Alternative causes of cancer

The relationship between cancer and apoptosis

Dr Chanda Siddoo-Atwal, President of Moondust Cosmetics, is a cancer biologist with a specific interest in the mechanisms that lead to cancer. The classical theory of carcinogenesis involving failure of DNA repair mechanisms and the clonal expansion of mutated cells does not fit all carcinogens (cancer-causing agents). More recently, it has become apparent that the aberrant regulation of apoptosis (programmed cell death) may provide another mechanism to explain these exceptions. Dr Siddoo-Atwal's research has centred around skin cancer and the need for effective novel sunscreens to protect against the development of UV-radiation induced skin cancer, which conforms to this new model.

Cancer is the second leading cause of death globally, accounting for around one in every six deaths in 2018. In particular, skin cancer is diagnosed in one in every three cases of cancer and this is set to increase due to climate change impacting the protective ozone layer around the Earth and allowing more UV radiation from the sun to reach the Earth's surface.

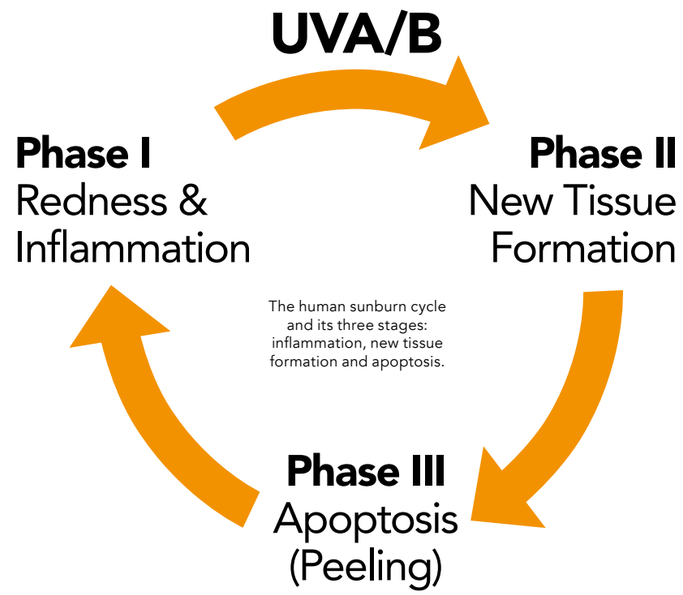
While it is well established that accumulation of cellular mutations and uncontrolled proliferation of cells contributes to the risk of developing cancer, this theory does not fit all models of carcinogenesis (cancer formation) and there may be other mechanisms at play. One such theory is that following exposure to a specific carcinogen (cancer-causing agent), an increased rate of apoptosis triggers carcinogenesis. This new theory explains a number of cancers that do not fit the classical view. It is this emerging subject area that Dr Chanda Siddoo-Atwal, President and Primary Biochemist of Moondust Cosmetics Ltd., is particularly interested in.

Cells from individuals with a genetic disorder called ataxia-telangiectasia provide important information in support of this new cancer theory, as they are at high risk of developing some forms of cancer. Dr Siddoo-Atwal reports that certain signalling molecules (interferons) are elevated in these patients, corresponding to stimulation of apoptotic pathways. This, in addition to a genetic predisposition, appears to confirm the role of apoptosis in cancer development and highlights the fact that we may need to move away from a more traditional way of thinking about carcinogenesis to focus on new mechanisms that do not simply consider uncontrolled cell proliferation. It is likely that the pathway is much more complex than previously thought, involving many different regulators of cell survival and cell death.

Apoptosis is also known as 'programmed cell death' and is the process by which damaged or defective cells are removed by the body's immune cells, thus making space for new cells and removing cells that are only required for tasks temporarily. Links between apoptosis and known carcinogens have been demonstrated for agricultural pesticides, mycotoxins, heavy metals and several different types of radiation, with many more studies ongoing.

Dr Siddoo-Atwal recently published a book on cancer risk assessment.

Dr Siddoo-Atwal has recently published a book, based on a collection of papers presented at scientific conferences, which explores novel approaches for assessing cancer risk, based on the relationship between apoptosis and cancer, and the carcinogenic potential of a variety of components, including those mentioned above.



The human sunburn cycle and its three stages: inflammation, new tissue formation and apoptosis.

Based on this information, Dr Siddoo-Atwal founded her cosmetics business, Moondust Cosmetics. The company sells sun care products, such as those reported to combat apoptotic sunburn.

THE HUMAN SUNBURN CYCLE

While the skin naturally sheds dead skin cells and replaces them with new healthy skin cells – a continuous process called desquamation – Dr Siddoo-Atwal wanted to observe what happens to living cells during sun exposure. She noticed that sunscreen protected her from the redness and inflammation caused by sunburn, but that she still experienced some skin peeling or apoptosis. This led her to learn more about the 'human sunburn cycle'. Dr Siddoo-Atwal believes that this cycle, lasting around 7 days in length, can be divided into three stages: inflammation, new tissue formation and apoptosis.

The initial inflammatory stage involves the reddening of the skin following sun exposure; this stage lasts around 2-3 days.

Dr Siddoo-Atwal's new cancer theory suggests that following exposure to a specific carcinogen, an initial increased rate of apoptosis can trigger carcinogenesis.

Dr Siddoo-Atwal has developed a new sunscreen with zinc oxide and melanin.

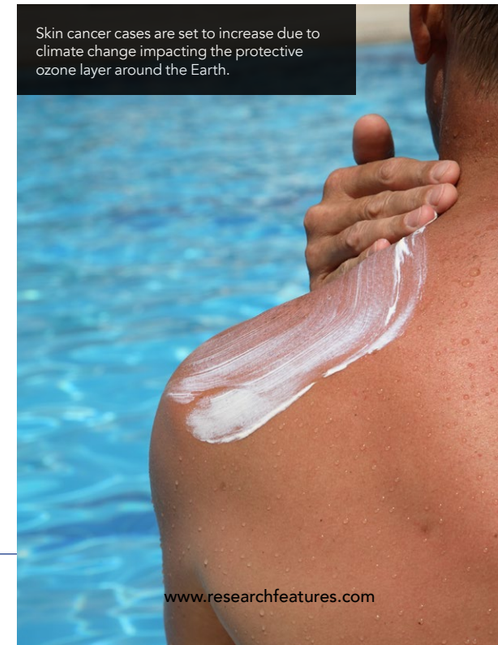
Next, formation of new skin is stimulated below the surface of the skin (although we cannot see this phase). Finally, the top layer of dead skin cells sloughs off to reveal the new layer of tissue below.

By using a combination of zinc oxide and melanin, Dr Siddoo-Atwal has developed a new sunscreen. After carrying out case studies on herself and other volunteer subjects, Dr Siddoo-Atwal concluded that this combination was able to protect against apoptotic sunburn, which is directly linked to skin cancer. Zinc oxide has a long history of use as an FDA approved ingredient in UVA/UVB sun protection and is responsible for the barrier formed on the skin by ointments such as sudocrem. Melanin is a naturally occurring skin pigment, made by specialist skin cells called melanocytes. Some people make more melanin than others, and higher levels of melanin may help protect the skin from UV radiation. It is already used in some sunscreens to maximise the tanning process, which is a distinct physiological process from sunburn.

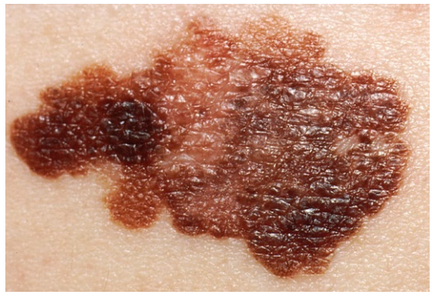
APOPTOSIS AND CANCER

It is already well-established that defective apoptotic pathways are associated with the risk of developing cancer as the loss of this organised cell death pathway can allow cancer cells to survive for longer and increases the length of time that they can acquire further mutations.

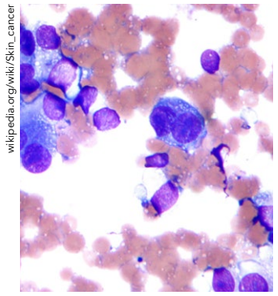
However, recent laboratory research has shown that in mice with uncontrolled levels of apoptosis in skin cells, there is an increased risk of developing skin



Skin cancer cases are set to increase due to climate change impacting the protective ozone layer around the Earth.



Malignant melanoma is commonly asymmetrical in shape and/or pigment distribution, with an irregular border.



wikipedia.org/wiki/Skin_cancer

Micrograph of melanoma, a type of skin cancer.

cancer. It is this relationship, in the context of skin cancer, that Dr Siddoo-Atwal was initially focused on, as well as the role of apoptosis in other types of cancer.

Interestingly, previous studies have explored this relationship and found that some changes within genes responsible for regulating apoptosis and DNA repair are associated with a higher risk of developing skin cancer. This is because failure to repair damage done by UV radiation from the sun can result in deregulation of cell proliferation and cell death pathways. This is observed as a higher rate of apoptosis, or sunburn in these individuals.

Studies have also provided support for this association by demonstrating that external factors also target apoptotic pathways in cancer. One example of this is through bioactive dietary agents, such as polyphenols. Polyphenols (like those found in black and green teas) have been shown to suppress tumour growth, in part due to their effects on apoptotic pathways in the affected cells. Other compounds of interest include resveratrol (from grape skin), procyanidins (from grape seeds), and the mineral selenium (abundant in Brazil nuts), which can also selectively initiate cell death pathways in different kinds of cancer cells while sparing normal cells. As a result, there is great potential for targeted cancer therapies with these compounds.

Another component of interest is a product produced by honey bees, which is thought to play a role in protecting against mycotoxins. Mycotoxins are metabolites produced by mould which can have adverse effects on the body, including increasing apoptosis levels in various tissues and, thus, elevating the risk of developing cancer. However, certain compounds found in bee propolis (the resinous substance used by bees to build their hives) have been demonstrated to have a possible detoxifying effect on mycotoxins and antiproliferative activity towards cancer cells.

Understanding more about underlying mechanisms of cancer may lead to novel treatment strategies, as well as screening and diagnostic procedures.

HEAVY METAL CARCINOGENESIS

Heavy metals are defined as naturally occurring elements in the periodic table with densities at least 5 times that of water, including lead, mercury and chromium. They are highly toxic, and many are known or probable carcinogens. While some aspects of heavy metal carcinogenesis are not yet known, all three of the heavy metals mentioned above have been associated with apoptosis.

Dr Siddoo-Atwal explains that there is likely to be a 'Two Stage Model of Tumour Formation'. While explained here in the context of heavy metals, this two-step model also applies to other carcinogens. For example, it may also apply to exposure to ultraviolet light from the sun, or carcinogens in cigarette smoke. The first phase in this proposed pathway is initial exposure to a carcinogen, such as a heavy metal, which influences gene expression and ultimately causes continuous apoptosis of cells in the target tissue. The second stage may or may not involve the presence of the carcinogen but occurs when resistance to apoptosis and continuous cell proliferation develops, facilitating tumour development.

AGRICULTURAL PESTICIDES

Given that we know apoptosis plays a key role in cancer risk, Dr Siddoo-Atwal proposes that screening potential carcinogens for their apoptotic abilities in human cells may be a way in which novel cancer risk assessment methods can be developed. While this carcinogen risk assessment method could be applied to all potential carcinogens, Dr Siddoo-Atwal uses the example of agricultural pesticides.

Many pesticides are known to be carcinogenic, including three classes known as organochlorides, organophosphates and dithiocarbamates. For example, exposure to insecticide DDT and its metabolites are likely risk factors for pancreatic and liver cancer, amongst others. Thorough testing and characterisation of pesticides is required before they are marketed and one way in which this could be done is through the use of cell culture studies. These cell culture studies can be used to test the effects of the chemicals against different types of human cells and to test their carcinogenic potential. This ability to cause cancer can be tested by evaluating the ability of the chemical to initiate apoptosis.

CONCLUSION

Understanding more about underlying mechanisms of cancer, such as the risks of increased rates of apoptosis, may lead to novel treatment strategies, as well as screening and diagnostic procedures. Furthermore, dysfunctional apoptosis is also linked to other conditions, such as neurodegenerative diseases and muscular dystrophies, suggesting that there is the possibility that much of this knowledge may be applicable to other fields of medicine and research.

Behind the Research

Dr Chanda Siddoo-Atwal

W: https://moondustcosmetics.com/ facebook.com/DrMoondust

Research Objectives

Dr Siddoo-Atwal explores alternative causes of cancer.

Detail

Bio

Chanda Siddoo-Atwal has a special association with the UK. As an undergraduate at University College London, she started off in Health Sciences studying epidemiology and genetics in a joint course with Richard Dawkins ("The Selfish Gene") at Oxford. Then, she moved to the Biology Department as genetics became her passion and, finally, ended by graduating with a degree from the Biochemistry Department before going on to become a cancer researcher. Her PhD was taken in Applied Sciences from Simon Fraser University in Burnaby (her research conducted at the BC Cancer Research Centre) and she did a Post-doctoral fellowship in the Biochemistry Department at the Medical College of Wisconsin.

Her research focuses mainly on mechanisms of carcinogenesis in various models including the AT disease state and ionizing radiation-induced cancer, mycotoxin-induced and chemically induced cancers, microwave-induced cancers, and ultraviolet radiation-induced skin cancer. She is the President and Primary Biochemist of Moondust Cosmetics Ltd. and her current research activity includes the formulation of a novel sunscreen to combat apoptotic sunburn that has been associated with skin cancer and other sun care products for the repair of skin damage related to sun exposure (Moondust skin protector plus has been named Best Sun Protection Product 2020 by Luxlife magazine).

References

Siddoo-Atwal, C. (2017). *A New Approach to Cancer Risk Assessment: An Overview.* Lambert Academic Publishing, Maritius. ISBN: 978-6202022262

Personal Response

What inspired you to conduct this research?

" The impetus for this research was the realisation that the parameter of SPF (sun protection factor) in sunscreen is not sufficient to block apoptotic sunburn, which is directly linked to skin cancer, and an additional protective factor was required. "

How can better understanding of the links between cancer and apoptosis be applied to diagnosis and treatment of disease?

" It is through understanding the mechanism of skin cancer, which involves repeated cell death or apoptosis, that we can prevent carcinogenesis by adding another level of protection called "APF" (apoptosis protection factor) to sunscreen. This is also a vital aspect of prevention in post-skin cancer patients. Moreover, the application of certain bioactive agents to damaged skin, such as resveratrol, can cause selective cell death in individual cancer cells and, possibly, even reverse the cancer process. "