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Evolution of Competing Diversities: Tumor vs. Immune

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T-cells, part of the human adaptive immune system, have T-cell receptors that recognize antigens (i.e. short amino acid sequences) presented by cells. Each T-cell clone responds to a different antigen, and therefore the T-cell repertoire is highly diverse. To prevent auto-immunity, this repertoire undergoes strong negative selection against “self” antigens during T-cell development, leading to a skewed diversity that primarily responds to “foreign” antigens (e.g. viral). Proto tumor cells initially start out presenting only “self” antigens typical of their cell-type of origin, since they arise from normal tissue cells. However, oncogenic mutations will cause the antigenic profile of a tumor cell to emerge from the protective shadow of self-antigen privilege. This exposure can occur through production of mutated antigens that appear “foreign”, or by over-production of self-antigens to a level at which they foment an auto-immune response. The accumulation and diversification of oncogenic strategies (i.e. acquisition of beneficial “drivers”) is therefore subject to increased exposure to immune attack, particularly in early-stage tumors where broad immunosuppressive strategies have not had time to develop. Here, we use a mathematical model to study how different aspects of tumor progression (cell turnover rate, radial growth rate, mutation rate, vascular density, and tissue density) stimulate different immune responses. These lead to either complete tumor eradication by the immune system, or immunologic escape and tumor growth. In the tumors that do escape, different patterns of heterogeneity emerge (e.g. big bang vs. clonal sweep vs. highly diverse). Additionally, a diversity of T-cell memory is developed over time, which has implications for the viability of future oncogenic alterations.