A great progress has been made in our understanding of cancer development, detection, and surgical removal of early and primary cancers in the past few decades. However, treatment of malignant cancers is still a challenge, and most of the chemotherapies developed in past years were centred on targeting general non-selective targets such as DNA replication/repair and tubulins. Obviously these treatments cause severe side effects and most patients succumb to the disease with miserable quality of life. Malignant cancer cells harbor multitude of mutations, chromosomal abnormalities and are resistant to most of the treatments. While maintaining rapid growth these cells do use different energy metabolism and face higher oxidative stress. Potentially all malignant cells could be differentially targeted for cell death by targeting these vulnerabilities. Indeed, we have demonstrated that natural compound pancratistatin and its synthetic analogues selectively target cancer cell mitochondria to induce apoptosis without affecting non-cancerous cells. On the other hand, compounds like piperlongumine and synthetic analogues of curcumins selectively kill cancer cells by inducing oxidative stress. Interestingly, some of the natural extracts also trigger cancer cell death by inducing oxidative stress and mitochondrial depolarization selectively in cancer cells. Gene expression profiling studies indicates that cancer cells and non-cancer cells respond very differently after treatment with these extracts or compounds. These findings open a new window of opportunity to develop new therapeutic regimens that are extremely selective to cancer cells and thus should be free of side effects.

Clinical experience: The grim reality of cancer therapeutics development is that in spite of tremendous efforts, more patients will die of cancer this year than the year before. The development of targeted and personalized therapies through cancer genomics is challenged by its complexity and cost and with the fact that some of the clinical data obtained to date are disappointing. Abundant scientific data show that some of the natural agents (nutrients and extracts) target cancer cells more selectively and efficiently, but there is no interest in bringing them to the clinical arena. Orthodox cancer therapies fall short and alternative treatment alone may not offer a solution; however, integrating them could significantly improve the odds for patients surviving this modern plague called cancer. Some successful example of this approach will be presented to prove this hypothesis.

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