Epidermal homeostasis and radiation responses in a multiscale tissue modeling framework

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The surface of skin is lined with several thin layers of epithelial cells that are maintained throughout life time by a small population of stem cells. High dose radiation exposures could injure and deplete the underlying proliferative cells and induce cutaneous radiation syndrome. In this work we propose a multiscale computational model for skin epidermal dynamics that links phenomena occurring at the subcellular, cellular, and tissue levels of organization, to simulate the experimental data of the radiation response of swine epidermis, which is closely similar to human epidermis. Incorporating experimentally measured histological and cell kinetic parameters, we obtain results of population kinetics and proliferation indexes comparable to observations in unirradiated and acutely irradiated swine experiments. At the sub-cellular level, several recently published Wnt signaling controlled cell-cycle models are applied and the roles of key components and parameters are analyzed. Based on our simulation results, we demonstrate that a moderate increase of proliferation rate for the survival proliferative cells is sufficient to fully repopulate the area denuded by high dose radiation, as long as the integrity of underlying basement membrane is maintained. Our work highlights the importance of considering proliferation kinetics as well as the spatial organization of tissues when conducting in vivo investigations of radiation responses. This integrated model allow us to test the validity

of several basic biological rules at the cellular level and sub-cellular mechanisms by qualitatively comparing simulation results with published research, and enhance our understanding of the pathophysiological effects of ionizing radiation on skin.