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Agent-based multi-scale modeling enhances understanding of the immune response to M. tuberculosis infection. Preliminary report.

Human infection with the bacteria *M. tuberculosis* (Mtb) produces a complex immune response that results in the formation of unique, emergent lung structures called granulomas. Due to the duration and dynamic nature of this immune response, as well as the involvement of processes that occur over tissue, cellular, and molecular scales, we take a multi-scale and mechanistic computational modeling approach. We build a hybrid agent-based model at the cellular scale which produces output at a tissue scale that incorporates mathematical elements including diffusion and recruitment, and we use a middle out approach to make this model multi-scale by adding molecular scale dynamics. We generate simulated granulomas whose range of spatial configurations reflects the heterogeneity observed experimentally, and through the use of uncertainty and sensitivity analyses, we identify parameters that drive such heterogeneous outcomes. We are particularly interested in how the behavior of neutrophils, a newly added model cell type, contributes to Mtb protection versus pathology. Through the parallel development of a 3D model, we analyze simulated output in 2D and 3D environments, and we present novel 3D visualization techniques to enhance conceptual understanding of the immune environment. (Received September 17, 2019)