List of Changes

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Title: Nanotopographical Surfaces for Stem Cell Fate Control: Engineering Mechanobiology from the Bottom
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According to the comments from the reviewers and the editor, we have carefully revised our manuscript. The main changes are listed as follows.

1. We added a few references as suggested by the reviewers.

[131] K. Lee, A. Mazare, P. Schmuki, Chem Rev, 114 (2014) 9385-9454.
[132] X.M. Zhou, N.T. Nguyen, S. Ozkan, P. Schmuki, Electrochem Commun, 46 (2014) 157-162.
[133] C. Yao, T.J. Webster, J Nanosci Nanotechno, 6 (2006) 2682-2692.
[134] C. Yao, V. Perla, J.L. McKenzie, E.B. Slamovich, T.J. Webster, J Biomed Nanotechnol, 1 (2005) 68-73.
[135] S.H. Oh, R.R. Finones, C. Daraio, L.H. Chen, S.H. Jin, Biomaterials, 26 (2005) 4938-4943.
[136] T. Ohgai, X. Hoffer, L. Gravier, J.P. Ansermet, J Appl Electrochem, 34 (2004) 1007-1012.
[137] K. Watanabe, M. Sakairi, H. Takahashi, S. Hirai, S. Yamaguchi, J Electroanal Chem, 473 (1999) 250-255.
[138] H. Tsuchiya, J.M. Macak, A. Ghicov, Y.C. Tang, S. Fujimoto, M. Niinomi, T. Noda, P. Schmuki, Electrochim Acta, 52 (2006) 94-101.
[136] M. Jarcho, C.H. Bolen, M.B. Thomas, J. Bobick, J.F. Kay, R.H. Doremus, J Mater Sci, 11 (1976) 2027-2035.
[137] T. Nishimura, M. Mitomo, H. Hirotsuru, M. Kawahara, J Mater Sci Lett, 14 (1995) 1046-1047.
[138] M. Nygren, Z.J. Shen, Solid State Sci, 5 (2003) 125-131.
[139] J. Rankin, B.W. Sheldon, Materials Science and Engineering a-Structural Materials Properties Microstructure and Processing, 204 (1995) 48-53.
[149] S. Namgung, T. Kim, K.Y. Baik, M. Lee, J.M. Nam, S. Hong, Small, 7 (2011) 56-61.
[150] D. Khang, S.Y. Kim, P. Liu-Snyder, G.T.R. Palmore, S.M. Durbin, T.J. Webster, Biomaterials, 28 (2007) 4756-4768.
[155] S. Lee, M.K. Leach, S.A. Redmond, S.Y.C. Chong, S.H. Mellon, S.J. Tuck, Z.Q. Feng, J.M. Corey, J.R. Chan, Nat Methods, 9 (2012) 917-+.
[156] J. Gerardo-Nava, T. Fuhrmann, K. Klinkhammer, N. Seiler, J. Mey, D. Klee, M. Moller, P.D. Dalton, G.A. Brook, Nanomedicine (Lond), 4 (2009) 11-30.
[197] J. Huang, S. Grater, F. Corbellini, S. Rinck, E. Bock, R. Kemkemer, H. Kessler, J. Ding, J. Spatz, Nano Lett. 9 (2009) 1111-1116.
[212] F. Kantawong, K.E.V. Burgess, K. Jayawardena, A. Hart, R.J. Burchmore, N. Gadegaard, R.O.C. Oreffo, M.J. Dalby, Biomaterials. 30 (2009) 4723-4731.
[218] J. Kim, H.N. Kim, K.T. Lim, Y. Kim, H. Seonwoo, S.H. Park, H.J. Lim, D.H. Kim, K.Y. Suh, P.H. Choung, Y.H. Choung, J.H. Chung, Sci. Rep. 3 (2013)

[220] L. Azzolin, F. Zanconato, S. Bresolin, M. Forcato, G. Basso, S. Bicciato, M. Cordenonsi, S. Piccolo, Cell 151 (2012) 1443-1456.
[230] S. Piccolo, S. Dupont, M. Cordenonsi, Physiol. Rev. 94 (2014) 1287-1312.

2. We corrected the typos suggested by the reviewers on page 12 and 56.

3. Following the suggestion by the reviewer and to make it clearer for readers, we made minor changes to the fabrication method section and added a table (Table 1) summarizing and comparing the advantages and disadvantages of each method.

4. Following the suggestion by the reviewer, we revised the manuscript thoroughly and reduced the descriptive words and added discussions about the potential future directions in the "Conclusion remarks and outlook". We also revised the manuscript thoroughly to provide more insight discussion of each applications.

5. Following the suggestion by the reviewer, we added balanced discussions on other potential signaling pathways in section "Adhesion-based mechanosensors and cytoplasmic transducers". Accordingly, we also revised the Figure 8 (original Fig. 7) to more appropriately present our hypothesis in a balanced way and covering a wider scope of prospective mechanisms.

6. Following the suggestion by the reviewer, we added a separate paragraph in section "Adhesion-based mechanosensors and cytoplasmic transducers" discussing in detail the recent studies on the nanotopography-sensing of integrins, as well as a few relevant hypothetical mechanisms. Accordingly, we added one figure (Fig. 7) to summarize published relevant results on this topic.

7. We wrote the section on "Nuclear mechanosensors" in a more condensed manner according to the review's suggestion.

8. We prepared a new Graphic Abstract.

9. Following the suggestion by the reviewer, we shortened the *"*Mesenchymal stem cells into neural differentiation" on page 22.

10. We deleted the sentences "Importantly, temporal down-regulation of E-cadherin with concurrent up-regulation of N-cadherin expression during differentiation of human ESCs on both planar and nanopit substrates was observed, indicating an epithelial to mesenchymal transition (EMT) during differentiation of human ESCs [146] Such an EMT-like morphological change demonstrated a slight preference to the nanopit array." on page 27-28.

11. Following the suggestion by the reviewer, we added a brief discussion and a few recent references about how nanotopography can influence the way ECM proteins adsorb to surfaces and in turn affect stem cell behaviors on page 21.