SUPPLEMENTARY INFORMATION

Cell mechanotatic and cytoxic response to Zinc oxide nanorods depends on substrate stiffness

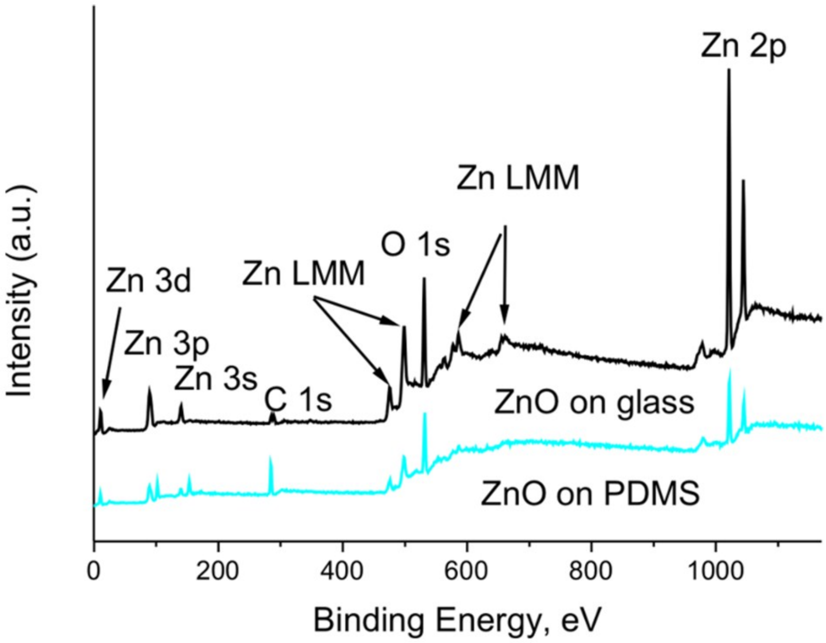

Fig. S1 X-ray photoelectron spectroscopy (XPS) survey of the ZnO-Nrd coated substrates: glass vs PDMS. The peaks show the presence of Zinc for as-prepared NRs as well as signals due to the Auger transitions.

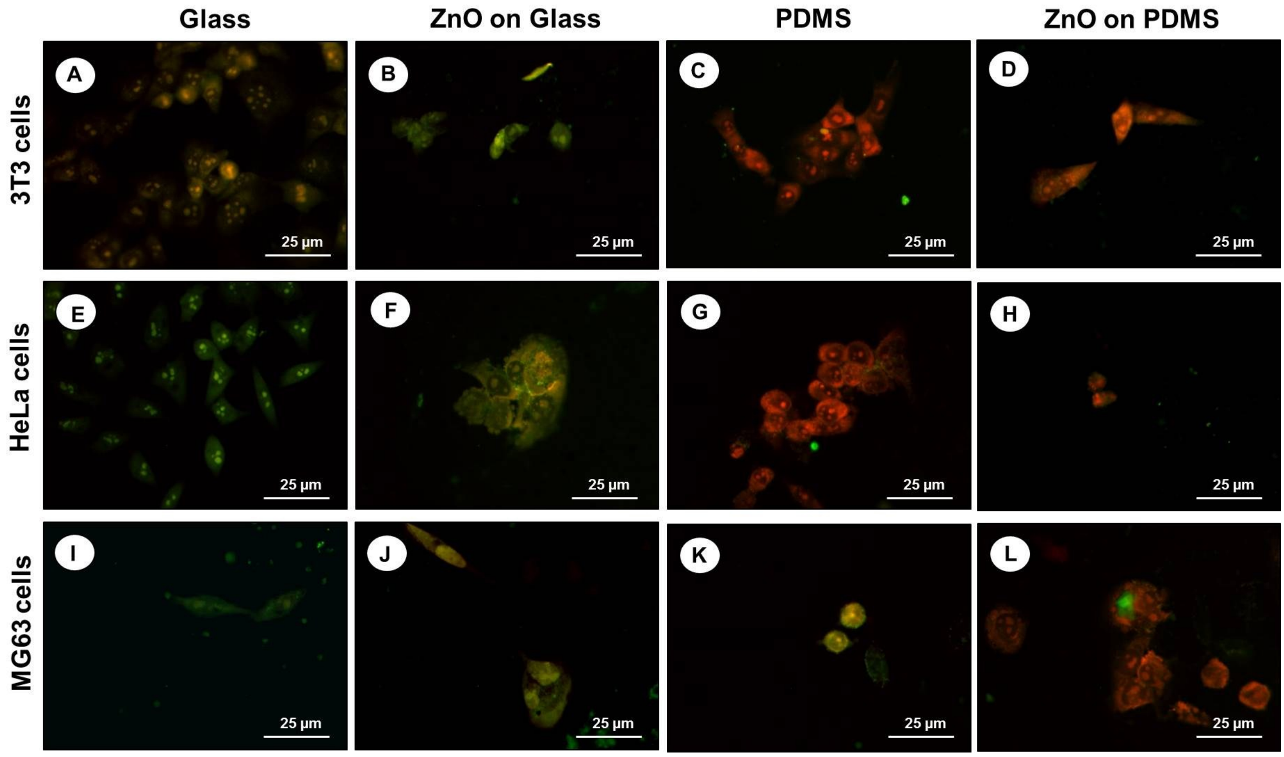

Fig. S2 Fluorescence images of Annexin V/Propidium Iodate staining after 24 hours of incubation of 3T3 fibroblasts (A,B,C,D), HeLa cells (E,F,G,H), and MG63 osteoblasts (I,J,K,L) on glass (A,E,I), ZnO-Nrds coated glass (B,F,J), PDMS (C,G,K) and ZnO-Nrds coated PDMS (D,H,L). A representative result of three independent experiments is shown. Scale bars: 25 µm.

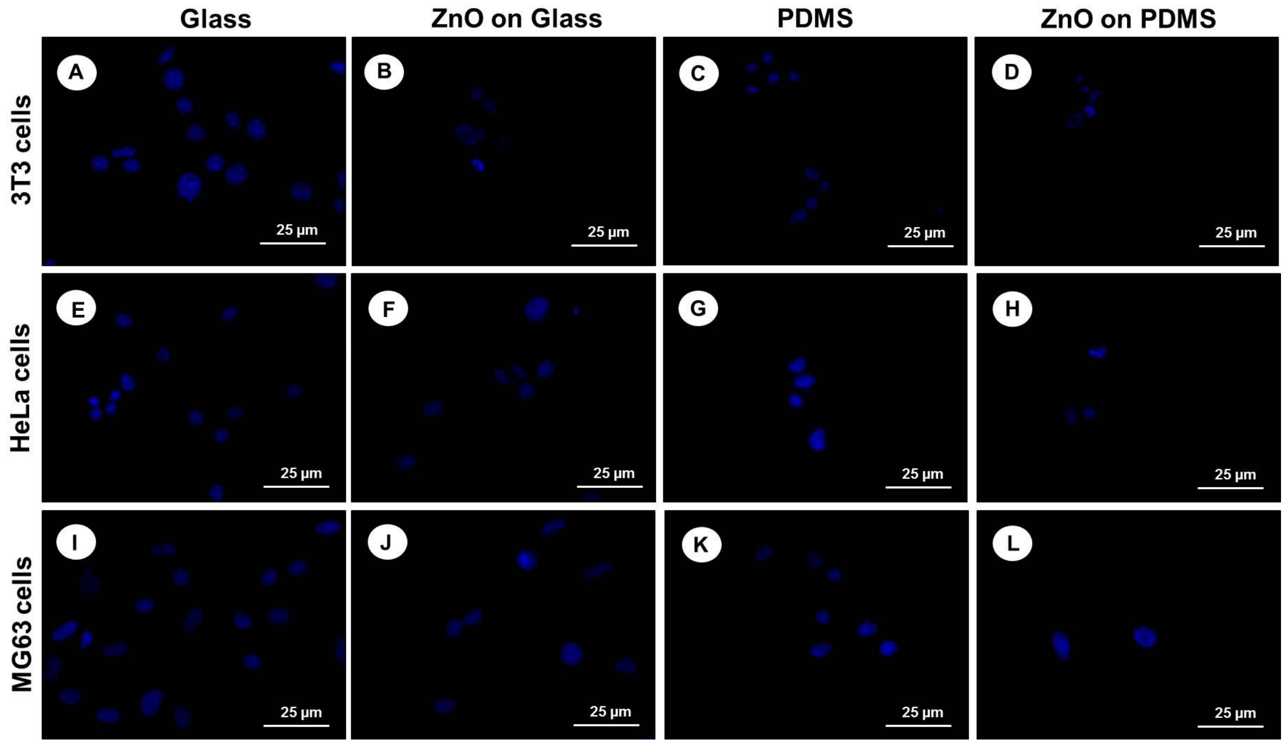

Fig. S3 Fluorescence images of Hoechst staining after 24 hours of incubation of 3T3 fibroblasts (A,B,C,D), HeLa cells (E,F,G,H), and MG63 osteoblasts (I,J,K,L) on glass (A,E,I), ZnO-Nrds coated glass (B,F,J), PDMS (C,G,K) and ZnO-Nrds coated PDMS (D,H,L). A representative result of three independent experiments is shown. Scale bars: 25 µm.

Substrates	**ZnO Morphology**	**Method of deposition**	**Cells**	**Mechanisms of ZnO toxicity**	**References**
Glass	ZnO NRs* and ZnO thin film relatively flat	Hydrothermal growth for NRs; Commercial film for flat	NIH 3T3 fibroblasts, Human umbilical cord vein endothelial cells (HUVECs) Bovine capillary endothelial cells (BCEs)	Toxicity due to chemically conjugating toxins and maybe nanotopography effect	Lee et al. [15]
Glass	ZnO NRs	Sonochemical growth	NIH 3T3 fibroblasts, bacterial culture	Glutathione oxidation, superoxide production, and membrane damage.	Okyay et al. [25]
PDMS	Ag NPs** on ZnO NRs	Hydrothermal growth for NRs	NIH 3T3 fibroblasts, bacterial culture	No significant toxic effect.	Chen et al. [24]
Glass	Ag NPs on ZnO NRs	Hydrothermal growth for NRs	Human hepatocarcinoma cells (HepG2), bacterial culture	No cytotoxic effects. Arginine may inhibit ROS-induced cytotoxicity.	Agnihotri et al. [26]
Glass and polyethylene terephthalate (PET) discs	ZnO NRs and ZnO thin film relatively flat	Hydrothermal growth for NRs; Sputtered ZnO for flat	Macrophages	Toxicity due to dissolved Zn and maybe nanotopography effect	Zaveri et al. [20]
Impregnated sterile gauze	ZnO ointment,	Commercial	Human dermal fibroblasts	The ointment vehicle induced cytotoxicity	Argen et al. [22]
Dispersion with culture medium	ZnO NRs	Hydrothermal synthesis	Bacterial culture	Particle size and morphology affect the antibacterial properties	Stanković et al. [18]Talebian et al. [19]
Dispersion with culture medium	ZnO NRs	Hydrothermal synthesis	Hela Cells (CCL-2)	No significant induction of oxidative stress and cell death	Gopikrishnan et al. [28]
Dispersion with culture medium	DNR loaded ZnO NRs	Hydrothermal synthesis	Human hepatocarcinoma SMMC-772	No cytotoxicity effects. Growth inhibition of cancer cells by photocatalysis of ZnO nanorods	Zhang et al. [27]
Dispersion with culture medium	ZnO tetrapods and ZnO NPs	Flame transport synthesis	Normal human dermal fibroblasts (NHDF)	Cytotoxicity depends on particle size and morphology and release of zinc ions	Papavlassopoulos et al. [16]
PDMS and glass	ZnO NRs	Hydrothermal synthesis	NIH 3T3 fibroblasts, Hela Cells,osteoblast-like cells MG63	Toxicity may depend on mechanotactic properties of the substrate.	Present work

* NRs: nanorods
**Nps: nanoparticles

Table S1 Literature reports on ZnO nanoparticles and nanorods structure, synthesis, substrates and cells.

PDMS				
Name	Peak BE	FWHM eV	Atomic %	Bond
Si_2p_3 - 1	102.4	1.37	24.3	$C_3 – Si – O$
Si_2p_3 - 2	103.0	1.37	5.5	$C – Si – O_2$
C1s	285.0	1.3	43.3	C – Si
O1s - 1	532.5	1.25	23.4	$C_3 – Si – O$
O1s - 2	533.4	1.25	3.5	H_2O

ZnO on Glass				
Name	Peak BE	FWHM eV	Atomic %	Bond
C1s – 1	285.0	2.53	9.8	C – C
C1s – 2	289.5	2.22	9.7	O – C = O
O1s	531.2	2.34	53.4	ZnO, O – C = O
$Zn2p_{3/2}$ – 1	1021.1	1.92	23.8	ZnO
$Zn2p_{3/2}$ – 2	1022.2	1.92	4.0	ZnO(OH)

ZnO on PDMS				
Name	Peak BE	FWHM eV	Atomic %	Bond
$Si2p_{3/2}$	102.3	1.33	23.1	C3 – Si – O
C1s	285.0	1.21	40.3	C3 – Si – O
O1s – 1	530.7	1.33	5.2	ZnO(OH)
O1s – 2	532.7	1.45	27.5	C3 – Si – O
$Zn2p_{3/2}$	1021.9	1.67	3.8	ZnO(OH)

Table S2 X-ray photoelectron spectroscopy (XPS) quantitative analysis and BE (eV) data for PDMS and ZnO-Nrd coated substrates on glass and PDMS.

Sample	**Surface Free Energy (mJ/ m^2)**		
	γ	γ^d	γ^p
PDMS	21.1	20.0	1.1
Glass	46.3	26.8	19.5
Glass-ZnO-Nrds	72.55	39.56	32.99
PDMS-ZnO-Nrds	89.22	64.37	24.88

Table S3 Surface free energies for ZnO-Nrd coated substrates.