Supplementary information for

Chitosan-coated cerium oxide nanocubes accelerate cutaneous wound healing by curtailing persistent inflammation

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Experimental Section

Cell culture. Rat insulinoma cell line INS-1 was purchased from the National Platform of Experimental Cell Resources for Sci-Tech (China). The cells were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum, 100 U/mL penicillin, 100 μg/mL streptomycin, 1 mM sodium pyruvate and 50 μM β-mercaptoethanol under 37 °C, saturated humidity and 5% CO2 (v/v). The cells were passaged every four to five days and the medium was changed every two days.

Cytotoxicity assay. Cell Counting Kit-8 (CCK-8, Dojindo, Kumamoto, Japan) was used to evaluate cell viability. Tetrazolium salt in the kit was reduced by dehydrogenases in cell mitochondria to a highly soluble yellow formazan, whose characteristic absorption at 450 nm can be employed as an indicator of cell viability. The cells were first plated in a 96-well plate with a density of 1.5×10^4 per well in 120 μL medium and pre-incubated for 24 h. 6 μL of CCNs of different concentrations were subsequently added, and the cells were further incubated for 48 h. Finally, the medium was replaced with fresh medium containing CCK-8 and further incubated for 2 h, after which the absorbance of each well at 450 nm and the reference wavelength of 650 nm was collected with a Synergy 4 multi-mode microplate reader (BioTek, USA).
Table S1. Description of primers used in RT-PCR

<table>
<thead>
<tr>
<th>Gene</th>
<th>Primer sequence</th>
<th>Product size</th>
<th>Annealing temp.</th>
<th>Accession number</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAPDH</td>
<td>F:5’-CTTCAACAGCAACTCCCATTC-3’&lt;br&gt;R:5’-GTAGCCATATTCATTGTCATACCAG-3’</td>
<td>106</td>
<td>60 °C</td>
<td>NC_005103</td>
</tr>
<tr>
<td>TNF-α</td>
<td>F:5’-ATCCGAGATGTGGAACTGGC-3’&lt;br&gt;R:5’-CGATCACCCCGAAGTTTCAGT-3’</td>
<td>153</td>
<td>60 °C</td>
<td>NM012675.3</td>
</tr>
<tr>
<td>IL-10</td>
<td>F:5’-TAAAAGCAAGGCAGTGGAGC-3’&lt;br&gt;R:5’-GTCACGTAGGCTTCTATGCAG-3’</td>
<td>161</td>
<td>60 °C</td>
<td>NM012854.2</td>
</tr>
</tbody>
</table>

![Cell viability of INS-1 cells incubated with CCNs of different concentrations for 48 h. Data are expressed as means ± SD, n = 6.](image_url)
Figure S2. Wound healing rate (%) of NS, as-prepared CeO$_2$ NCs and CCN-treated groups on day 2, 5, 8 and 12 post-wounding. Data are expressed as means ± SD. *$p<0.05$, **$p<0.01$ vs. other group(s) on the same day.

Figure S3. Representative image of H&E stained histopathological sections of normal rat skin (scale bar: 400 μm).