

The neurons which contribute to cancer development

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A quite stunning and remarkable study has shown that tumors recruit immature neurons produced by the brain to form new nerve fibers essential for the progression of the cancer.

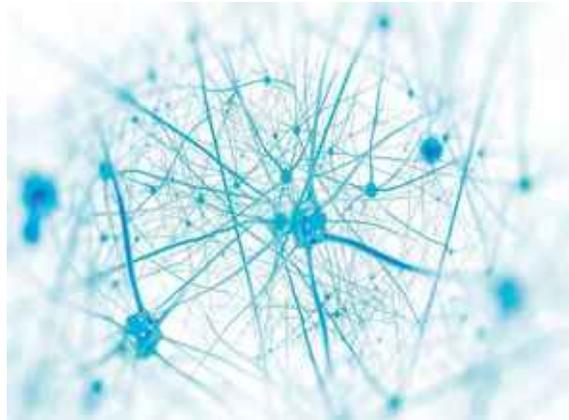
PERMISSIVE MICROENVIRONMENT

Despite their genetic instability, which allows them to grow much more rapidly than normal cells, cancer cells alone are unable to invade the tissues in which they wind up. To do this, they must absolutely have an environment which is amenable to their growth, a sort of welcoming location which allows them to obtain the elements necessary to evolve and reach the stage of a mature cancer.

It is now well established that solid tumors have more than one strategy for developing a microenvironment favorable to their progression. For example, they secrete biochemical messengers which create new blood vessels, a phenomenon known as tumoral angiogenesis, which allows them to obtain the oxygen and nutrients they need. The cancer cells also attract certain immune cells which create a microenvironment of chronic inflammation that favors both their survival and the acquisition of genetic mutations which are indispensable for their progression into mature cancer.

NERVE FIBRES

During a study on prostate cancer, a team of French researchers reported the presence of another type of cells in solid tumors: nerve fibres¹. This discovery was completely unexpected, because these peripheral nerve fibres are the extensions of neurons which conduct the nervous impulses necessary for the activity of various organs (heartbeats, breathing, etc.), which had no prior link to cancer progression. However, it seems that this link exists: the elimination of these nerve fibres by surgery or their blockade by medications considerably slowed the development and progression of prostate cancer in animal models and the analysis of samples from biopsies of prostate cancers showed that the cancers which contained the highest quantities of nerve fibres were the most aggressive and were associated with a lower level of survival. The progression of cancer could thus interfere with the nervous system, which would explain why patients treated by chemotherapy who were also taking beta-blocker medications for the heart (these block the action of adrenaline, a neurotransmitter in sympathetic nerve fibres) exhibited a better rate of survival than those treated solely by chemotherapy².



RECRUITMENT OF NEURONS

Not only are tumors infiltrated by nerve fibres already present in the proximity of the organs where the cancer develops, but the latest results indicate that they also possess new neurons formed from stem cells³. This is quite surprising because the production of new neurons is limited to only two regions of the brain, i.e. the dentate gyrus (a region of the hippocampus) and the subgranular zone (SGZ) found close to the fluid-filled spaces (ventricles) within the brain.

The researchers were able to show that the new neurons present in the prostate tumors were derived from the SGZ; thanks to a temporary rupture in the blood-brain barrier, the neuronal stem cells succeed in reaching the blood circulation and migrating to the prostate tumor where they differentiated into adrenergic neurons (neurons that use adrenaline as a neurotransmitter). This phenomenon seems crucial for the development of prostate cancer in humans because the density of neuronal stem cells present in these tumors is strongly correlated with the aggressiveness of the cancers and with a high rate of recurrence. It thus seems that these tumors manage to communicate with the brain to recruit immature nervous cells which are necessary for their growth.

These results thus suggest that medications which target the autonomic nervous system could represent a new therapeutic approach against cancer, not only that of prostate but also others in which the presence of nerve fibres has been identified (stomach, colon, pancreas, breast).

- (1) Magnon C et al. Autonomic nerve development contributes to prostate cancer progression. *Science* 2013; 341: 1236361.
- (2) Melhem-Bertrandt A et al. Beta-blocker use is associated with improved relapse-free survival in patients with triple-negative breast cancer. *J. Clin. Oncol.* 2011; 29: 2645-2652.
- (3) Mauffrey P et al. Progenitors from the central nervous system drive neurogenesis in cancer. *Nature* 2019; 569: 672-678.