THE SUFFICIENT COMPONENT CAUSE MODEL: EXPLAINING LOW-DOSE RADIOBIOLOGY THROUGH AN EPIDEMIOLOGIC LENS

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October 12, 2021

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One of the major challenges in understanding space radiation-induced carcinogenesis is the uncertainty from translating radiobiological research in cellular and animal models to humans, especially at doses below 100 mSv. Biological studies have shown a host of potential outcomes at low doses in animal and cellular models. The existence of non-targeted effects as bystander and abscopal effects is well-documented from clinical research and basic science[1,2,3]. While some studies have shown increased effects at low doses, others have shown evidence of hormetic bystander effects, where radiation exposure may be beneficial[4,5,6]. Despite these varied and diverse findings, epidemiologic studies largely support the linear-no threshold (LNT) assumption used by radiation protection guidance[7,8]. Translational animal-to-human models have predominantly considered ratio values such as the relative biological effectiveness (RBE) and dose and dose-rate effectiveness factor (DDREF) that rely on the assumption of LNT rather than implementing specific dose-response shapes in the low-dose region, and translational cell-to-human models are uncommon.

The sufficient component cause model presents an opportunity to examine biological findings at low doses from an epidemiological lens[9]. In this model, exposures “sufficient” to cause an outcome of interest are presented in pie charts, such that when all slices of a pie chart are fulfilled, the outcome will occur. Multiple pie charts may exist for a single outcome, illustrating individual differences[9]. In 1988, Greenland and Poole adapted the sufficient component cause model to incorporate interaction with other exposures (such as genetics or lifestyle factors)[10]. They show that a range of biological processes are possible in a population, but that an epidemiologic study will only reveal the mean outcome from the population at large[10,11]. Using this construct, the multiple outcomes presented in radiobiological models to date can be explained in the context of epidemiologic studies.

This presentation aims to demonstrate a causal framework that can integrate radiobiological and epidemiological models to date. It is intended as a conversation starter to spur future research.

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