**Microarray and Bioinformatics analysis**

For Affymetrix® microarray profiling, the total RNA was isolated from 30 zebrafish embryos per SiNPs-treatment group (3 ng/nL) by the TRIzol reagent (Invitrogen, Carlsbad, Canada) and purified with an RNeasy Mini Kit (Qiagen, Hilden, Germany) according to the manufacturer’s protocol. The amount and quality of RNA were determined by a UV-Vis Spectrophotometer (Thermo, NanoDrop 2000, USA) at the absorbance of 260 nm. The mRNA expression profiling was measured using Zebrafish Gene 1.0 ST Array (Affymetrix GeneChip®, USA), which contains 59,302 gene-level probe sets. The microarray analysis was performed by Affymetrix® Expression Console Software (version 1.2.1). Raw data (CEL files) were normalized at transcript level using robust multi-array average method (RMA workflow). Median summarization of transcript expressions was calculated. Gene-level data was then filtered to include only those probe sets that are in the ‘core’ metaprobe list, which represent RefSeq genes.

For microarray data analysis, differential expression genes were identified based on random variance model (RVM) t-test. And the differential expression genes were considered to be up or down regulated with at least *p* < 0.05. Genes with similar expression patterns often facilitate the overlapping functions. Accordingly, the cluster analysis of gene expression patterns was analyzed by Cluster and Java Treeview software. Pathway analysis was used to find out the significant pathway of the differential genes according to Kyoto Encyclopedia of Genes and Genomes (KEGG) database, Biocarta and Reatome databases. Fisher’s exact test was performed to select the significant pathway, and the threshold of significance was considered as *p* < 0.05.

**Results from Microarray and Bioinformatics analysis**

Microarray data analysis demonstrated that SiNPs-induced toxicity in zebrafish embryos affected expression of 2515 genes, including 1107 genes were up-regulated and 1408 genes were down-regulated. The significant pathways were analyzed according to the functions and interactions of differential genes based on KEGG database: the up-regulation significant pathways are Ribosome, Herpes simplex infection, Adipocytokine signaling pathway, Salmonella infection, Toll-like receptor signaling pathway, Apoptosis, Arachidonic acid metabolism, JAK-STAT signaling pathway, Cytokine-cytokine receptor interaction, and MAPK signaling pathway. While the down-regulation significant pathways induced by SiNPs are involved in Calcium signaling pathway, Phototransduction, Neuroactive ligand-receptor interaction, Purine metabolism, Cardiac muscle contraction, Gap junction, Glycine, serine and threonine metabolism, Vascular smooth muscle contraction, Tryptophan metabolism, and Metabolic pathways.

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Figure S1. The knockdown effect of *i6st*-MO was verified by RT-PCR. A, 2.625 ng MO; B, 5.25 ng MO; C, 10.5 ng MO.

Table S1. Gene sequence for morpholino oligo (MO).



Table S2. Gene probes for whole-mount in situ hybridization.



Table S3. Primers used for qRT-PCR.



Table S4. Endotoxin detection by LAL assay

