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The Swamp of Cancer

Invasion of cancer in metastasis

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Introduction

What is metastasis? Metastasis is the process in which a tumor cell migrates through the circulatory system and settles in a new tissue or organ to form a secondary tumor.

How does it take place? The main tumor grows and there's a migration of malignant cells through the blood to form the secondary tumor. Thereafter, there's an invasion of the new tissue or organ by different biological molecules which are important in physiological processes. And finally, tumor cells proliferate to develop the secondary tumor.

Objectives

Understand why metastasis takes place in our bodies.
Which are the ecological factors that carry out this development:

- Interaction between two species in the same environment
- Differences between the fitness of two species

Parallelism with ecology

Cancer cells generate their own niche within the tumor ecosystem, they displace normal cell function and lead to the creation of an hypoxic, acidic, nutrient-poor environment. This new environment has effects to promote metastasis. In table 1 there is the relation between ecology and cancer biology that we are going to comment below.

Their interactions with other species and their habitat are critical to the survival of an individual organism. The interactions between organisms in a community and the abiotic environment form an ecosystem. The structure of an ecosystem is governed by the stoichiometry of species, the differentiation of niches, environmental disturbances and the availability of resources.

In cancer, the homeostasis of our body is unbalanced by the introduction of a non-native species into our ecosystem. Invaders are characterized by rapid growth, high reproduction rates, and phenotypic plasticity.

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CHARACTERISTIC	ECOLOGY	CANCER BIOLOGY
Biosphere	Earth	Patient
Ecosystem	Lake	Organ system
Species	Animals and plants	Cell types
Abiotic factors	Land or water	Extracellular matrix
Invasive species	Beavers, kudzu	Cancer
Ecosystem collapse	Mass extinction	Organ failure and death

Table 1: Modified from Amend, S. R., & Pienta, K. J. (2015). Ecology meets cancer biology: the cancer swamp promotes the lethal cancer

Fitness

We can define "fitness" by the rate of the cell replication. To do this we will use the population growth equation with two populations: healthy cells (A) and mutant cells (B). If we assume that both replicate at a constant rate (α for population A and β for population B).

Both populations growth exponentially, and we compare the ratio α/ β.

- α/β>1 = the normal cell population will outnumber the mutant population
- α/ β<1 = the mutant cell population will outnumber the normal cell population

$$\frac{dN_A\,(t)}{dt} = \alpha N_A\,(t) \rightarrow N_A\,(t) = N_A\,(0)e^{\alpha t}$$

$$\frac{dN_B\,(t)}{dt} = \beta N_B\,(t) \rightarrow N_B\,(t) = N_B\,(0)e^{\beta t}$$

The population in which the cells replicate at a higher rate will compete with the other. Like we said, resources are limited and this means that the total population size is conserved. The fact that cancer cells replicate more quickly makes it natural to say that have greater fitness than others.

Competition

Competition is the antagonistic interaction where two individuals use the same limiting resource and as a result the fitness of both is reduced.

Gause exclusion principle.

"If one species is more efficient than the other, one will end up displacing the other. Invasive species enter the ecosystem because they are more efficient than others. They can't coexist because they use the same resources and the best competitor uses those resources more efficiently."

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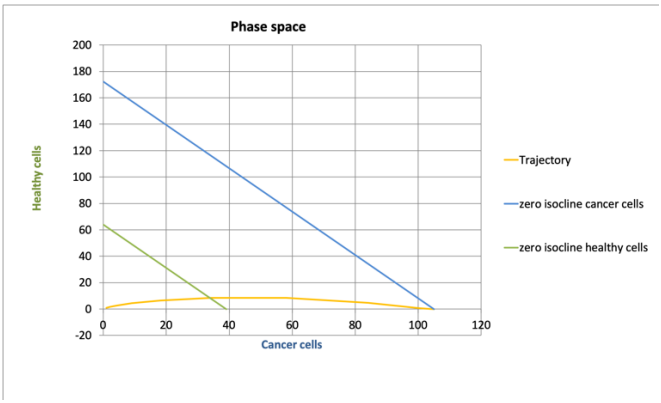
In this principle we can extrapolate the term efficiency to fitness. And we can also make an analogy with the first theorem of natural selection. Given the spontaneity of the process, the individuals who have the most fitness are the ones who dominate the next generation, only those who have most fitness remain. And this promotes an erosion of genetic variance.



$$Species\ 1: \frac{dN_1}{dt} = r_1 N_1 \left(\frac{K_1 - N_1 - \alpha N_2}{K_1}\right)$$

$$Species\ 2: \frac{dN_2}{dt} = r_2 N_2 \left(\frac{K_2 - N_2 - \beta N_1}{K_2}\right)$$

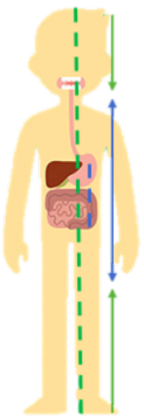
Two species that have the same resource requirements cannot coexist, as long as there are no disturbances (the patient enters in treatment). The best competitor will displace the other, which will use the resources more efficiently, being able to live in values for which the other can no longer use them. Only the one with the greatest fitness will persist. It implies that there are extinctions due to competition.

Niches

As a result of competition, niche segregation or extinction occurs. Cancer cells produce their own niche. As tumor cells design their environment, they simultaneously create a habitat that will exert selective pressure on subsequent generations of daughter cancer cells.

Without the selective pressure of the designed ecosystem, cancer cells are much more likely to remain restricted to the primary tumor rather than metastasize to distant sites.

Remember that we can have different niche definitions:
Hutchinson: Overlap of niches because of competition. Cancer cells would live in the fundamental niche and host cells would be limited to a realized niche.
Elton: Considering resource splitting each cell has optimums for a given resource. When there is an invasive species it is much more efficient than the other species and displaces them. It causes the extinction of healthy species.



Healthy cells have fundamental niche distribution, they live all over our body. When an invasive species such as cancer cells arrives, its niche is redistributed. Cancer cells have a selective pressure to metastasize and displace healthy cells. In this why we only find healthy cells where there are no mutant cells. Cancer competes and by interference kills healthy cells of essential tissues and organs for the functioning of the human body. There is a war for space and resources.

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LEGEND:
FUNDAMENTAL NICHE OF CANCER CELLS // THEORETICAL NICHE OF CANCER CELLS
FUNDAMENTAL NICHE OF HEALTHY CELLS // THEORETICAL NICHE OF HEALTHY CELLS

Conclusion

To conclude, we can say that cancer cells have more fitness and there's a selective pressure that pushes them to progress around the body and produce metastasis. These cancer cells act like invasors that disrupt our health basal conditions. That means that they create their own home. Our body detects all these negative effects as a swamp.

Metastasis creates their own microenvironment generating an ecosystem to promote the reproduction of cancer cells and their invasion to other tissues or organs. A swamp acts the same way to provide a place where plants and animals can live altering the natural landscape.

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