

Cancer Cells Turn Cannibal!

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A study has shown that in tumors treated by chemotherapy, certain cancerous cells feed by cannibalizing neighboring cells, which allows them to resist treatment and thus leading to tumor recurrence.

THE PROBLEM OF RECURRENCE

The resistance of cancerous cells to chemotherapy medications remains one of the principal obstacles to the treatment of cancer and a major cause of the mortality linked to this disease. These treatments usually succeed in eliminating nearly all the cancerous cells, but it frequently turns out that some of them succeed in adapting to the medications and manage to remain alive. The presence of these residual cancerous cells is a major problem because they can eventually resume their growth, causing recurrence or even expanding to other essential organs (lungs, liver or brain, amongst others) in the form of metastases. To improve the effectiveness of anticancer treatments, one of the biggest challenges for research is thus to better understand the factors responsible for this resistance.

SLEEPING RATHER THAN DYING

The success of chemotherapy medications is due in large part to their ability to provoke such significant damage to the DNA of cancerous cells that they have no option but to kill themselves, a phenomenon called apoptosis. Generally, to acquire resistance to chemotherapy, the cancerous cells must avoid being directed towards this apoptotic path, which usually occurs by acquiring mutations in certain key genes involved in apoptosis. For example, nearly half of all cancers exhibit mutations in the tumor suppressor gene p53, which is one of the principal organizers of apoptosis, and these mutations play an important role in the resistance of several types of cancers to chemotherapy.

Curiously, it sometimes happens that certain types of cancers possess two normal versions of p53 but nonetheless acquire a strong resistance to multiple medications. For example, breast cancers which express a normal p53 respond far less to chemotherapy and are associated with a poor prognosis¹. Studies have shown that, rather than die by suicide, these cancerous cells instead enter a dormant state from which they can be reactivated, thus allowing the cancer to recur.

EATING THEIR NEIGHBOURS

One study suggests that this stationary condition of dormancy is made possible by the surprising ability of certain cancerous cells to literally eat their neighbours when they are submitted to treatment by chemotherapy with doxorubicin². This phenomenon is observed both with cultured cells as well as with tumors grafted into animals and is caused by the activation of genes which are normally used by the immune cells (such as macrophages) to “swallow” bacteria by the process of phagocytosis. The authors showed that the



dormant cancerous cells which cannibalize their neighbours live longer, which strongly suggests that this phenomenon allows them to acquire the elements necessary both for their survival and for production of the growth factors which will ultimately allow the cancer to recur after the end of treatments.

The identification of this cellular cannibalism as a factor in cancer recurrence could thus open a way for new therapeutic approaches which specifically target this phenomenon and improve the effectiveness of many chemotherapy medications.

- (1) Wang Y et al. TP53 mutations are associated with higher rates of pathologic complete response to anthracycline/cyclophosphamide-based neoadjuvant chemotherapy in operable primary breast cancer. *Int. J. Cancer*. 2016; 138: 489-96.
- (2) Tonnessen-Murray CA et al. Chemotherapy-induced senescent cancer cells engulf other cells to enhance their survival. *J. Cell Biol.* 2019; 218: 3827-3844.