Malformations in heart, eyes and nervous system: Nanoplastics found to disrupt growth

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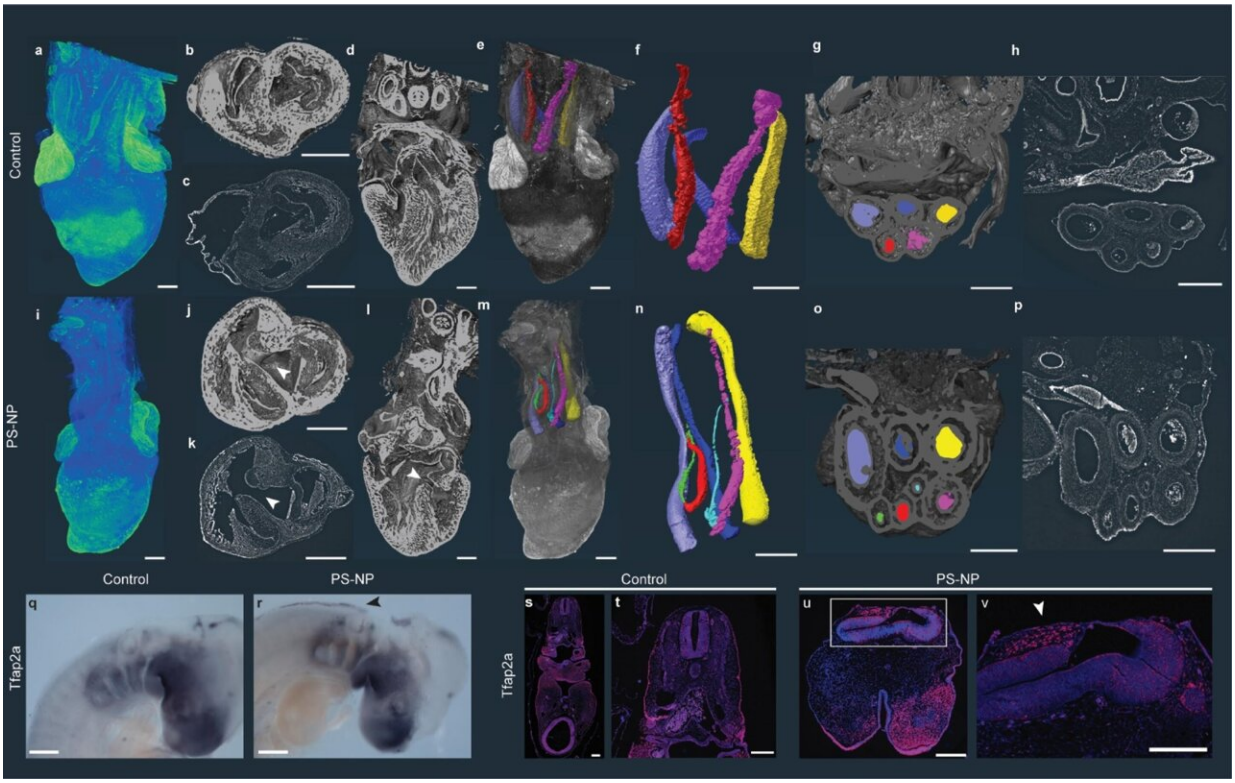

25 nm PS-NPs cause cardiac malformations by disrupting the development of the cardiac neural crest. a-p, synchrotron tomographic scans of hearts and great vessels at 8 dpe; a-h, control embryo, stage 35. n = 2. a and e, segmentation and volume rendering of heart and vessels. (b, d, g), virtual transverse sections. (c, h) two-dimensional (2-D) view of virtual transverse sections. (f), three-dimensional (3-D) model of great vessels produced by manual tracing. (i-p), PS-NP treated, stage 35. n = 2. (i, m), volume rendering of PS-NPs treated heart. (n), 3-D model of great vessels produced by manual tracing. (j, n, o), 3-D view of virtual transverse sections. (k, p), 2-D view of virtual transverse sections. (q, r),

wholemount in situ hybridization of TFAP2A. (q), control embryo, stage 19. n = 2. (r), PS-NPs treated embryo, stage 18. n = 3. s-v, immunohistochemistry showing TFAP2A and DAPI stained transverse sections. n = 2 for control and n = 5 for PS-NPs-treated group. (s, t), control chicken embryo, stage 19. (u, v), PS-NPs treated chicken embryo, stage 17. Note, The treated heart in (i-p) has both a ventricular septal defect (arrowhead) and supernumerary pharyngeal arch arteries (seven in place of the normal five). The two supernumerary pharyngeal arch arteries (green and light blue) are aberrant subclavian arteries. In this embryo, the brachiocephalic artery is abnormally short. The sixth pharyngeal arch arteries are normal in all of our specimens from control group. The wholemount in situ hybridization for the cardiac neural crest marker TFAP2A shows that PS-NP treatment causes a failure of the cardiac neural crest to completely populate the pharyngeal arches; it also disrupts migration of the cardiac neural crest, such that some crest cells never leave the neural tube (arrows). Key: purple, right aorta; red, right brachiocephalic artery; yellow, left pulmonary artery; pink; left brachiocephalic artery; blue, right pulmonary artery; green right subclavian artery; light blue, left subclavian artery; PS-NP, embryos treated with polystyrene nanoparticles (25 nm, 5 mg/mL); dpe, days post-exposure. Scale bars, 500 μm in (a-p), 300 μm in (q, r), 200 μm in (s, v). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.). Credit: *Environment International* (2023). DOI: 10.1016/j.envint.2023.107865

Nanoplastics cause malformations. This is the conclusion of Meiru Wang, researcher at the Institute of Biology Leiden, who looked at the extreme effects polystyrene nanoparticles could have, using chicken embryos as a model.

"We see malformations in the nervous system, heart, eyes and other parts of the face," Wang says. "We used a high concentration of polystyrene particles, that would normally not be present in an organism. But it shows what nanoplastics can do in extreme cases on very young embryos. And it also gives us guidelines on what can happen less

severely in the developmental stage," says Wang.

The results are now published in *Environment International*.

Nanoplastics target stem cells

Nanoplastics target the embryonic neural crest cells, Wang found. These stem cells are formed very early in all vertebrates at the beginning of their existence. The neural crest cells start in what will be the spinal cord , and migrate to create part of the nervous system. They also form parts of several important organs, such as the arteries, heart and face.

However, when nanoparticles surround the neural crest cells, the migration of those cells is disrupted. This results in growth disturbances.

Michael Richardson, Wang's supervisor says, "When you know the mechanism, everything else falls into place. We think they stick to the neural crest cells, which causes the cells to die. Neural crest cells are sticky, so nanoparticles can adhere to them and thereby disrupt organs that depend on these cells for their development. I like the metaphor of making dough. When making bread, for example, you put flour on it to make it not sticky anymore. However, in this case, it ruins the migration of the neural crest cells."

Finding mechanisms with 3D reconstructions, X-rays and expertise

The research project involved multiple research centers in Leiden and abroad including CML, whose new director, Martina Vijver, is Wang's supervisor. "Because nanoplastics are so small, it is impossible to see them using conventional microscopes. That is what makes it difficult to research. We can only see them when they are fluorescently tagged,"

Richardson explained. "Collaboration was the way to go, as this type of research can't be done as a one-man band."

The researcher continues, "At Naturalis Biodiversity Center in Leiden, Martin Rücklin and Bertie Joan van Heuven were able to make 3D reconstructions of the embryos, so we could clearly see the malformations. And with the high-resolution synchrotron Switzerland, we could see what happens in the heart. Experienced researchers from the LUMC helped define what we saw."

Wang is very happy with her research, even with its worrying results. "Everything is a question mark in research, and you get the chance to fill in the gaps. I have many great supervisors and colleagues, who encourage me and make me braver. This research is only one step to see what are the ultimate effects of nanoplastics in our environment. And especially as people are now looking into using them in human medicines, we believe that we should take care before these drastic effects are seen in humans."

More information: Meiru Wang et al, Nanoplastics causes extensive congenital malformations during embryonic development by passively targeting neural crest cells, *Environment International* (2023). DOI: 10.1016/j.envint.2023.107865

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