Diffusion dynamics play an essential role in regulating stem cells and tissue development

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Gradients of molecular signaling factors play an essential role in numerous events in embryonic development, from patterning limb and organ formation to the intricate shaping of the brain and neuroanatomical architecture. These gradients are a consequence of diffusion dynamics in tissues, and newly published work describes two vital aspects of these diffusion processes in tissue development—first, the influence of molecular diffusion gradients on stem cell signaling pathways is described in detail, including a summary of recent discoveries in how gas and nutrient concentrations can influence stem cell potency, differentiation, and metabolism. Secondly, the paper describes novel applications of diffusion equations to model concentration gradients of nutrients and signaling factors in three-dimensional (3D) tissue constructs under a variety of conditions, including with or without cellular metabolism of the diffusing substance.

With the recent advent of complex stem-cell-derived 3D tissue constructs (e.g., organoids or mini-organs) in forming and modeling innate tissues and organ structures like the brain, and with recent discoveries that gas and nutrient concentrations can have a vast number of effects on stem cell state and function, a novel role of diffusion modeling will be immensely important to rigorous study of developmental processes, disease modeling, and regenerative medicine. This work provides several tools and resources that will enable researchers from many backgrounds to understand and model diffusion processes for their specific types of tissue constructs, including models for diffusion either into or out of the tissue, and for any type of diffusant

molecule, biomaterial scaffold, and cell type.

Although many mechanisms of how stem cells self-organize at the proper place and time into mature tissues and organs still remain to be elucidated, it is clear that the architecture, composition, and function of numerous tissues is influenced by many overlapping diffusion signals during development, and this work helps open the door for many more complex and unique diffusion solutions to be explored and studied as they relate to developmental events.

"Understanding these mechanisms requires a synthesis of stem cell biology and mass transfer physics, where physical diffusion phenomena affect neurodevelopmental cues that define cell identities and ultimately help shape the cellular architecture of the brain," said Dr. Richard McMurtrey, the author of the work. "The dynamics of all this cross-talk are complex and still beyond our complete comprehension, but it is fascinating that the layout of the brain and all the processing of information that flows through it ultimately depend on numerous critical signaling events that organize these cellular systems early in development."

More information: Richard J. McMurtrey, Roles of Diffusion Dynamics in Stem Cell Signaling and Three-Dimensional Tissue Development, *Stem Cells and Development* (2017). DOI: 10.1089/scd.2017.0066

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