Why We Should Study Cancer Like We Study Ecosystems

By Rachel Nuwer

1 When pine beetles invaded North American forests, they threw a delicate ecosystem out of balance. Cancer cells, too, behave like damaging invasive species.

当松甲虫入侵北美森林时,它们使脆弱的生态系统失去了平衡。癌细胞的行为也像 破坏入侵物种一样。

2 Sometimes, thinking about an old problem from a refreshing new angle is just the thing needed to find that eureka moment.

有时候,从一个崭新的角度思考一个老问题仅仅是找到尤里卡时刻的必要。

3 Cancer, one of the most **notorious** medical **maladies**, has been studied intensely in the current era of modern medicine. But a growing number of researchers think that bringing a fresh, out-of-the-box approach to understanding the disease may lead to some novel insights and, perhaps, solutions. And the subject that they're hoping can serve as a window into the study of cancer may surprise you: ecology.

癌症是最臭名昭著的医学疾病之一,在当今的现代医学时代已经进行了深入研究。但 是,越来越多的研究人员认为,采用一种全新的,开箱即用的方法来了解这种疾病可能会 带来一些新颖的见解,甚至可能是解决方案。他们希望它可以作为癌症研究的窗口,这可 能会让您感到惊讶:生态学。

4 On face value, oncology and ecology seem vastly different. For example, one is localized to specific cells in the body, while the other by definition spans the entire globe. But rather than labeling cancer as a group of mutated cells, as the thinking goes, we should see cancer as a disruption in the balance of a complex microenvironment in the human body. 1) Like a damaging invasive beetle eating its way through forests in Colorado, a novel disease breaking out in populations of wild birds, or loggers mowing down parts of the Amazon rainforest, cancer throws a **monkey wrench** into an otherwise **placid**, balanced system.

从表面上看,肿瘤学和生态学似乎有很大的不同。例如,一个位于人体的特定细胞中, 而另一个则定义为遍布整个地球。但是,正如人们所认为的那样,我们应该将癌症视为对 人体复杂微环境平衡的破坏,而不是将癌症标记为一组突变的细胞。1)就像破坏性的甲 虫在科罗拉多州的森林中觅食一样,一种新的疾病在野鸟种群中爆发,或者伐木工人在亚 马逊雨林的一部分上砍伐,癌症使猴子扳手陷入了原本平静的平衡系统中。

5 This way of thinking makes cancer seem even more complex than it already is, but it could provide insights that ultimately make cancer more treatable, propose researchers from the Moffet Cancer Center in a paper published in the journal *Interface Focus*.

Moffet癌症中心的研究人员在《Interface Focus》杂志上发表的一篇论文中提出,这种 思维方式使癌症看起来比现在更加复杂,但是它可以提供最终使癌症更易于治疗的见解。

6 "Einstein is known to have said that everything should be made as simple as possible, but not simpler," they write. 2) "It turns out that complexity has its place and, as convenient as it would be for cancer biologists to study tumor cells in isolation, that makes as much sense as trying to understand frogs without considering that they tend to live near swamps and feast on insects."

他们写道: "众所周知,爱因斯坦曾说过一切都应尽可能简单,而不是简单。" 2) "事实证明,复杂性是有其地位的,对于癌症生物学家来说,隔离肿瘤细胞的便利性与试 图理解青蛙而不考虑它们倾向于生活在沼泽和盛宴的意义一样有意义。在昆虫上。"

7 We tend to think of cancer only in terms of mutated cells, the authors continue. But adopting this narrow approach is like trying to understand why a frog has a sticky tongue without taking into account that frogs use their tongues to catch insects. Cancer cells, likewise, need context. A voracious cancer cell, for example, may situate itself next to a blood vessel not by chance, but by choice so it can obtain more nutrients and oxygen to support its unlimited division.

作者继续说,我们倾向于仅从突变细胞的角度来考虑癌症。但是,采用这种狭窄的方 法就像试图理解为什么青蛙的舌头发粘,而没有考虑到青蛙用舌头抓昆虫的原因。同样, 癌细胞也需要环境。例如,一个贪婪的癌细胞可能不是偶然地而是自身定位在血管旁,而 是通过选择使它能够获取更多的营养和氧气以支持其无限分裂。

8 Cancer cells must compete within the body for nutrients and other resources, just like animals living in an environment must compete with one another in order to survive. This means that cancer, like any organism, must adapt to its environment in order to **thrive**. The researchers explain:

癌细胞必须在体内争夺营养和其他资源,就像生活在环境中的动物为了生存而必须相 互竞争一样。这意味着癌症,像任何生物一样,必须适应其环境才能蓬勃发展。研究人员 解释:

9 It is now beginning to be widely accepted that cancer is not just a genetic disease but the one in which evolution plays a crucial role. This means that tumor cells evolve, adapt to and change the environment in which they live. The ones that fail to do so will ultimately become extinct. The ones that do will have a chance to invade and metastasize. 3) The capacity of a tumor cell to adapt to a new environment will thus be determined by environment and the cellular species from the original site, to which it has already painstakingly adapted.

现在开始被广泛接受,癌症不仅是一种遗传疾病,而且在进化中起着至关重要的作用。 这意味着肿瘤细胞会进化,适应并改变其生存环境。没有这样做的人将最终灭绝。这样做 的人将有机会入侵和转移。 3) 因此,肿瘤细胞适应新环境的能力将取决于环境和原始位 置的细胞种类,而这些部位已经经过艰苦的适应。

10 So how can all of this theory be applied in real life? The environmental approach to understanding cancer is so complex that it rules out normal experiments; they could easily go away with so many different components to consider. Instead, the researchers suggest turning to mathematics and computation for understanding the greater environmental context that leads to cancer. Ecologists use one such mathematical approach, game theory, as a way to study evolutionary biology and the way animals interact:

那么,如何将所有这些理论应用到现实生活中?理解癌症的环境方法是如此复杂,以 至于排除了正常的实验。他们可以轻松考虑许多不同的组件。相反,研究人员建议转向数 学和计算以了解导致癌症的更大环境。生态学家使用一种这样的数学方法,即博弈论,作 为研究进化生物学和动物相互作用的方法:

11 The force of natural selection keeps ecosystem denizens focused on optimizing the bottom line: long-term reproduction. In the games studied by evolutionary game theoreticians, individuals compete for available resources using a variety of strategies. These features and

behaviors, known as the phenotypic strategy, determine the winners and losers of evolution. 自然选择的力量使生态系统居民专注于优化底线:长期繁殖。在进化游戏理论家研究 的游戏中,个人使用各种策略竞争可用资源。这些特征和行为(称为表型策略)决定了进

化的赢家和输家。 12 Behavioral strategies may change depending upon both an animal's nature and the situation's context. Here's a hypothetical example, based upon game theory thinking: If two **hyenas** are digging into a large, tasty wild beast carcass, they'll happily share that resource. But if two

lions find that same carcass, they will fight for exclusive rights to eating it, meaning one lion

emerges victorious and takes all the meaty spoils, while the other gets no food or even gets injured. Finally, if a lion meets a hyena at the carcass, the hyena will **bolt**, surrendering its goods to the stronger lion. In other words, game theory players can react one of the three ways depending upon who they are and what's going on: they can share, fight or forfeit.

行为策略可能会根据动物的天性和情况的不同而改变。这是一个基于博弈论思想的假设示例:如果两个鬣狗正在挖掘大型美味的野兽尸体,那么他们将很乐意共享该资源。但是,如果两只狮子发现了相同的尸体,他们将争取获得它的专有权,这意味着一只狮子会胜利,并吞下所有的肉,而另一只狮子则没有食物甚至受伤。最后,如果狮子在尸体上遇到鬣狗,则鬣狗会栓住,将其货物交还给较强的狮子。换句话说,博弈论玩家可以根据自己是谁以及发生了什么事来做出三种反应之一:他们可以分享,战斗或没收。

13 **Similar games may be played with tumor cells**. "A good example would be a tumor with cells that move away when confronted with scarce resources and cells that stay to use them," the authors write. To make things even more complicated, however, tumor cells are known to change their behavior as they **proliferate** and metastasize throughout the body, meaning they could switch from a hyena to a lion.

肿瘤细胞可能会玩类似的游戏。这组作者写道:"一个很好的例子是一种肿瘤,它的细胞在遇到稀缺资源时会移动,而细胞会继续使用。"然而,使事情变得更加复杂的是,众所周知,肿瘤细胞会随着其在体内的增殖和转移而改变其行为,这意味着它们可以从鬣狗变成狮子。

14 One crucial thing that game theory at an ecosystem level shows us, they continue, is that **indiscriminately** focusing on killing as many tumor cells as possible might not provide the best outcome for the patient. According to game theory models, the eventual long-term result of the game depends upon specific interactions between the players, not on the number of players involved. Lions will continue to fight one another for food, regardless of whether two lions or 2,000 lions meet. "A treatment based exclusively on indiscriminately removing most (but not all) cancer cells may only have a temporary effect; as in most cases, the original number of tumor cells will eventually be restored and exceeded," the authors write.

他们继续说,在生态系统层面上,博弈论向我们展示的一个至关重要的事情是,不加选择地专注于杀死尽可能多的肿瘤细胞可能无法为患者提供最佳的治疗效果。根据博弈论模型,最终的长期游戏结果取决于玩家之间的特定互动,而不取决于参与的玩家数量。狮子会继续争夺食物,而不管是两只狮子还是2,000狮子见面。"仅基于不加选择地去除大多数(但不是全部)癌细胞的治疗可能仅具有暂时效果,在大多数情况下,原始肿瘤细胞的数量最终将被恢复并超过。"作者写道。

15 Instead, game theory indicates that a more effective alternative would be based on trying to change the ways that cells interact with one another and with their environment. This may affect the cells' behavior, strength and reproductive success, the authors explain, which could drive a tumor's evolution towards less aggressive cell types, or to a more stable coexistence with non-cancerous cells.

相反,博弈论表明,一种更有效的替代方法是基于试图改变细胞相互之间以及与环境相互作用的方式。这组作者解释说,这可能会影响细胞的行为,强度和生殖成功,这可能会促使肿瘤向侵袭性较小的细胞类型发展,或与非癌性细胞更稳定地共存。

16 "The ecosystem view is, ultimately, a holistic one that sees cancer progression as a process that emerges from the interactions between multiple cellular species and interactions with the tumor microenvironment," the authors write. 4) "An ecosystem perspective presents us with intriguing implications," they say, along with a host of questions about how far the analogy between ecosystem and cancer can be taken.

作者写道:"生态系统的观点最终是一种整体的观点,认为癌症的发展是多种细胞物种之间的相互作用以及与肿瘤微环境之间相互作用的过程。"4)他们说:"生态系统的观点给我们带来了有趣的启示,"以及一系列关于生态系统和癌症之间的相似性可以被采用的问题。

17 For example, if cancer cells spread like an invasive species through an ecosystem, what evolutionary gain is achieved when the closed off ecosystem (a body) is irreparably damaged (through a person's death) such that the pestilence also dies? Unlike a virus, which may kill its host but spread to other hosts in the process, cancer cells themselves, for the most part, have no means of spreading from individual to individual. And are cancer cells taking their cues from processes driven by competition or from cooperation? Thinking more proactively, can non-cancerous cells be triggered so that they behave like lions and usurp cancerous cells' resources until the cancer is manageable?

例如,如果癌细胞像入侵物种一样在整个生态系统中扩散,那么封闭的生态系统(身体)受到不可挽回的损害(通过人的死亡),从而使瘟疫也消亡,将会获得什么进化收益?与病毒可能杀死其宿主但在此过程中扩散到其他宿主不同,癌细胞本身在大多数情况下无法在个体之间传播。癌细胞是从竞争还是合作驱动的过程中汲取线索?更加积极地思考,是否可以触发非癌细胞,使其表现得像狮子,并吞噬癌细胞的资源,直到可以控制癌症为止?

18 While ecology and mathematics likely will not defeat cancer on their own, viewing the disease from this perspective could allow doctors to better predict where in the body tumor cells have the best and worst chances of survival, and how to most effectively prevent them from proliferating.

虽然生态学和数学方法可能无法独自克服癌症,但从这种角度看待疾病可以使医生更好地预测肿瘤细胞在体内哪些地方存活的最佳和最差的机会,以及如何最有效地防止它们扩散。

- 19 5) "The heart of the matter is that an ecological view of tumors does not invalidate but complements and builds upon decades of cancer research and undoubtedly this will lead to a better understanding of the biology of cancer and to new and improved therapies," the researchers conclude. "We need to properly understand the trees (e.g. every leaf, twig and branch) before we can understand the forest but we cannot afford to ignore the forest because the trees are so interesting on their own."
- 5)"问题的核心是,对肿瘤的生态学观点不会无效,而是会在数十年的癌症研究中得到补充和建立,毫无疑问,这将使人们对癌症的生物学有更好的了解,并寻求新的和改进的疗法,"研究人员得出结论。"在了解森林之前,我们需要正确地理解树木(例如,每片叶子,树枝和树枝),但是我们不能忽视森林,因为树木本身非常有趣。"

NOTES

- 1. **eureka**: a cry of joy or satisfaction when one finds or discovers something. The word came from Greek *heurēka* "I have found it", said to have been uttered by Archimedes when he hit upon a method of determining the purity of gold.
- 2. **game theory:** the branch of mathematics concerned with the analysis of strategies for dealing with competitive situations where the outcome of a participant's choice of action depends critically on the actions of other participants. Game theory has been applied to contexts in war, business, and biology. 博弈论
- 3. **holism**: the belief that everything in nature is connected in some way. 整体主义; 整体论 holistic *a*.