Malignancy from cooperation

Cooperation among tumor cells may improve their odds of survival and eventual malignancy, as proposed by Robert Axelrod, Kenneth Pienta (University of Michigan, Ann Arbor, MI), and David Axelrod (Rutgers University, Piscataway, NJ). By applying the theoretical analysis of cooperation known as game theory, the authors offer a new way to view cancer progression.

Originally an economic analysis, game theory is now widely used. “In terms of societies, businesses, even political parties,” says David Axelrod, “competition, where one wins and one loses, is not necessarily the best strategy. But cooperate, and both can win.” He and his colleagues argue that the same can be said for tumor cells.

Tumors are a mixed bag of cells that have acquired different mutations, creating unique lineages. Malignancy is thought to result only when a subclone gains all of the necessary mutations, while many others die out due to genetic instability or host defenses. Game theory, say the authors, adds to this thinking by suggesting that different tumor subclones share resources and thereby help each other survive and multiply.

In a theoretical analysis, the authors discussed a few examples in which a hallmark of cancer is also a sharable resource. For example, one hallmark is the ability to produce growth factors. A lineage that secretes a necessary soluble growth factor may help nearby tumor cells that lack this factor but express its receptor. It may, in turn, get another growth factor from a second lineage. Another hallmark is angiogenesis. Tumor cells may produce diffusable angiogenic factors that induce blood vessels, which support neighboring cells that lack these factors.

According to the authors, the theory is consistent with what is known about tumor biology and makes predictions that can be tested, such as the presence of different growth factors expressed by nearby cells. But even before the theory’s validity is tested, they hope that biologists and publishers will be open to theoretical reports that stimulate new experiments. “New ways of thinking can be as powerful as obtaining new data,” says Axelrod. “As biologists, we’ve been in the business of collecting data. Now we have to start thinking about how this data can be put together.”

Reference: Axelrod, D., et al. 2006. Proc. Natl. Acad. Sci. USA. 103:13474–13479.