Creating “right” microenvironments for controlling stem cell phenotypes

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Cellular microenvironments play critical roles in precisely regulating cell functions and tissue organization, and dysfunctions of tissue microenvironments cause tumor formation, progression, and metastasis. Therefore, understanding the mechanisms through which microenvironments exert their effects facilitates the establishment of accurate and efficient methods for manipulating cellular functions and the development of cell-based therapies, drug development and screening, and cancer diagnosis and therapy. However, our understanding of these microenvironments remains limited because we lack proper tools to perturb environmental factors precisely and investigate cellular phenotypic responses systematically. In this study, we integrated microfluidics and nanofibers to create various artificial cellular environments on a single platform: we call this the Multiplexed Artificial Cellular MicroEnvironment (MACME) array. In this platform, image-based cytometry followed by statistical analysis is used for systematically analysing cell behaviour under the influence of multiparametric environment factors. Combining image-based and statistical analyses enables quantitative interpretation of individual cellular phenotypic responses to environmental cues.

We applied our strategy by testing how environmental cues affect the functions of self-renewing human pluripotent stem cells (hPSCs) can potentially be used in drug development, cell-based therapies, tissue engineering, and regenerative medicine, due to the unique characteristics, such as unlimited self-renewal and capacity for directed differentiation into most cell types. In this context, we expect our strategy for identifying optimal conditions for maintaining hPSC self-renewal to be appropriate for this challenge, and we elucidate how environments altered cellular phenotypes.

Furthermore, we confirm that the optimal conditions identified here can be scaled-up for macroscopic cultures. The use of this combinatorial approach provides insights into the underlying chemical and physical mechanisms that govern stem-cell fate decisions.

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