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Evolution of cooperation among tumor cells

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The evolution of cooperation has a well established theoretical framework based on game theory. This approach has made valuable contributions to a wide variety of disciplines, including political science, economics, and evolutionary biology. Existing cancer theory suggests that individual clones of cancer cells evolve independently from one another, acquiring all of the genetic traits or hallmarks necessary to form a malignant tumor. It is also now recognized that tumors are heterotypic, with cancer cells interacting with normal stromal cells within the tissue microenvironment, including endothelial, stromal, and nerve cells. This tumor cell–stromal cell interaction in itself is a form of commensalism, because it has been demonstrated that these nonmalignant cells support and even enable tumor growth. Here, we add to this theory by regarding tumor cells as game players whose interactions help to determine their Darwinian fitness. We marshal evidence that tumor cells overcome certain host defenses by means of diffusible products. Our original contribution is to raise the possibility that two nearby cells can protect each other from a set of host defenses that neither could survive alone. Cooperation can evolve as by-product mutualism among genetically diverse tumor cells. Our hypothesis supplements, but does not supplant, the traditional view of carcinogenesis in which one clonal population of cells develops all of the necessary genetic traits independently to form a tumor. Cooperation through the sharing of diffusible products raises new questions about tumorigenesis and has implications for understanding observed phenomena, designing new experiments, and developing new therapeutic approaches.

carcinogenesis | hallmarks | tumorigenesis | cancer

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