Apoptosis:

A Key Trigger Mechanism for Cancer



Chanda Siddoo-Atwal, B.Sc., Ph.D.



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Chanda Siddoo-Atwal

B.Sc. University College London
Ph.D. Simon Fraser University
Post-Doctoral Fellowship Medical College Wisconsin
President and Primary Biochemist of Moondust Cosmetics Ltd.
Vancouver, Canada



DEDICATION

This book is dedicated to the memory of my parents,

Dr. A.S. Atwal and Dr. S.K. Siddoo,

two enlightened souls,

who always knew I was born a rebellious,

free spirit of the Sixties,

and nobody was ever going to tie me down,

tell me what to think,

or tame me,

so they lovingly let me find my own way.

And, to the friends, family, and all others who have been sacrificed on the altar of this terrible disease called "Cancer".

FOREWARD

Some years ago, I discovered that sunscreens were not working for me. Most of the sunscreens I tried would eliminate the redness and inflammation caused by sunburn, but to my surprise, the peeling of skin cells continued despite my sunscreen use [A Case-Study of Apoptotic Sunburn with Sunscreen. Indian Journal of Ecology 2011; 38(2): 300-301]. As a biochemist and cancer biologist, I was horrified since I had a vague conception that peeling was part of the physiological process called "sunburn". I also remembered from my graduate courses that it was connected to skin cancer. Thus, I embarked upon a thorough study of the subject in order to understand this mystery. As I delved deeper into the scientific literature, it became clear that Sun Protection Factor (SPF) was not engineered to block scientific sunburn or "apoptosis" but to prevent tanning/pigmentation and to decrease redness and inflammation. However, I could find nothing in the literature about a human sunburn cycle, which I knew to exist from personal experience.

Then, I started a series of case-studies on myself to elucidate the human sunburn cycle, which consists of three discrete phases - *Inflammation, New Tissue Formation, and Apoptosis* (peeling). The last phase of apoptosis (or peeling) involves the removal of dead skin cells that have been damaged beyond repair by ultraviolet (UV) radiation in the form of sunlight. This cycle repeats itself over and over again upon sun exposure and can become the cause of skin cancer on susceptible areas of the skin if it is not stopped. One of my case-studies followed the formation of an abnormal growth (or "tumour") on the tip of my nose as a result of such unchecked sunburn during a summer of continuous sun exposure.

The next step for me was to prepare a sunscreen that would prevent apoptosis since I could not envisage a life trapped indoors. The first idea was to try an ointment of zinc oxide since it is a very mild chemical used for diaper rash which can act as a physical block that effectively



prevents UVA and UVB light from penetrating the skin. The second idea was to use melanin. This chromophore is the natural defense of the human body against UV radiation and black melanin is the most effective in this regard. Why look further for a cure for sunburn? In further case-studies, it was shown that both these compounds could effectively prevent apoptotic sunburn [published as A Case-Study of Two Sunscreens that May Prevent Apoptotic Sunburn. Indian Journal of Ecology 2012; 39(1): 131-134]. Eventually, I dubbed this novel feature Apoptosis Protection Factor (APF).

During my research, it also became increasingly clear that apoptosis was the physiological process linked not only to skin cancer, but to many other types of cancer. In effect, dysregulation of the apoptotic mechanism was slowly becoming a central feature of cancer research and there was a movement away from the classical model of a failure of DNA repair mechanisms followed by the clonal expansion of damaged cells. In fact, such a link to apoptotic cell death could be found for carcinogens ranging from agricultural pesticides to mycotoxins to heavy metals or air pollution to alpha-and gamma-radiation and microwaves. This book is a compilation of papers that I have presented world-wide on this fascinating subject and a new mode of cancer risk assessment which is based upon it.

At the same time, I found that my research was overlapping more and more with current topics such as the understudied biological and botanical effects of radioactive contamination, new information & communications technologies, the overuse of chemical pesticides, global climate change including the increasing incidence of wildfires, and the preponderance of plastic pollution, which may all be of interest to environmentalists.

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Figure 1. The Human Sunburn Cycle

The natural human sunburn cycle (without the use of any sun lotions or sunscreens) is approximately one week in length (7 days) from start to finish. Macroscopically, it consists of three phases including Inflammation, New Tissue Formation, and Apoptosis (visible peeling). The inflammatory phase consists of redness and inflammation commencing 20-30 minutes from the time of initial sun exposure. It spans grossly 2-3 days, but can last up to 5 or 6 days depending upon UV intensity. New tissue formation is stimulated sometime after initial exposure and it is complete within one week. In the last apoptotic phase, the top layer of dead skin cells sloughs off to reveal a new tissue layer beneath. This process follows on from the inflammatory phase and is complete approximately 7 days following sun exposure. (The photos below are based on an initial exposure time of 20-30 min at Ambleside beach in February).

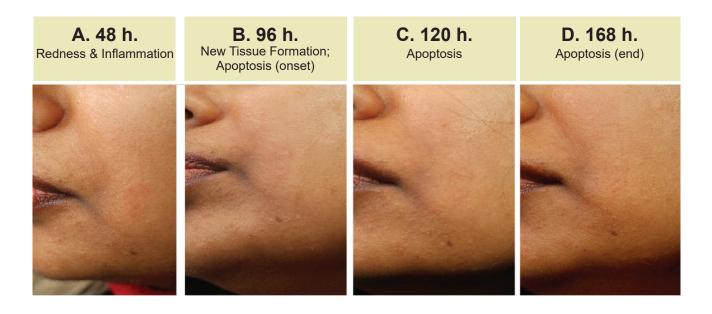
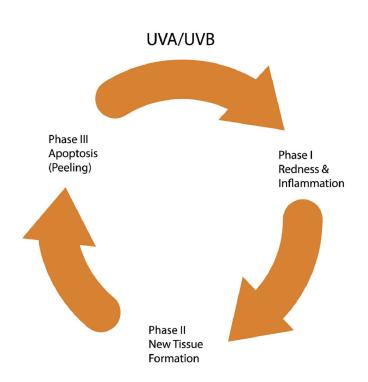




Diagram 1. The Human Sunburn Cycle



^{*} If this cycle continues unchecked in a specific area, it may result in skin cancer.

TABLE I – The Three Phases of Sunburn*

I. Inflammation 0 - 72 Hours

II. New Tissue Formation 24 - 168 Hours

III. Apoptosis 36 - 168 Hours

^{*} This table is based on an initial exposure of 20 - 30 min at noon at the beach [This data is based on a set of experiments conducted at Ambleside beach in West Vancouver (British Columbia), Canada in February 2010; the results were published as [A Case-Study of Apoptotic Sunburn with Sunscreen. Indian Journal of Ecology 38(2): 300-301, 2011]

TABLE II – The Human Sunburn Cycle*

0-1 Hours (Initial exposure) redness and inflammation

24 Hours (Day 1) Redness and inflammation; pain

48 Hours (Day 2) Redness and inflammation peak; pain

72 Hours (Day 3) Minor peeling; less redness and inflammation

96 Hours (Day 4) Major peeling

120 Hours (Day 5) Minor peeling; itching

140 Hours (Day 6) Minor peeling; itching

168 Hours (Day 7)** Recovery; visible new tissue

(*no use of sun preparations, sunscreen, or suntan lotion)

^{**} Approximately a one week/7-day cycle without the use of any sun preparations

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