

**Nanoscale Dual-enzyme Cascade Metal-organic Frameworks
through Biomimetic Mineralization as a ROS Generator for
Synergistic Cancer Therapy**

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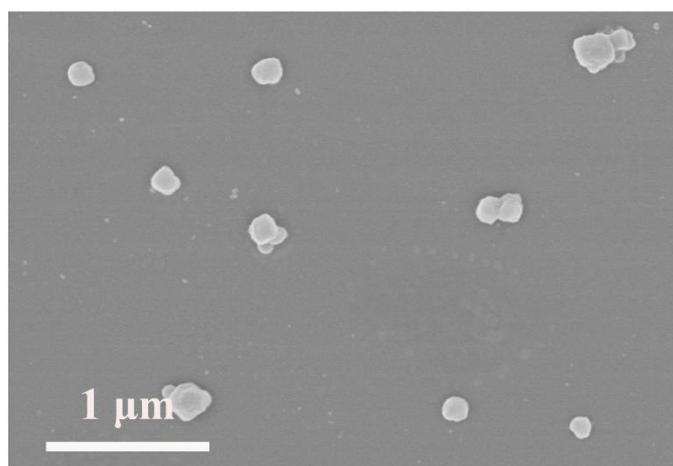


Fig S1. SEM image of GOx@Pd@ZIF-8.

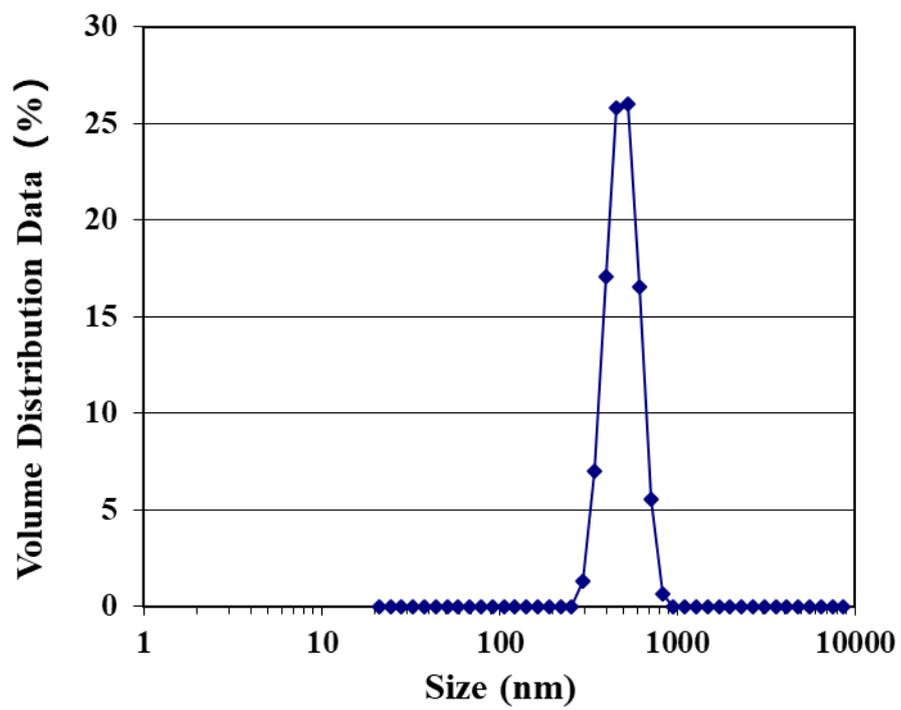


Fig S2. DLS of GOx@Pd@ZIF-8

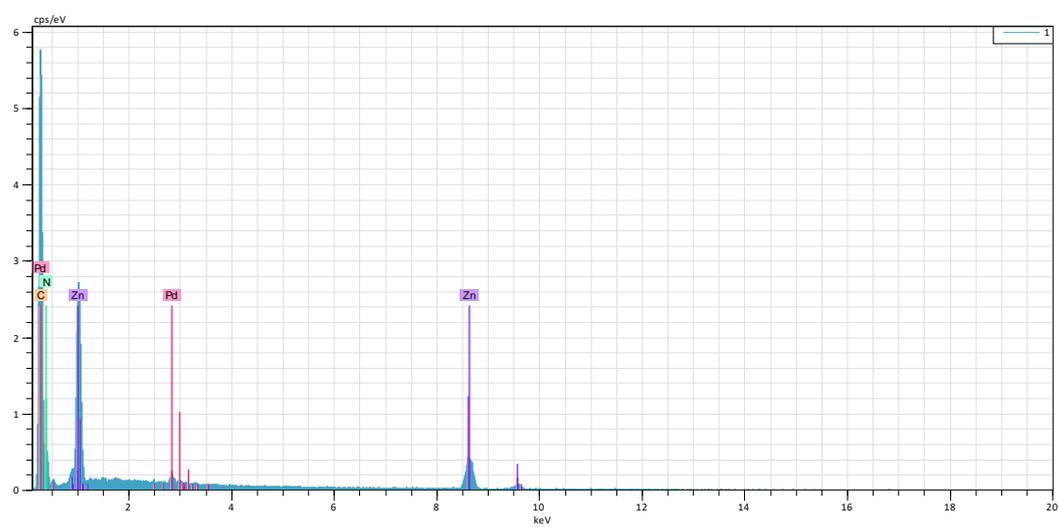


Fig S3. EDS of GOx@Pd@ZIF-8.

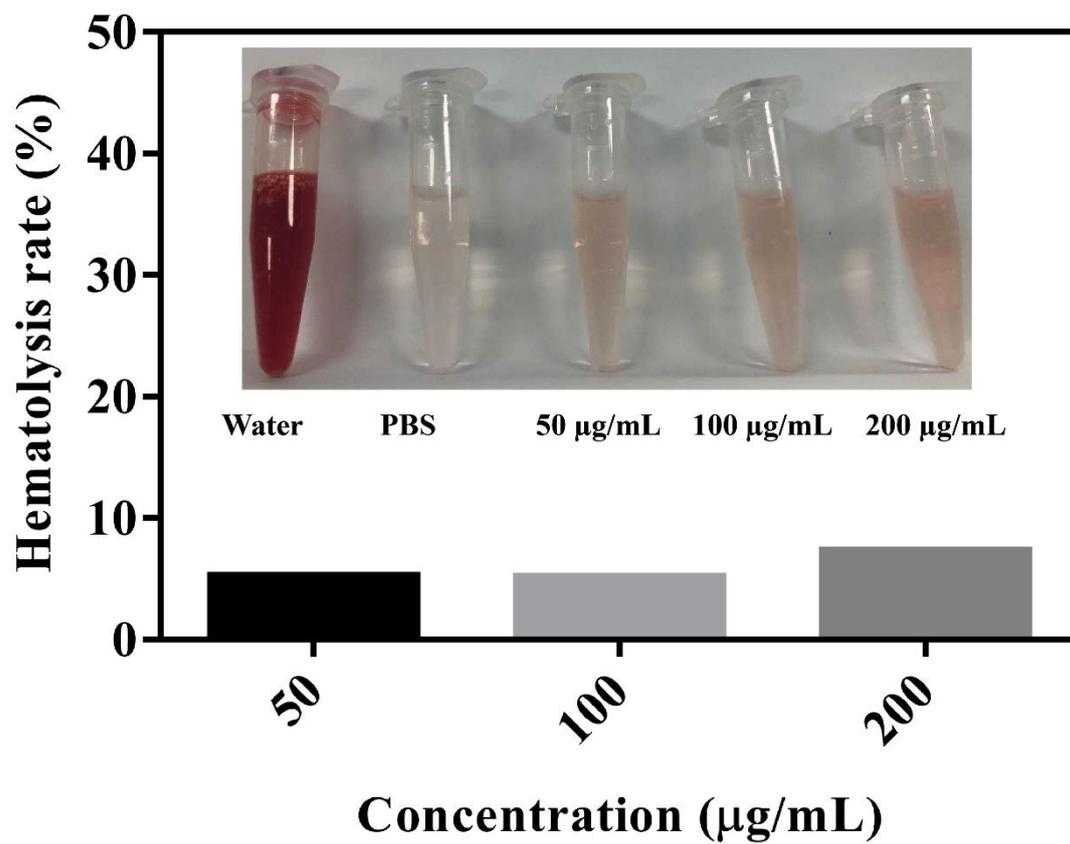


Fig S4. Hemolysis ratio of GOx@Pd@ZIF-8 at different concentrations. The inset shows the corresponding hemolysis images.

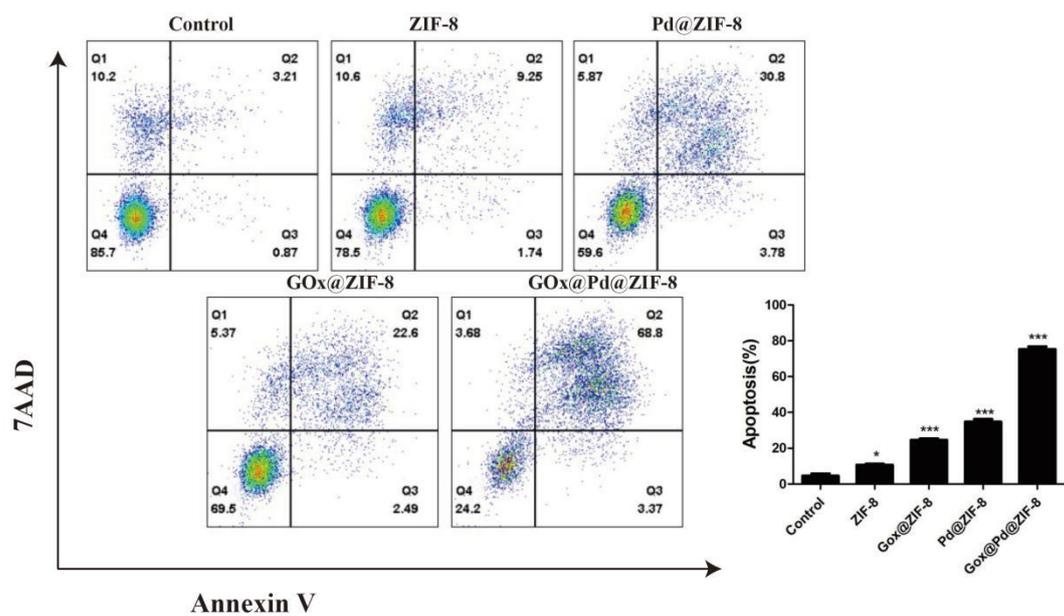


Figure S5. The A549 cells were treated with ZIF-8, Pd@ZIF-8, GOx@ZIF-8, GOx@Pd@ZIF-8 for 48 hours, the apoptosis rates were analyzed.

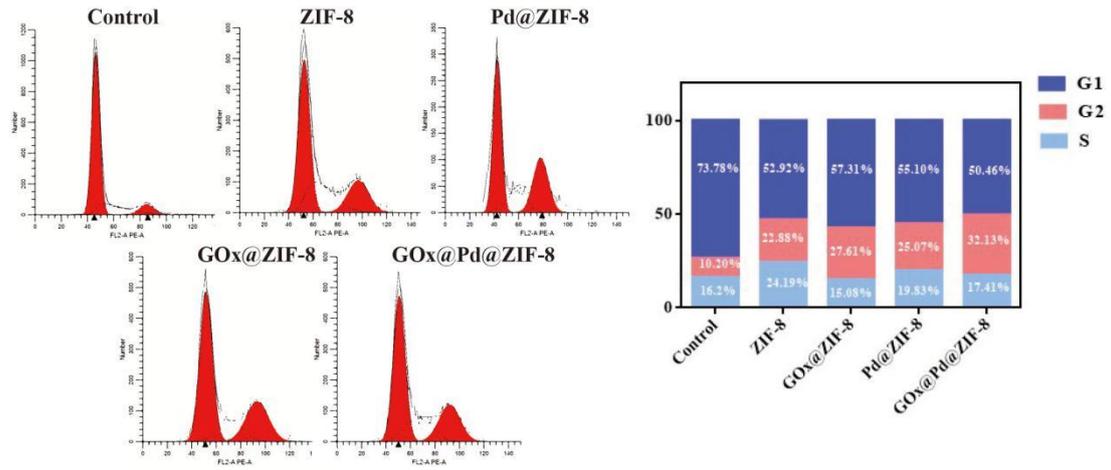


Figure S6. The A549 cells were treated with (A) untreated, (B) ZIF-8, (C) Pd@ZIF-8, (D) GOx@ZIF-8, (E) GOx@Pd@ZIF-8 for 48 h, G0/G1 and S/G2/M phases of A549 cells were quantified.

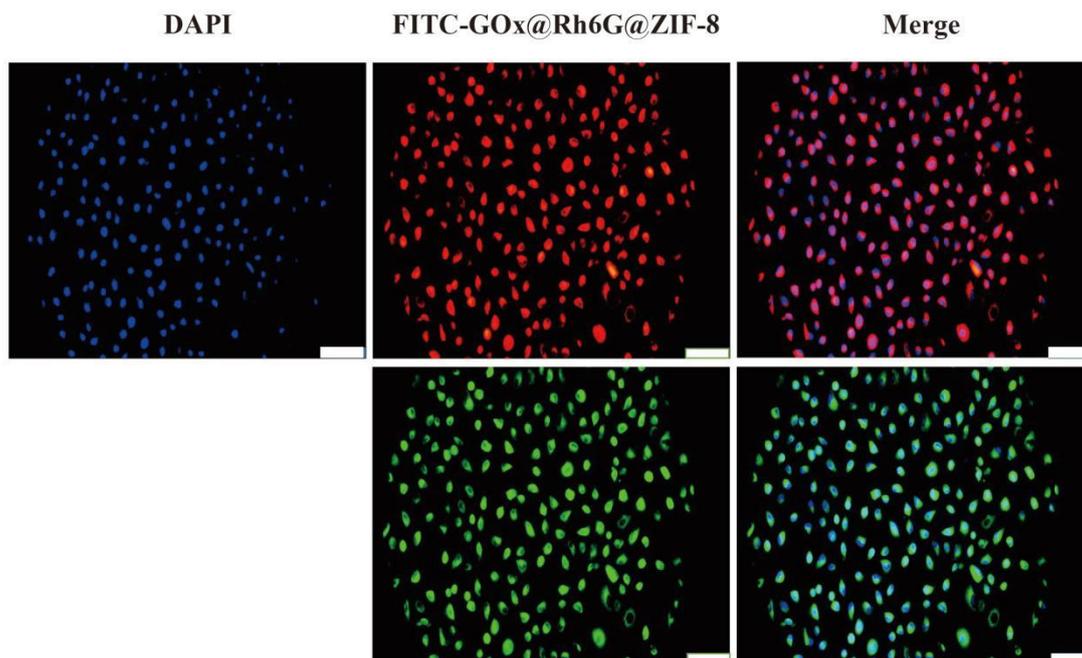


Figure S7. Endocytosis assay. We used FITC-GOx and Rh6G as a cargo to modify ZIF-8 simultaneously, and then detected the fluorescence distribution 6 h later. FITC-GOx emits a red fluorescent signal, Rh6G emits a green fluorescent signal, and the lower layer is the pictures after merge with DAPI. These results showed the nanomaterials entered the cytoplasm within 6 hours, Objective 10X, eyepiece 10X.

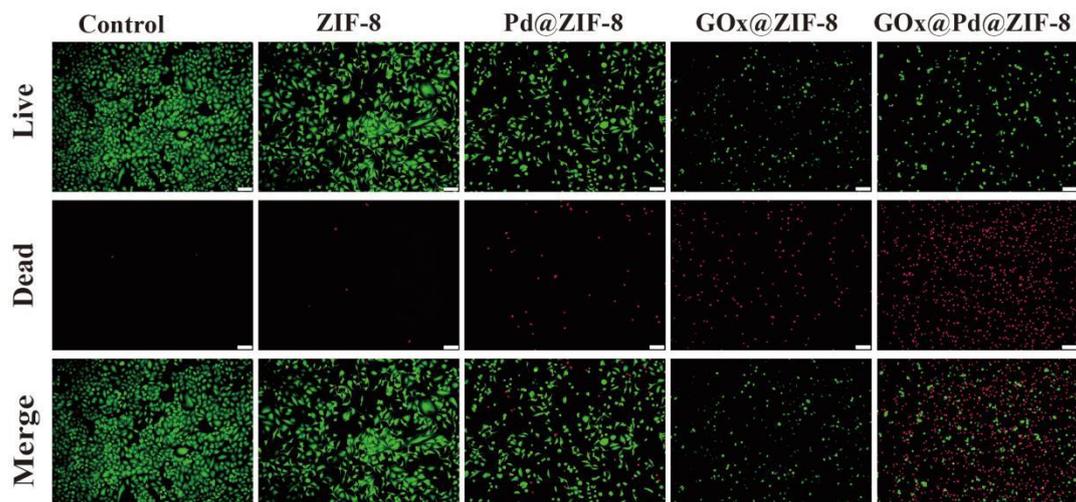


Figure S8. Inhibitory effect of various nanoparticles on A549 cells detected by Live & Dead assays. Red fluorescence represents dead cells, green fluorescence represents living cells. Objective 10X, eyepiece 10X.

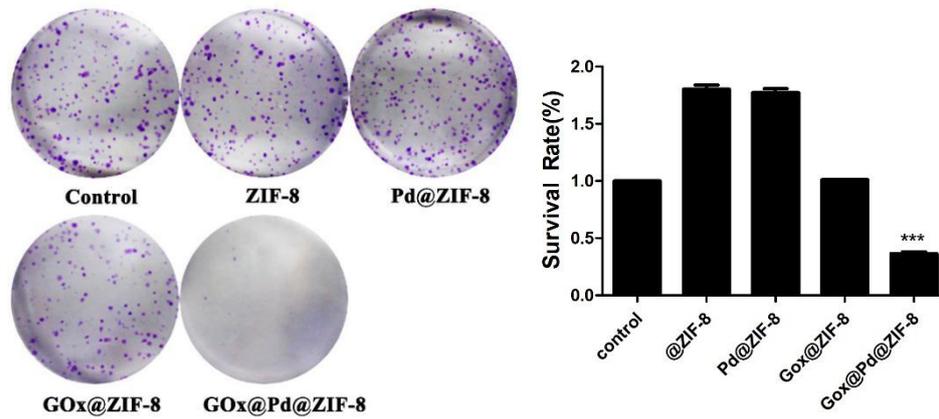


Figure S9. The A549 cells were treated with ZIF-8, Pd@ZIF-8, GOx@ZIF-8 and GOx@ZIF-8 for 24 hours, A549 cells were trypsinized and collected. Data are means \pm SD. * $P < 0.05$ and *** $P < 0.001$, compared with control.

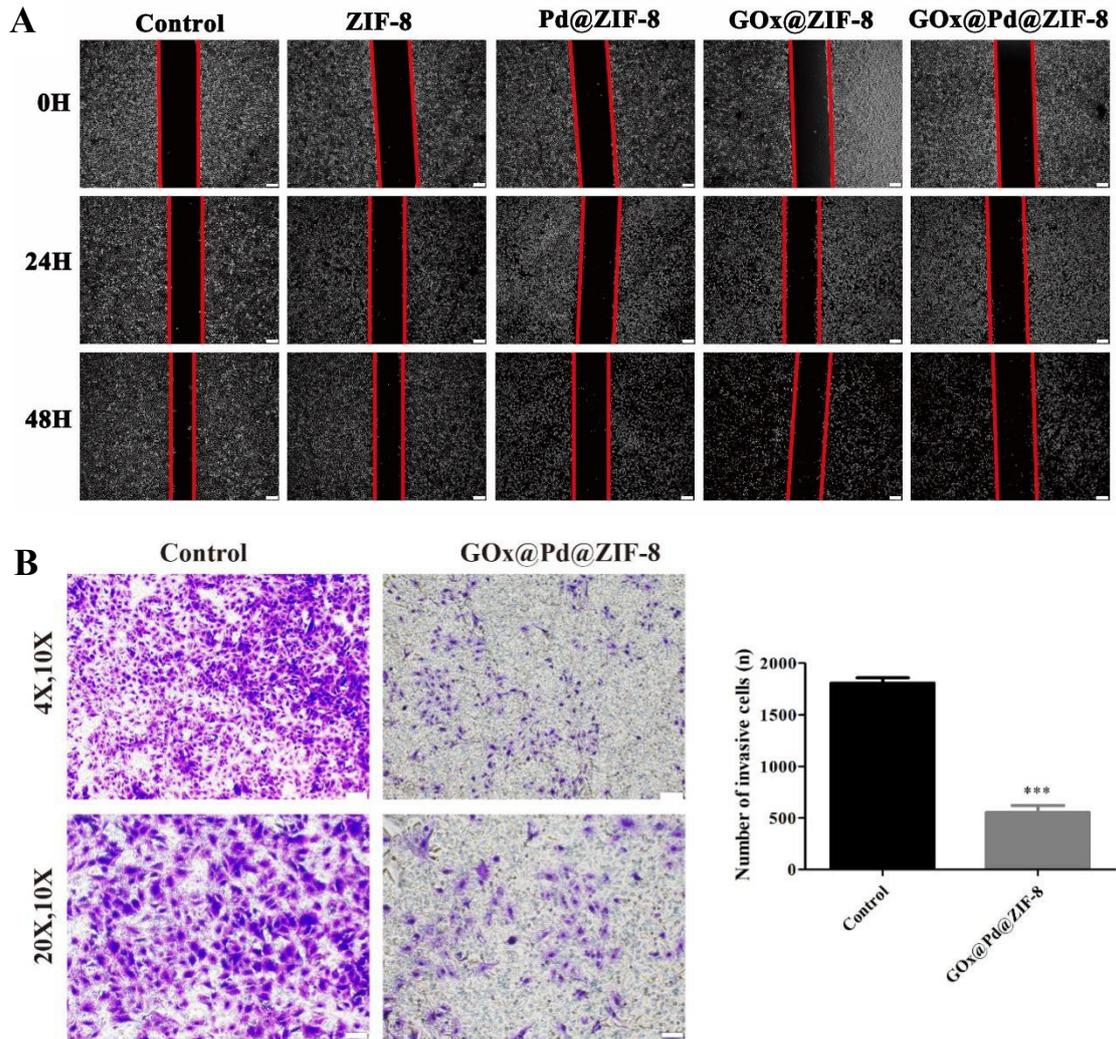
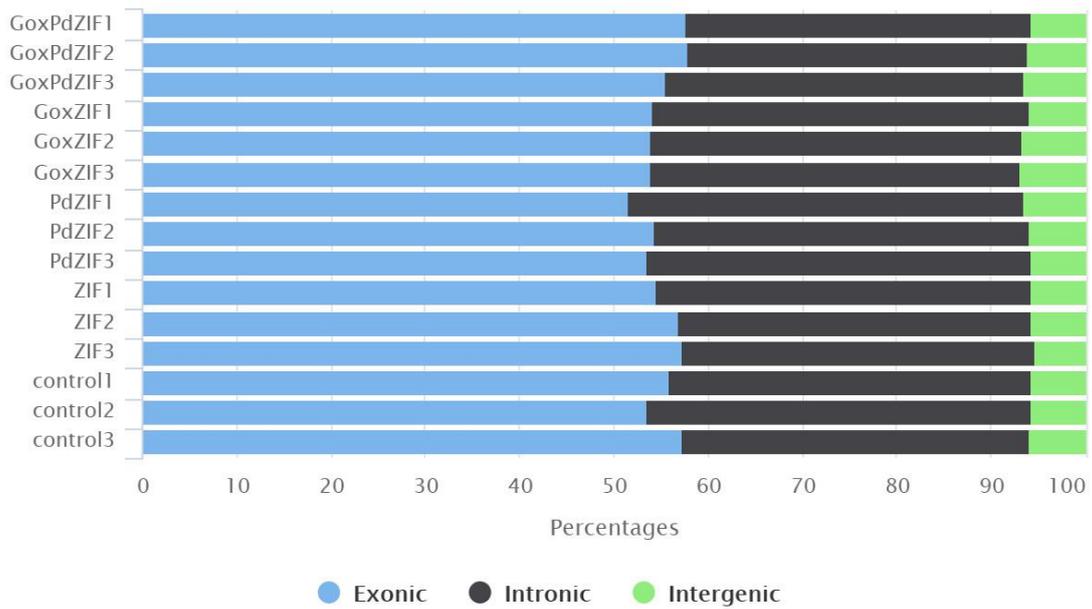


Figure S10. The A549 cells were treated with ZIF-8, Pd@ZIF-8, GOx@ZIF-8, GOx@Pd@ZIF-8, respectively. (A) the width of the wound was measured at 24 h and 48 h. (B) the number of invaded cells was counted in images taken with a fluorescence microscope at 30 h. Objective 10X, eyepiece 10X.

Qualimap RNAseq: Genomic Origin



Created with MultiQC

Figure S11. Genomic origin distribution of RNA-seq data from qualimap software. It shows more than 50% of the obtained reads mapped to exonic regions, and more than 30% of the obtained reads mapped to intronic regions in the annotated human genome (GRCh37).

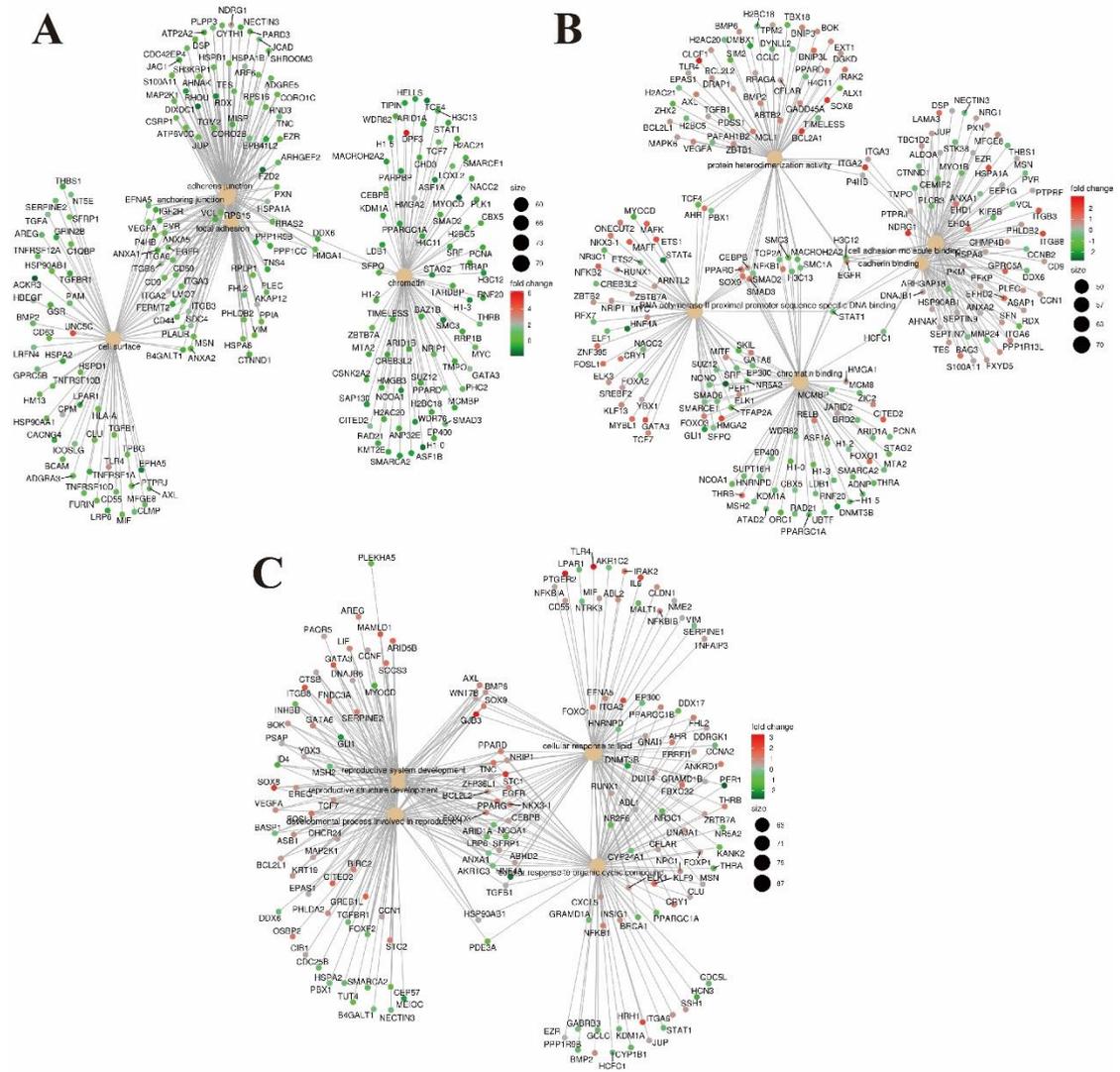


Figure S12. Gene Map. In order to consider the potentially biological complexities in which a gene may belong to multiple annotation categories, and provide information of numeric changes if available. (A) cellular components; (B) molecular function; (C) biological process. This picture shows several genes colored by LFC for top 5 most significant GO terms

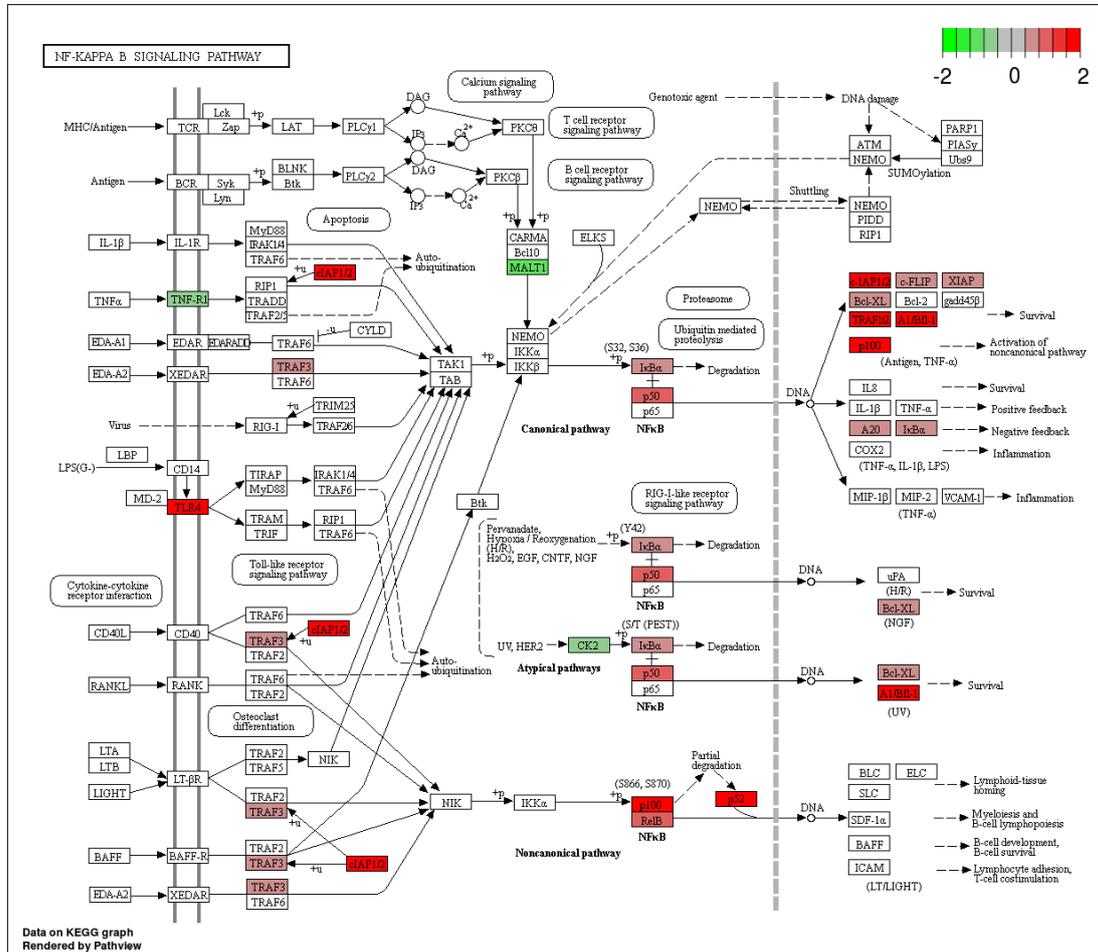


Figure S13. Genes dysregulated in NFκB signaling pathway from KEGG enrichment analysis. KEGG enrichment analysis showed that NFκB signaling pathway was activated after 4 h treatment of GOx@Pd@ZIF-8.