From nano to macro: biomaterials for a synthetic stem cell niche

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Abstract

Blood is replenished with billions of fresh cells every day throughout the entire life span. The source of these cells are the so-called hematopoietic (= blood forming) stem cells (HSCs). Their ability to reconstitute the entire blood system makes them the key to the cure of many hematological diseases. Upon transplantation from a healthy donor, they are able to replace the diseased hematopoietic system of the patient. However, this treatment is restricted by the limited availability of HSCs. To overcome that limitation, controlling HSC behavior in terms of proliferation or differentiation *in vitro*, is an important goal of nowadays HSC research.

In vivo HSCs are controlled by a highly specialized microenvironment – the niche – within the bone marrow. In this niche HSCs are supported by mutual cell-cell as well as cell-matrix interactions. While it is clear that biological and/or chemical parameters play an important role in this interplay, surprisingly little attention was paid to physical signals that are transmitted by the niche microenvironment. In the last years, we found that these physical signals include nanostructure[1,2], matrix stiffness[3], as well as the three-dimensional architecture[4]. In reductionist approaches, in which we studied only one parameter at a time, we could show that all of these parameters impact HSC behavior.

In order to achieve the goal of a synthetic stem cell niche to guide HSC behavior, the complexity of the natural HSC niche, which combines a variety of different signals, has to be taken into account. For this purpose, we increased the complexity of our systems to study the synergistic effects of different biological and/or physical signals[5,6]. With these experiments we hope to get one step closer towards a synthetic stem cell niche that is as simple as possible but as complex as necessary to instruct HSCs.

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[1] Altrock et al. (2012) *Biomaterials*, doi: 10.1016/j.biomaterials.2012.01.002
[2] Muth et al. (2013) *PloS ONE*, doi: 10.1371/journal.pone.0054778
[3] Lee-Thedieck et al. (2012) *J Cell Sci*, doi: 10.1242/jcs.095596
[4] Raic et al. (2014) *Biomaterials*, doi: 10.1016/j.biomaterials.2013.10.038
[5] Rödling et al. (2017) *Sci Rep*, accepted
[6] Winkler et al. (2017) *Adv Funct Mater*, doi: 10.1002/adfm.201606495