amount of Ringer Lactate, AD-MSC-EVs, or UC-MSC-EVs via the right quadriceps muscle. The control group was shared with our previous study[27], conducted in parallel under identical conditions, to avoid unnecessary duplication of animals in line with the 3R principles. The temperature at the site of injection was measured daily. Four days after the treatment, the rabbits were sacrificed. The injection sites were collected and fixed in 4% paraformaldehyde, embedded in paraffin and cut into serial 5-µm sections, which were then subjected to hematoxylin and eosin (HE) staining. The degree of vascular stimulation and muscle stimulation was assessed via macroscopic observation and histopathological examination. A positive

response was defined as a ≥ 1.5 °C temperature increase or evidence of local inflammation. Images were captured using a microscope (Olympus, Japan)."

In the "Method" section, under subheading "Subchronic toxicity test",

"Wistar white rats (200–300 g, 8–10 week old, total 36 animals) were randomly distributed into 6 groups ($n = 6$). The rats were intravenously injected with UC-MSC-EVs or AD-MSC-EVs, with either 50 μg/animal (low dose) or 150 μg/animal (high dose), three times at 10-day intervals via the tail vein. A group of rats injected with Ringer Lactate and another group that did not receive injections were used as controls. Exercise status, the amount of food consumed, convulsions, diarrhea, and death were monitored throughout the experiment. Blood cell counts were conducted before injection and on day 10 after each injection to determine the WBC, RBC, and platelet counts and hemoglobin levels. Liver and kidney damage was examined by measuring the serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine before injection and on day 10 after each injection. Histology of the liver, kidney, and spleen was examined using HE staining on day 10 after the final injection."

now reads:

"Wistar white rats (200–300 g, 8–10 week old, total 36 animals) were randomly distributed into 6 groups ($n = 6$). The rats were intravenously injected with UC-MSC-EVs or AD-MSC-EVs, with either 50 μg/animal (low dose) or 150 μg/animal (high dose), three times at 10-day intervals via the tail vein. A group of rats injected with Ringer Lactate and another group that did not receive injections were used as controls. The Ringer Lactate control group was shared with our previous study[27], conducted in parallel under identical conditions, to avoid unnecessary duplication of animals in line with the 3R principles. Exercise status, the amount of food consumed, convulsions, diarrhea, and death were monitored throughout the experiment. Blood cell counts were conducted before injection and on day 10 after each injection to determine the WBC, RBC, and platelet counts and hemoglobin levels. Liver and kidney damage was examined by measuring the serum concentrations of aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, and creatinine before injection and on day 10 after each injection. Histology of the liver, kidney, and spleen was examined using HE staining on day 10 after the final injection."

The original Figures legends are shown below.

Figure 2. Vascular and muscular stimulation of UC-MSC-EVs and AD-MSC-EVs. New Zealand rabbits were injected with either Ringer Lactate (control), 50 μg of UC-MSC-EVs, or 50 μg of AD-MSC-EVs. (**A**) The temperatures of the injected ears were measured at the indicated time points. (**B**–**G**) HE staining of injected ears on day 4 post-injection to evaluate vascular stimulation, including the number of blood vessels per mm^2 (B), blood vessel diameter (C), blood vessel area (D), number of WBCs (E), percentage of lesion area (F), and representative HE staining of injected ears (G). (**H**) The temperatures of the injected muscles were measured at the indicated time points. (**I**–**J**) HE staining analysis of injected muscle on day 4 post-injection to measure the blood vessel diameter (I) and percentage of lesion area (J). The data are presented as mean ± SEM. Significant differences between groups were analyzed by ANOVA//Bonferroni. Ns indicate not significant.

Figure 6. Effects of UC-MSC-EVs and AD-MSC-EVs on hematological indices of rats. Wistar rats were injected with either Ringer Lactate, UC-MSC-EVs or AD-MSC-EVs at low (50 μg) or high doses (150 μg) on days 0, 10, and 20. Groups of rats injected with Ringer Lactate or untreated were used as controls. (A) The experimental scheme. (B) The body weights of the injected animals were monitored for 29 days. (C–F) The number of WBCs (C), number of RBCs (D), hemoglobin levels (E), and number of platelets (F) in blood collected before and 10 days after each injection were determined. The data are presented as mean ± SEM.

Figure 7. UC-MSC-EVs and AD-MSC-EVs administration does not damage the liver, kidney, or spleen. Wistar rats were injected with either Ringer Lactate, UC-MSC-EVs or AD-MSC-EVs at low (50 μg) (UC-MSC-EVs-L and AD-MSC-EVs-L, respectively) or high (150 μg) (UC-MSC-EVs-H and AD-MSC-EVs-H, respectively) doses on days 0, 10, and 20. The levels of AST and ALT (**A**) and urea and creatinine (**B**) in blood collected before and 10 days after each injection were measured. On day 30 post-injection, the liver, kidney, and spleen were collected for macroscopic and microscopic observation via H&E staining (**C**). The data are presented as mean ± SEM.

Moreover, in the "Conclusion" section, the specific extracellular vesicles were missing. Consequently,

"In this study, we sucessfully isolated EVs from UC-MSCs and AD-MSCs cultured in xeno- and serum-free media and primed with 5% oxygen. Our study is the first to evaluate the safety of the EVs using animals. Overall, our results confirm the safety of both UC-MSCs and AD-MSCs in rabbits and rodents (Fig. 8). Additionally, we believe that the comprehensive approach employed in our study will provide other researchers with a framework to assess the immunogenicity and toxicity of their EVs, facilitating the development of therapeutic EVs for various disease models and human studies."

now reads:

"In this study, we successfully isolated EVs from UC-MSCs and AD-MSCs cultured in xeno- and serum-free media and primed with 5% oxygen. Our study is the first to evaluate the safety of the EVs using animals. Overall, our results confirm the safety of both UC-MSC-EVs and AD-MSC-EVs in rabbits and rodents (Fig. 8). Additionally, we believe that the comprehensive approach employed in our study will provide other researchers with a framework to assess the immunogenicity and toxicity of their EVs, facilitating the development of therapeutic EVs for various disease models and human studies."

In addition, original images from three representative animals have been added in Supporting Materials 2 (Figures S3-S6) to support the data in Figures 2G and 7C.

The original Article has been corrected, and Supplementary Material 2 was added to the original Article.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1038/s41598-026-36511-4.