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Response

Oleander extract induces cell death in human but not murine cancer cells

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We agree with the premise of Björn Stenkvist that studies like the one we reported[1] should be performed on a much larger scale using extracts of other potential medicinal plants on a variety of human cancer types. The purpose of our studies was several fold: (i) to evaluate the cancer cell-killing mechanism of Anvirzel™ *in vitro*, (ii) to determine whether human, canine and murine cancer cells are equally sensitive to the cell-killing activity of Anvirzel and its active ingredient Oleandrin, and (iii) to evaluate if telomere erosion is directly involved in cancer cell death. Other aspects of Oleandrin effects were studied by some colleagues at the University of Texas MD Anderson Cancer Center, Houston, Texas. For example, Dr Aggarwal and his group showed that Oleandrin suppresses the nuclear transcription factor-κB (NF-κB), and c-JUN NH_2-terminal kinase in a concentration- and duration-dependent manner.[2] From our own department, David J McConkey and his associates demonstrated that cardiac glycosides stimulate Ca^{2+} increases and apoptosis in androgen-independent, metastatic human prostate adenocarcinoma cells.[3] All three of these articles were published from our cancer center at about the same time with the idea of showing the cell-killing activity of Anvirzel and its active ingredient Oleandrin in different human cancer cells. In addition, Robert Newman's group is concentrating on the pharmacology of various plant products including the Oleander extract.[4] Currently, my group is actively involved in testing many crude plant products, and some homeopathic and Chinese medicines for their cancer cell-killing activity with minimal or no effects on normal somatic cells.

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Dr P Banerjee, a homeopathic doctor from Calcutta, India, has successfully treated some brain cancer patients with Ruta-6, an extract of *Ruta graveolens*. My associates and I are currently studying the molecular mechanism of cancer cell-killing of this medicine. A major problem of conventional cancer chemotherapeutic drugs is that they not only kill the cancer cells but also kill rapidly growing normal cells. Since we have earlier reported amplification of telomeric DNA in human and murine metastatic cancer cells of different histologic origin[5] as compared to their non-metastatic counterparts, and also since telomeres are a survival factor for the cells, it would be rewarding to discover/develop new therapies that target telomeric DNA selectively, with the promise that such extracts would kill cancer cells primarily with minimal or no side effects on normal cells. Such drugs are being tested in various hospitals, even some in the USA.[6]

The present commentary 'Cardenolides and cancer' written by Stenkvist is timely, because it showed positive effects of digitalis on human patients suffering from breast cancer. His previous follow-up work on breast cancer patients who were on digitalis has clearly shown smaller-sized tumors or less death as compared to those who were not on a digitalis treatment regimen.[7,8] Recent reports have further demonstrated that digitalis could serve as a potential anti-tumor agent in several types of cancers.[9]

The time has come to test natural plant products in conjunction with conventional cancer drugs for the treatment of various malignancies. Such extracts should have little or no side effects and may even promote cell division in normal body cells while showing killing activity specifically against the cancer cells. Our group is committed to carry on such research at the University of Texas MD. Anderson Cancer Center (Houston, TX).

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