Cancer as an open system

Our prevailing approach to cancer is the crash or crash through strategy, know to older Australians as the Gough Whitlam strategy (he crashed); the strategy of the direct approach. Here we say 'there is the enemy, go get 'em'. This current strategy revolves around curing the cancer, ridding our bodies of it or at the least, bullying it into a state where we can manage it, keep it under control. As many know, the result is variable depending on which one you cop and even if you do survive, the process is a long drawn out one of pain, suffering and uncertainty.

Finally, some intelligence has surfaced in this all out assault on cancer; a group of scientists are trying a radically different approach, one based in open systems and the strategy of indirect approach. Rather than declaring war on cancer, researchers are building on its known malleability to turn it into a different and benign state, "persuading them to adopt a new identity" (Ainsworth, 2025, p41).

Other strategies involve changing the abnormal environment surrounding the cancer – "this is all the system in its entirety, that is changing" (p43). This is tricky because the system and environment are constantly determining each other as the tumour is known to be changing the surrounding tissue so it better supports the growth of the cancer. All our interventions will be met by counter moves by the cancer so a more effective approach is to change its nature so it cannot act in those ways.

As early as 1959, pathologist Barry Pierce and his team discovered that embryonic tumour cells grafted into adult mice could differentiate into benign cell types to aid healthy tissue growth. This supported observations of cancers spontaneously regressing in some patients. They realized that ***the tissue environment surrounding the cancer cells seemed to influence their behaviour*** so they began looking for the mechanisms responsible. They learnt that cancer cells could be retrained through exposure to tissue environments in which closely related cell types were generated.

However it was not until much later that two Chinese doctors Zhen-Yi Wang and Zhu Chen applied this idea in the clinic, following Confucius' advice to educate rather than punish. Now cells from varieties of aggressive cancers are being treated, some directly but others on their surrounding tissue.

Examples are several: acute promyelocytic leukemia (APL), a blood cancer which can be quickly fatal is treated by administering retinoic acid, a derivative of vitamin A to immature APL cells. This "beneficially alters the shape of a protein involved in causing APL" (p42), causes those cells to differentiate into mature white blood cells. Used in combination with an arsenic compound and conventional chemotherapy, it has turned APL into a highly curable condition.

These treatments are based on the knowledge that embryonic stem cells start out with the ability to form any kind of cell, pluripotency. They draw on signals from their neighbours and environment to make a sequence of decisions that progressively restrict their ability to form different cell types. This is essentially an epigenetic process and can be reversed as the cells retain their the plasticity. Just four proteins known as the Yamanaka factors can push cells all the way back to pluripotency.

This knowledge and techniques are being exploited to turn breast cancer cells into harmless fat cells and glioblastoma cells are being turned into neurons and microglia. In this

latter case, the original drug used, cAMP, is not suitable but forskolin which boosts cAMP in cells can be used in combination with radiation.

Cancer as we now understand it is a combination of genetic and epigenetic factors at many levels of biological organization. It is a crafty enemy necessitating a full bag of approaches employing far more intelligence and strategy than the 'war on cancer'. Fortunately, our researchers have advanced from the primitive closed systems approach of the past and are exploring much more fertile approaches based on open systems. Hopefully, soon more of these advances will be available for clinical application.

Reference: Ainsworth, Claire. (2025). Rehabilitating cancer. *New Scientist*, 30 August, 40-43.