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Fig. S1. Characterization of synthesized AgNPs. (A) The TEM image of AgNPs. (B) Size distribution of AgNPs.



Fig. S2. The extracellular dissolution of AgNPs in cell culture medium and the intracellular bioaccumulation of AgNPs in oyster hemocytes. The dissolution of 1.0 mg/L AgNPs was determined at 0 h and 3 h (A). The intracellular Ag concentrations were determined after oyster hemocytes were exposed to AgNPs from 0.2-3.0 mg/L for 3 h (B). Data are expressed as mean  $\pm$  SEM (n=6). \*\*p < 0.01, and \*\*\*p < 0.001 compared with the control.



Fig. S3. Live cells stained with CellTrace calcein red-orange.



Fig. S4. Cellular viability (A), mitochondrial membrane potential (B), and mitochondrial ROS (C) detected in oyster hemocytes in vitro experiments. Mean fluorescence intensity (MFI) was acquired. Data are expressed as mean  $\pm$  SEM (n=6). AG, agranulocytes; SG, semigranulocytes; G, granulocytes; All, all hemocytes. \*\*p < 0.01 and \*\*\*p < 0.001 compared with the control.



fluorescence intensity in oyster hemocytes. (B) Intracellular Ag<sup>+</sup> contents in oyster hemocytes. (C) Intracellular dissolution rate of AgNPs. Data are expressed as mean  $\pm$  SEM (n=6).



Fig. S6. Distinction of oyster hemocyte subtypes. (A) A representative flow cytometric plot of forward scatter (FSC) versus side scatter (SSC) including three hemocyte subtypes, including agranulocytes (AG) possessing low SSC, semigranulocytes (SG) possessing mid-high SSC, and granulocytes (G) possessing high SSC. (B) Distribution of hemocyte subtypes according to SSC values.



Fig. S7. Mitochondrial ROS (A), mitochondrial membrane potential (B), cellular viability (C), and lysosomal membrane permeabilization (D) detected in oyster hemocytes by flow cytometry *in vitro* experiments. Mean fluorescence intensity (MFI) was acquired. Data are expressed as mean  $\pm$  SEM (n=6). AG, agranulocytes; SG, semigranulocytes; G, granulocytes; All, all hemocytes. \**p* <0.05, \*\**p* < 0.01, and \*\*\**p* < 0.001 compared with the control. #*p* <0.05, ##*p* <0.01, and ###*p* <0.001 compared with AgNP treatment groups.



Fig. S8. Quantification of minimum duration of mitochondria–lysosome contacts in agranulocytes (A), semigranulocytes (B), and granulocytes (G). Data are expressed as mean  $\pm$  SEM (from 30 cells in each group). AG, agranulocytes; SG, semigranulocytes; G, granulocytes. \*p < 0.05, \*\*p < 0.01, and \*\*\*p < 0.001 compared with the control.



Fig. S9. The dissolution of AgNPs in artificial seawater (A) and the intracellular bioaccumulation of AgNPs in oyster hemocytes (B) *in vivo* experiments. Data are expressed as mean  $\pm$  SEM (from 3 oysters in each group). \*\*\*p < 0.001 compared with the control. ###p < 0.001 compared with AgNP treatment groups.