Cancer 2020

Directed Adaptive Evolution Metabolic Centric Biology 2020

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work in progress

Life/Cancer

All life is dependent on flowing energy and mass.
Physically we are flow dependent structures in time and space.

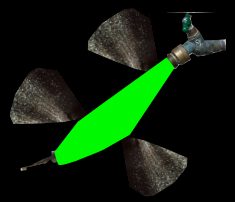
Flowing energy and mass create solutions for generating greater complexity – evolution leading to life.

The balance of creation and destruction determines health or illness, greater or lesser health respectively.

Free radical changes to flowing biochemicals are the homeostatic agents of flow dependent structures created by redox metabolic reactions.

Life was not created from DNA. DNA was created by evolved/evolving, complex, flow dependent structures to record metabolic success. Life is an adaptive, dynamic fractal.

Carbohydrate Metabolism

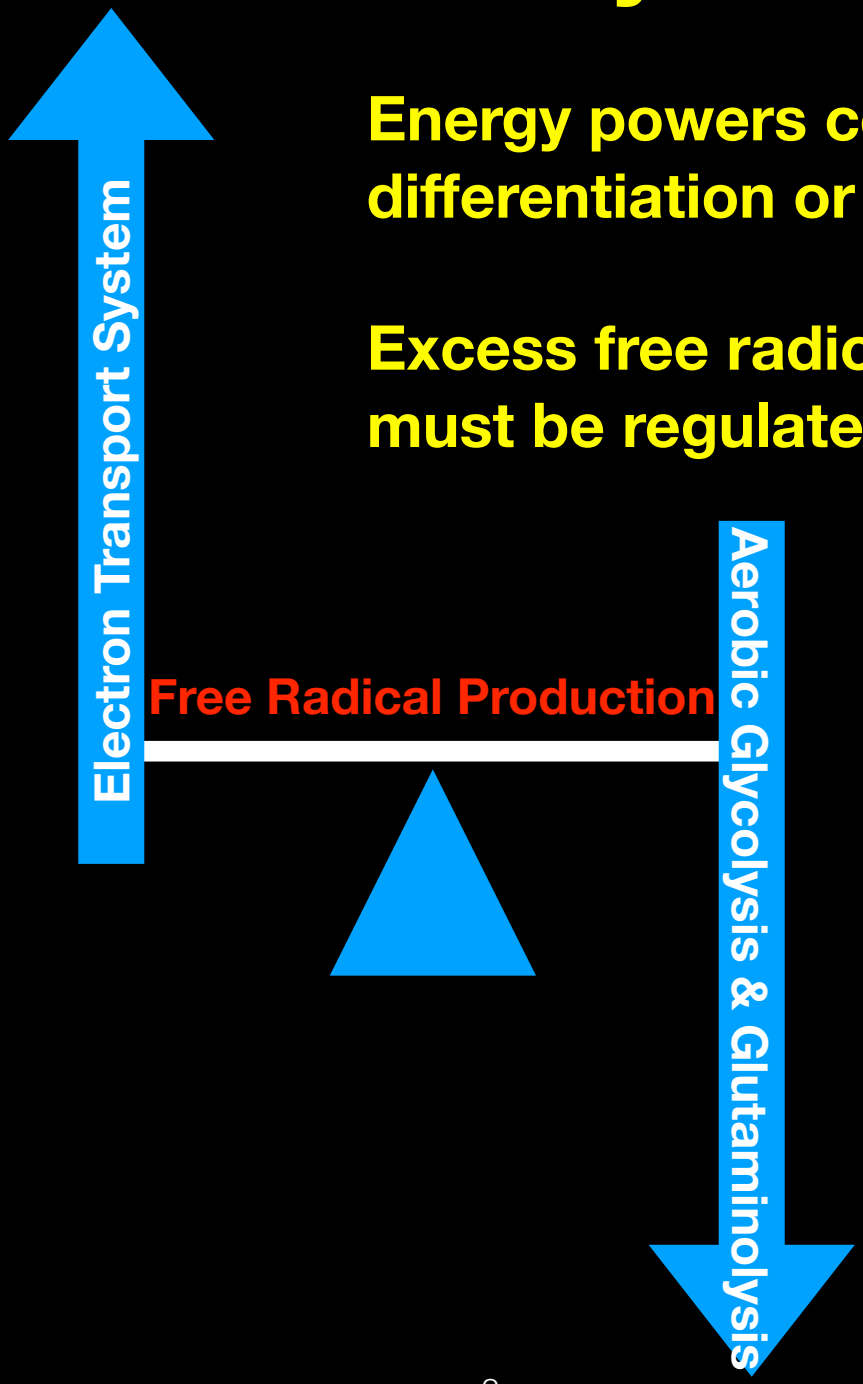


Too much flow
leaks free radicals

Balanced electron
transport system

Energy powers cell growth leading to differentiation or division.

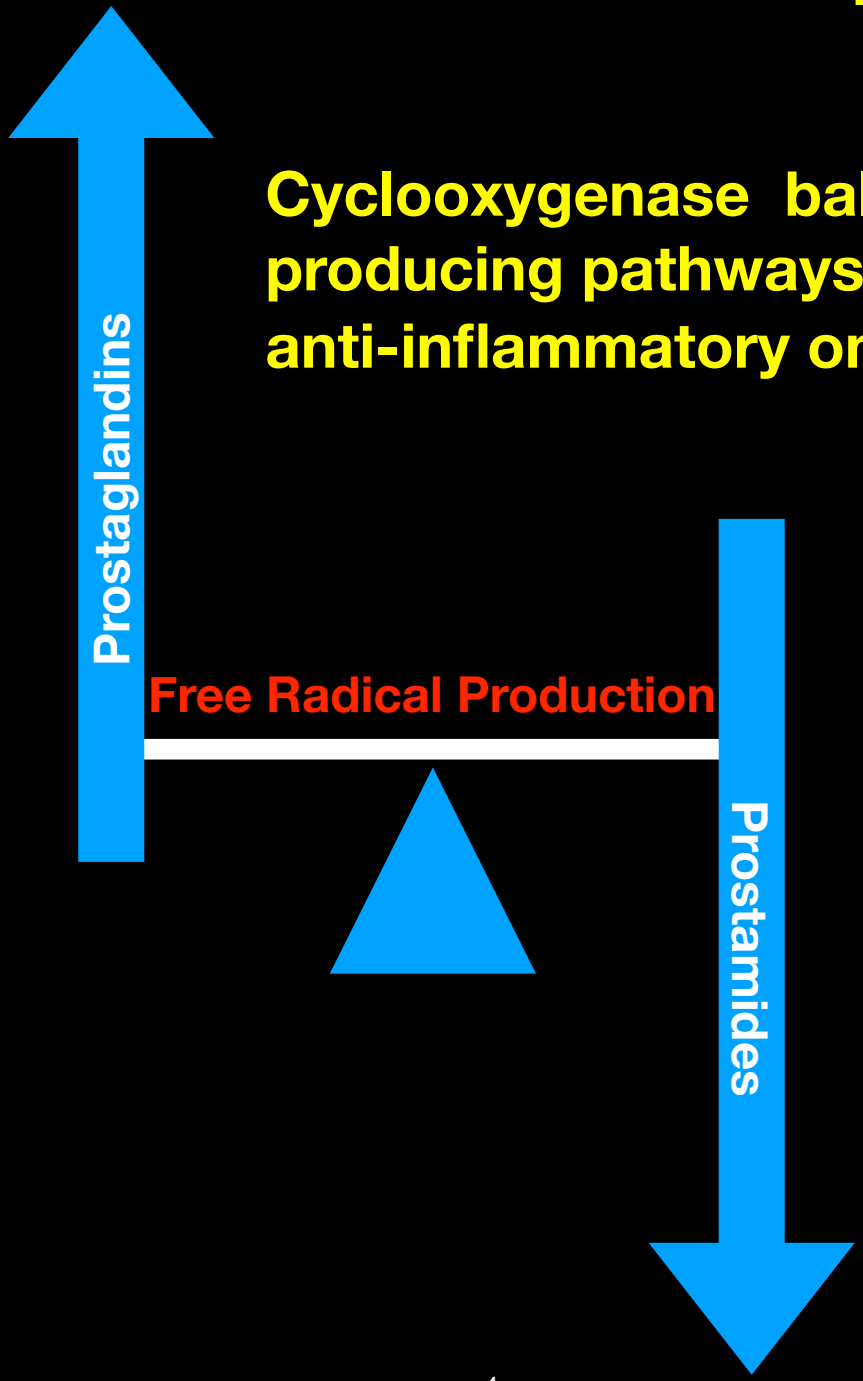
Excess free radical production must be regulated



Sugars
Glutamine
Amino acid

Complexity of Redirected flow produces Sugar burning anti-oxidants
Fat
Fibre
Migration
Cell division
Cycloogygenase

Non-beta Lipid Oxidation



Cyclooxygenase balances free radical producing pathways (prostaglandins) with anti-inflammatory ones (prostamides)

Complexity of Redirected flow produces Sugar burning anti-oxidants
Fat
Fibre
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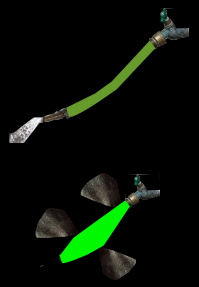
Cell division
Cycloogygenase



Carbohydrate Metabolism

- Regulates Free radial production
  - evolution
  - cell division
  - differentiation
  - COX ↑

CB1 Cyclooxygenase is part of differentiated metabolic pathways responsible for Non-beta oxidation of cyclooxygenase precursors

Free Radical Production

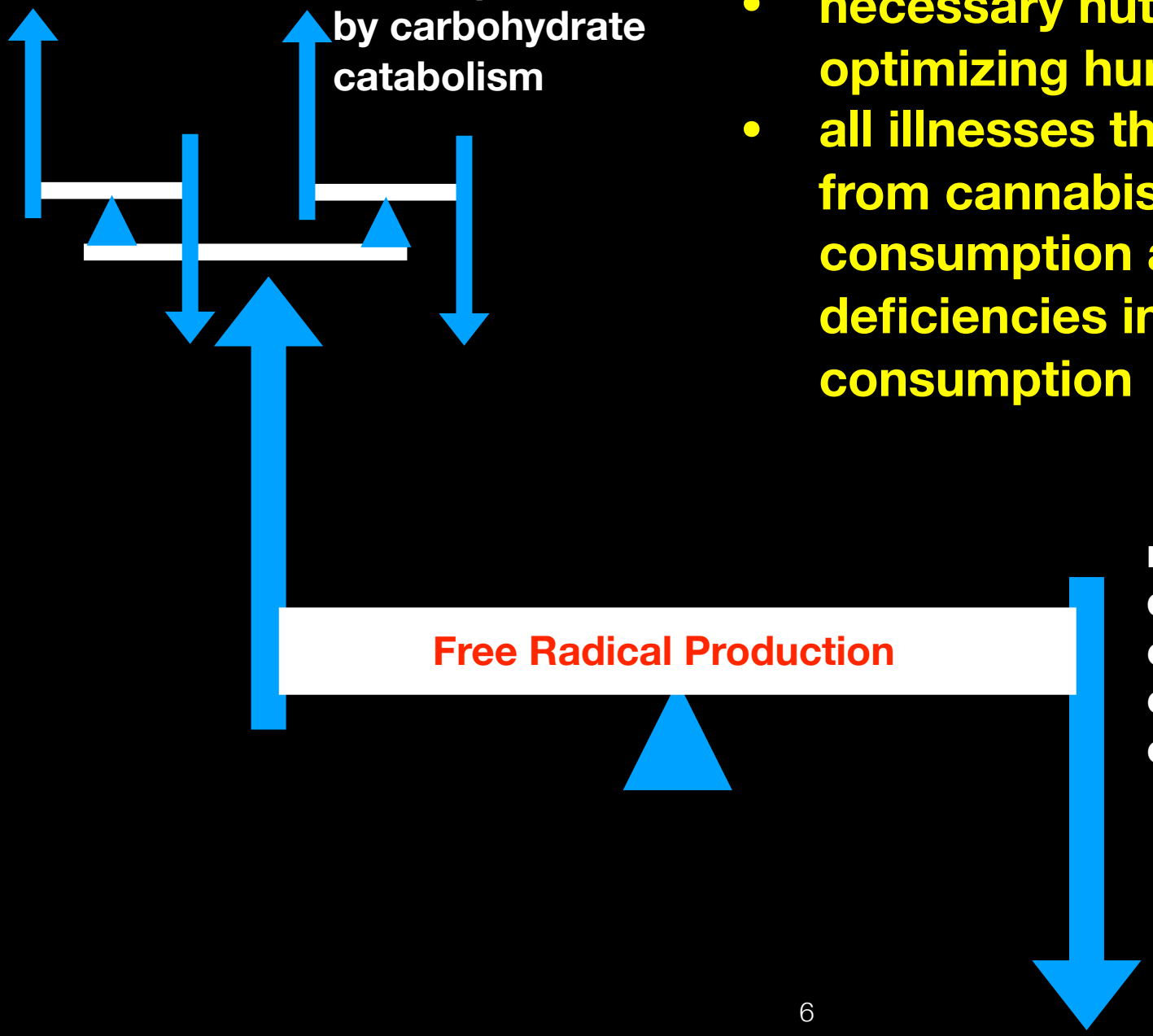
CB2

- Reduces Activating Ca++ flow
- Recycling of free radical
- Damaged cellular components
- Anti-aging
  - osteogenesis
  - telomere repair
  - COX ↓

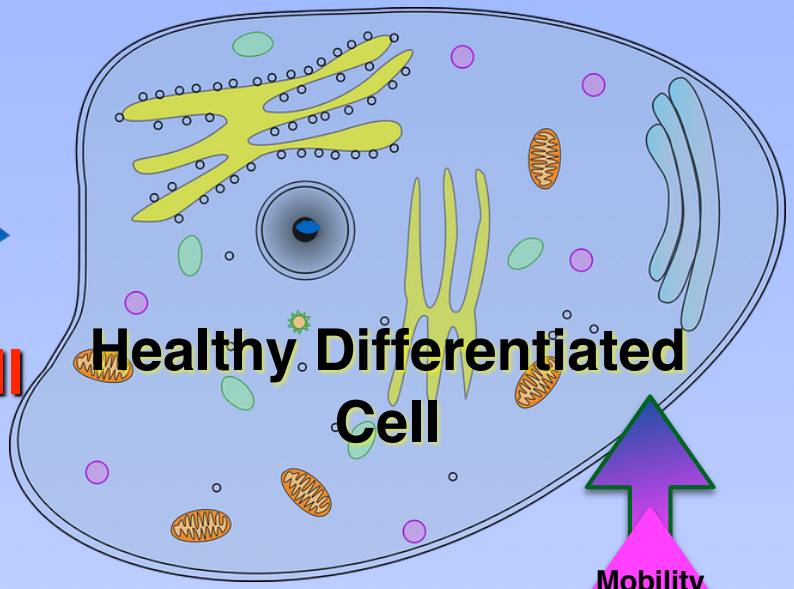
Fat-Burning

Cannabinoids

- necessary nutrients for optimizing human health
- all illnesses that benefit from cannabis consumption are nutritional deficiencies in cannabis consumption



CELLULAR ENERGY Flow



Healthy Differentiated Cell

Cancer Cell

Metastasis

Cancer Stem Cell

De-differentiated Cancer Stem

(Treatment Resistent)

Mobility

Adult Stem Cell

EMT

Epidermal/MesenchymalTransition

Electron Transport System

Carbohydrate Burning

Aerobic Glycolysis

Amino acid catabolism

FREE RADICAL Increase

Beta-Oxidation

Fat burning

Embryonic Stem Cell

De-differentiated State

(totipotent)

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Life/Cancer

Different cancers have survived organismic and cellular defense mechanisms by appropriately expanding and contracting survival-determining metabolic pathways so as to prevent cell death.

Different cancers have different metabolic flow patterns that have unique susceptibilities and resistances that characterize success or failure for any treatment.

Life/Cancer

Critically, the flow must be maintained for life to exist, with or without corresponding genetics as is proposed to have occurred when life first evolved and when senescent cells are created by chemotherapy or radiation.

A healthy cell is part of a healthy organism. A cancer cell no longer contributes to organismic health only to its selfish survival.

Healthy homeostasis involves a balance between efficient, but dangerous, electron transport driven ATP production, and alternative pathways that protect a cell from electron transport driven excess free radical production that leads to apoptosis.

When excess free radical production is no longer homeostatically controlled for organismic health, metabolic flow must be adjusted to prevent cell death.

Chronic, constitutive excess free radical production, as occurs in cancer cells, will direct genetic changes that will correspond to an existing gene expression profile and associated post-translational modifications that are holistically responsible for cell survival and carcinogenesis.

Life/Cancer

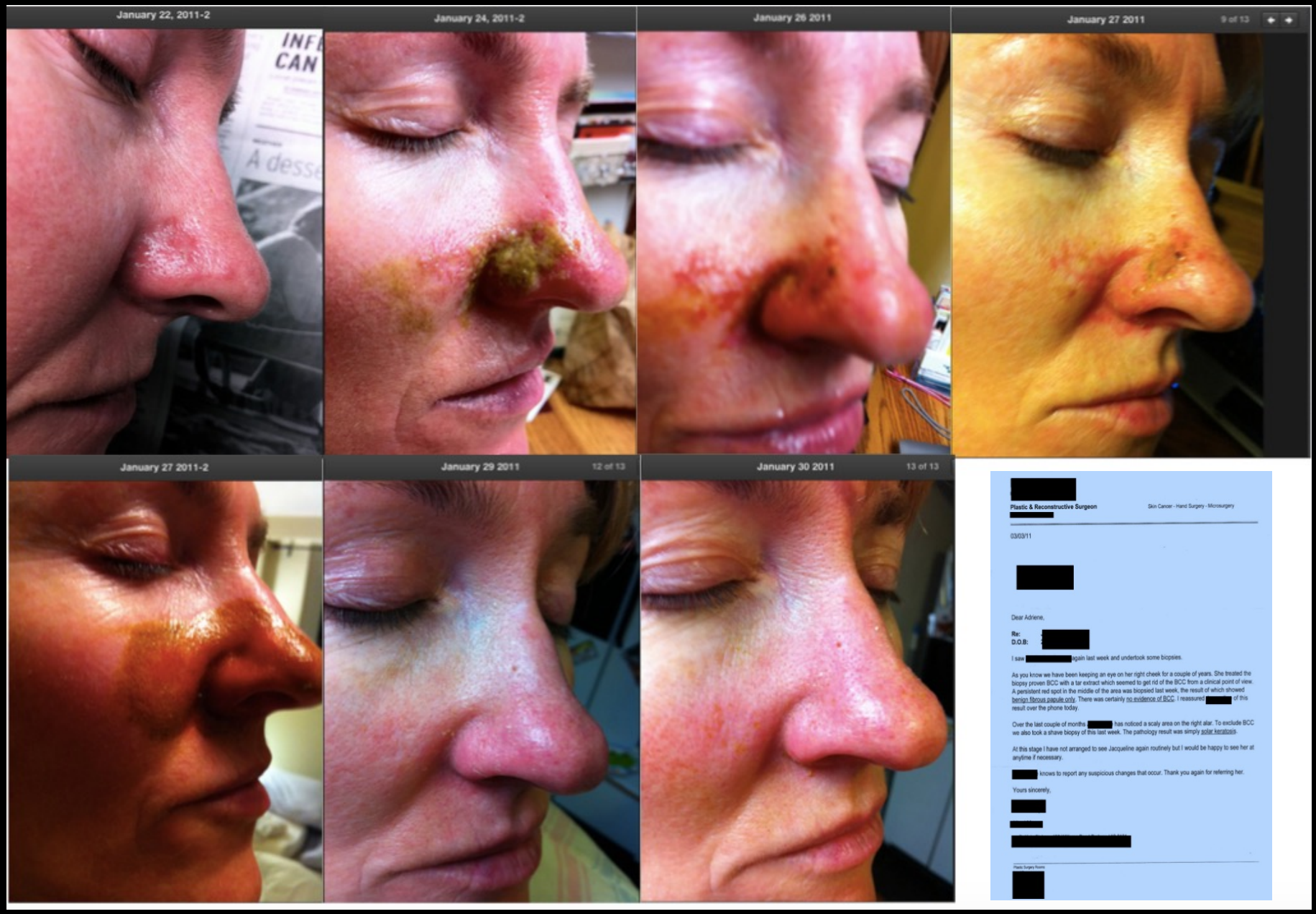
The following slides demonstrate metabolic principles visually.

They show that cancers that survive still heavily dependent on the electron transport system (differentiated cancers, squamous cell). They have different characteristics than those that are predominantly driven by inefficient, but safer means of carbohydrate metabolism (anaerobic glycolysis, glutaminolysis).

Beta-oxidation (fat burning), when the dominant survival mechanism of a cancer cell, actually ***generates*** the genetic diversity that characterizes tumors.

Chemotherapy and radiation actually create, in a nonrandom targeted fashion, the genetic changes that are characteristic of drug resistance cancer cells. They cannot undergo apoptosis since their electron transport system is turned off.

Basal Cell Cancer

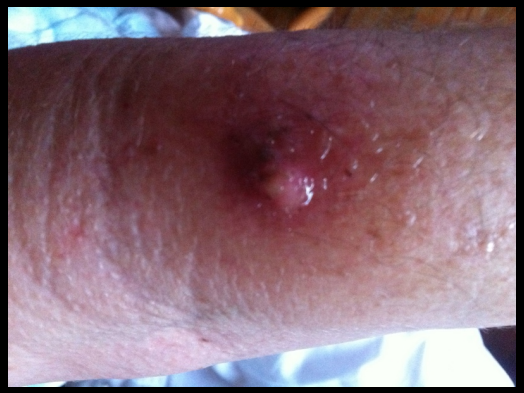
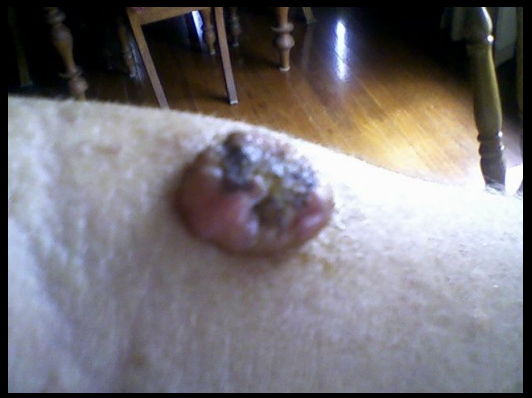
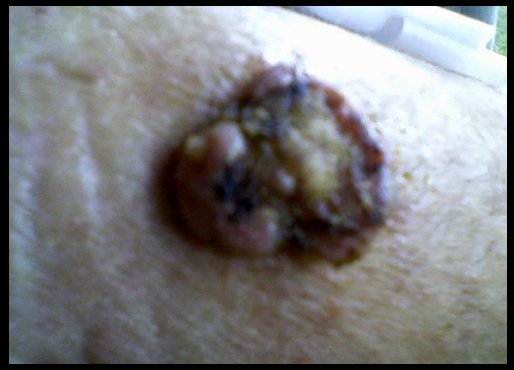
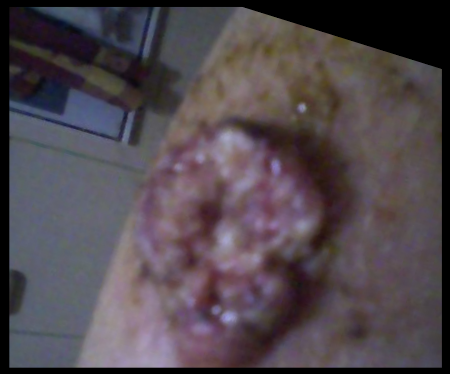


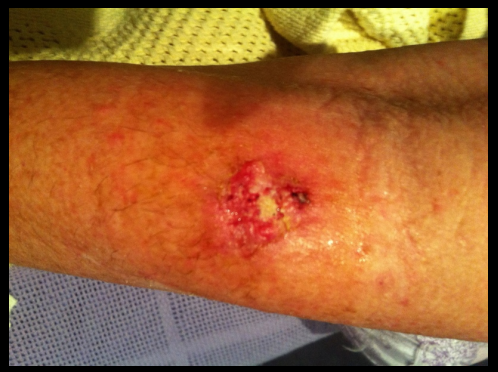
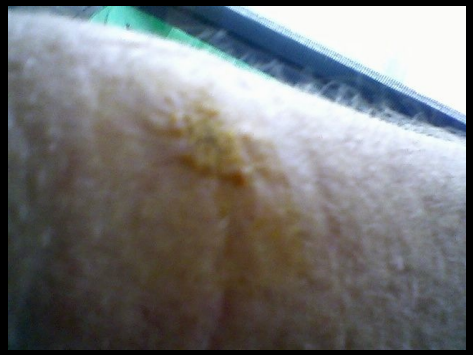
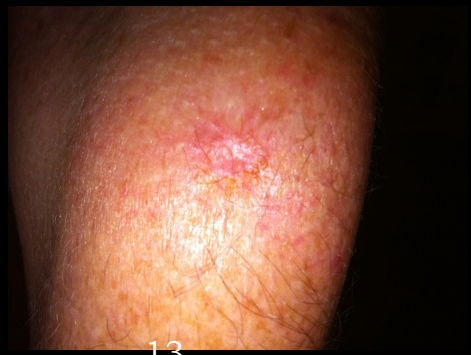
Life/Cancer

Basal cell carcinomas typically respond extremely well to topical full plant, high THC extracts. These cells readily undergo apoptosis when forced to burn fat by THC (also true of most traditional herbal remedies for cancer).

THC treated basal cell carcinoma typically fall of, painlessly, leaving no scar, in a few day to a few weeks.

Squamous Cell Cancer

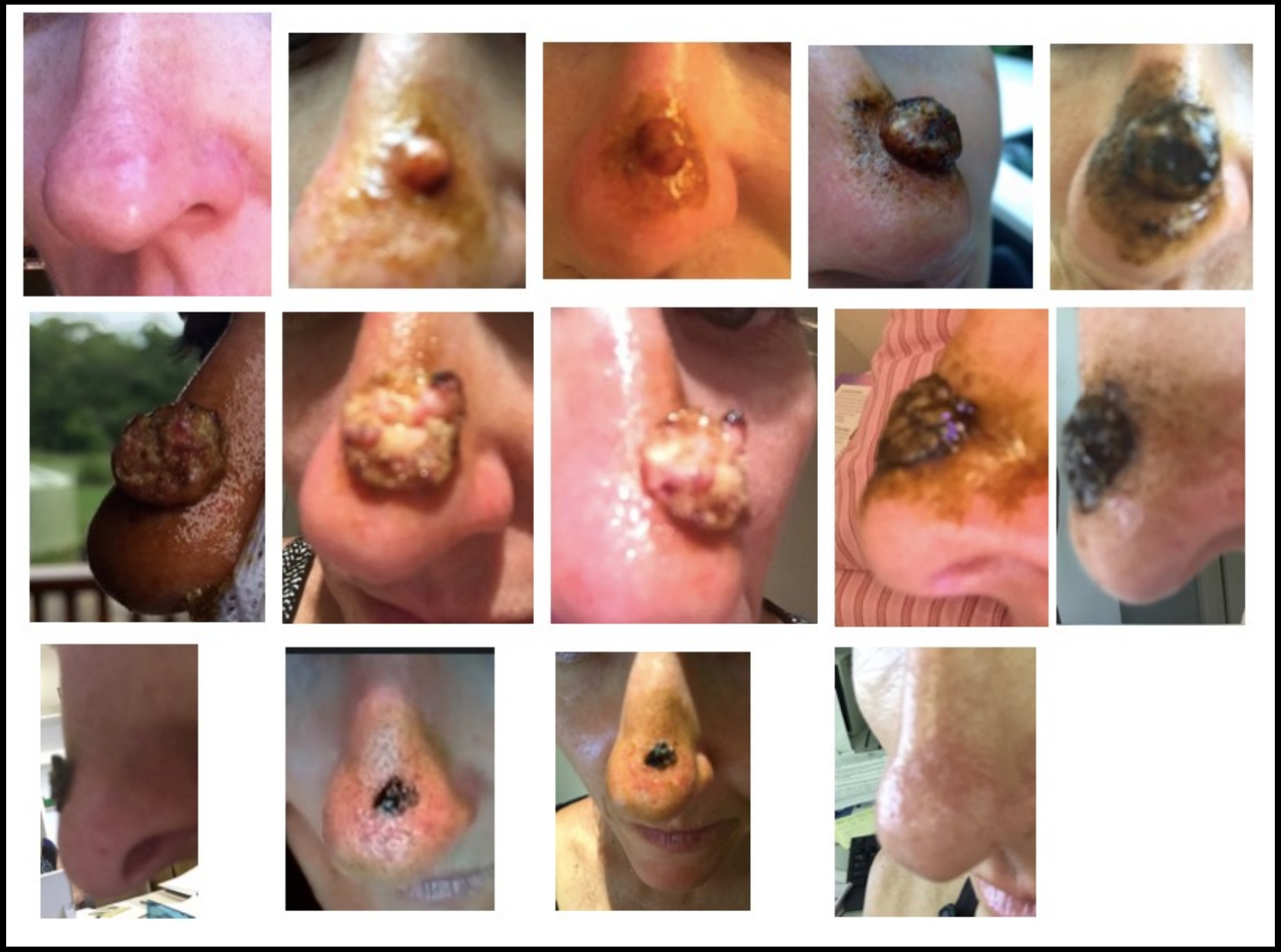




Life/Cancer

Squamous cell skin cancers typically initially grow when topical full plant, high THC extracts are applied. These cells do not undergo apoptosis when forced to burn fat by THC via the CB2 because CB1 activity is stimulating safer use of the electron transport system via its regulation of CA++ influx while the electron transport system is operational.

Squamous cell cancers, like all cancers, are metabolically imbalanced and and continue to produce excess free radicals. The complexity of the system decreases until the living state collapses and necrosis results.

Squamous Cell Cancer

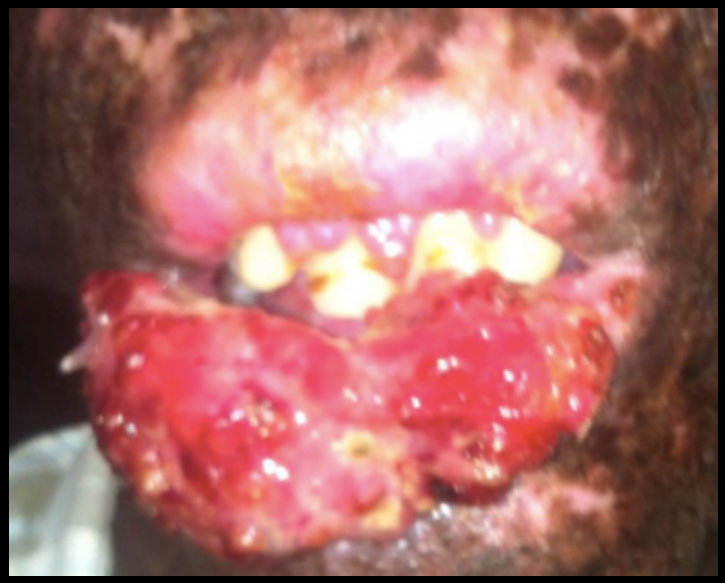


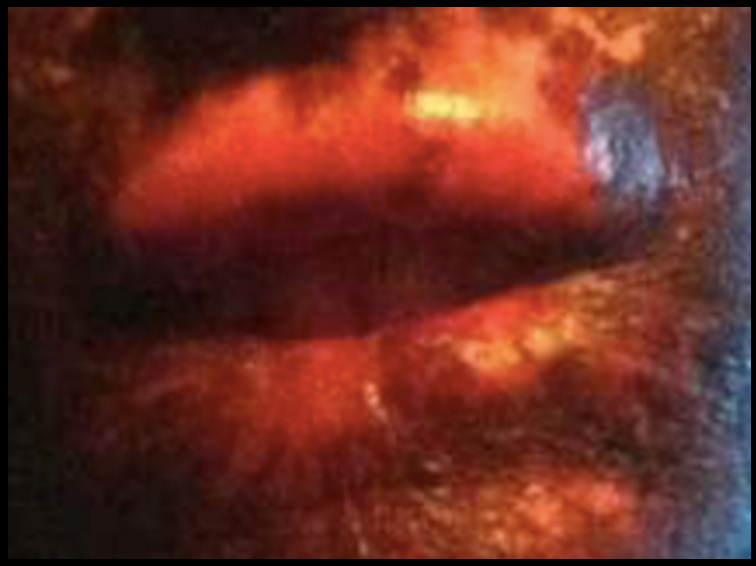
Life/Cancer

The patient had successfully treated numerous basal cell lesions with cannabis extract. It was an unpleasant surprise when a new cancer started to grow with topical THC extract application.

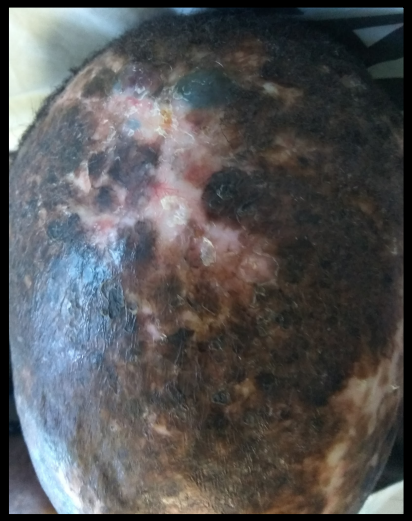
The tumor grew for a few months before hydrogen peroxide was topically applied to promote a free radical overload. Within an hour of application, the tumor started to collapse. After healing there was no scarring.

Xeroderma pigmentosum



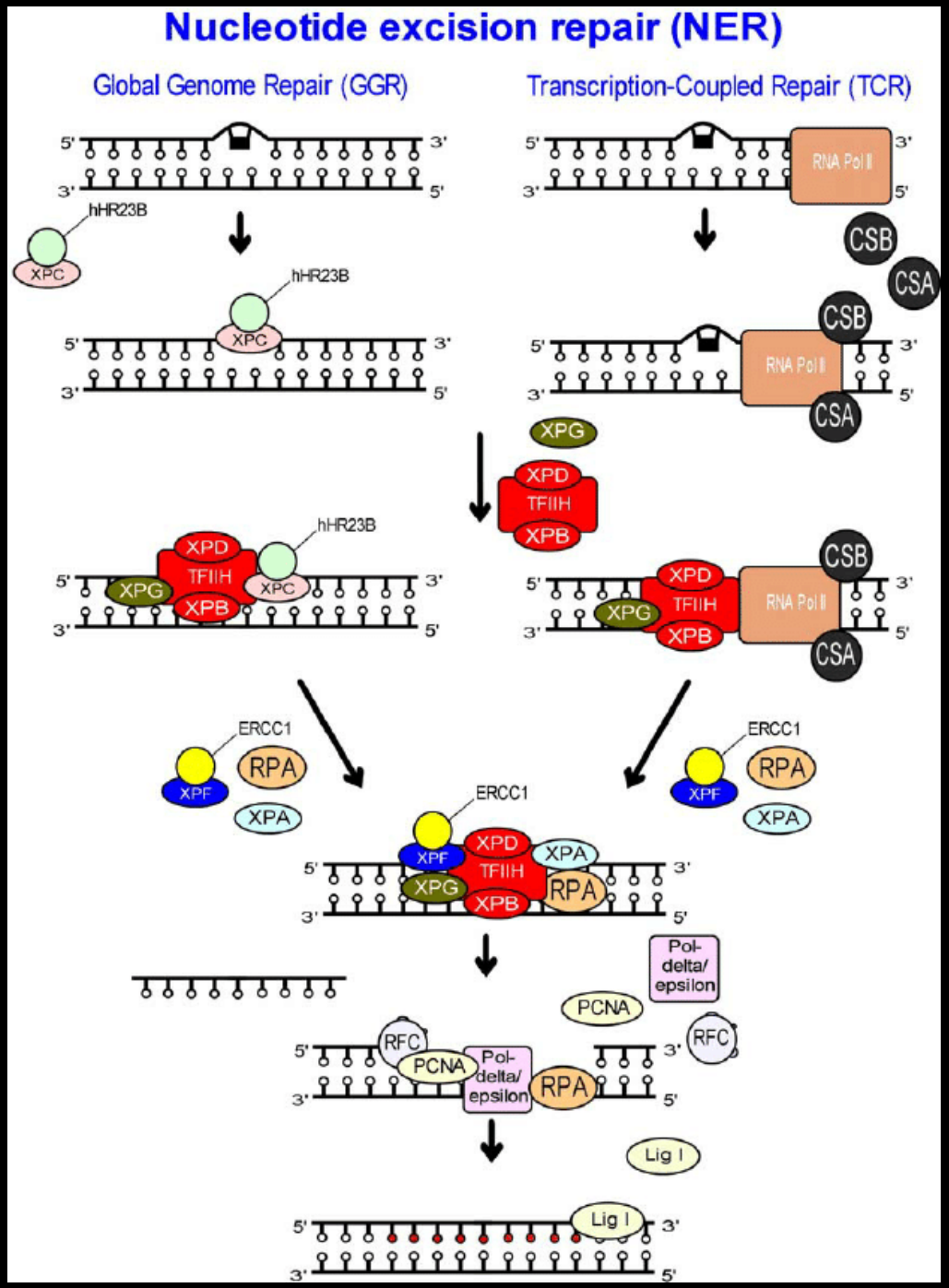


The human body has greater than 15 trillion, Every day suffer each cell suffers at least 30,000 oxidative base damages. Over the course of one year, cannabis medications metabolically reversed cancers caused by a genetic deficiency in a cell's ability to repair UV light induced DNA damages (Xeroderma pigmentosum). How can cannabis help? Note that XP cells have normal base excision repair abilities that repair free radical induced DNA damages.



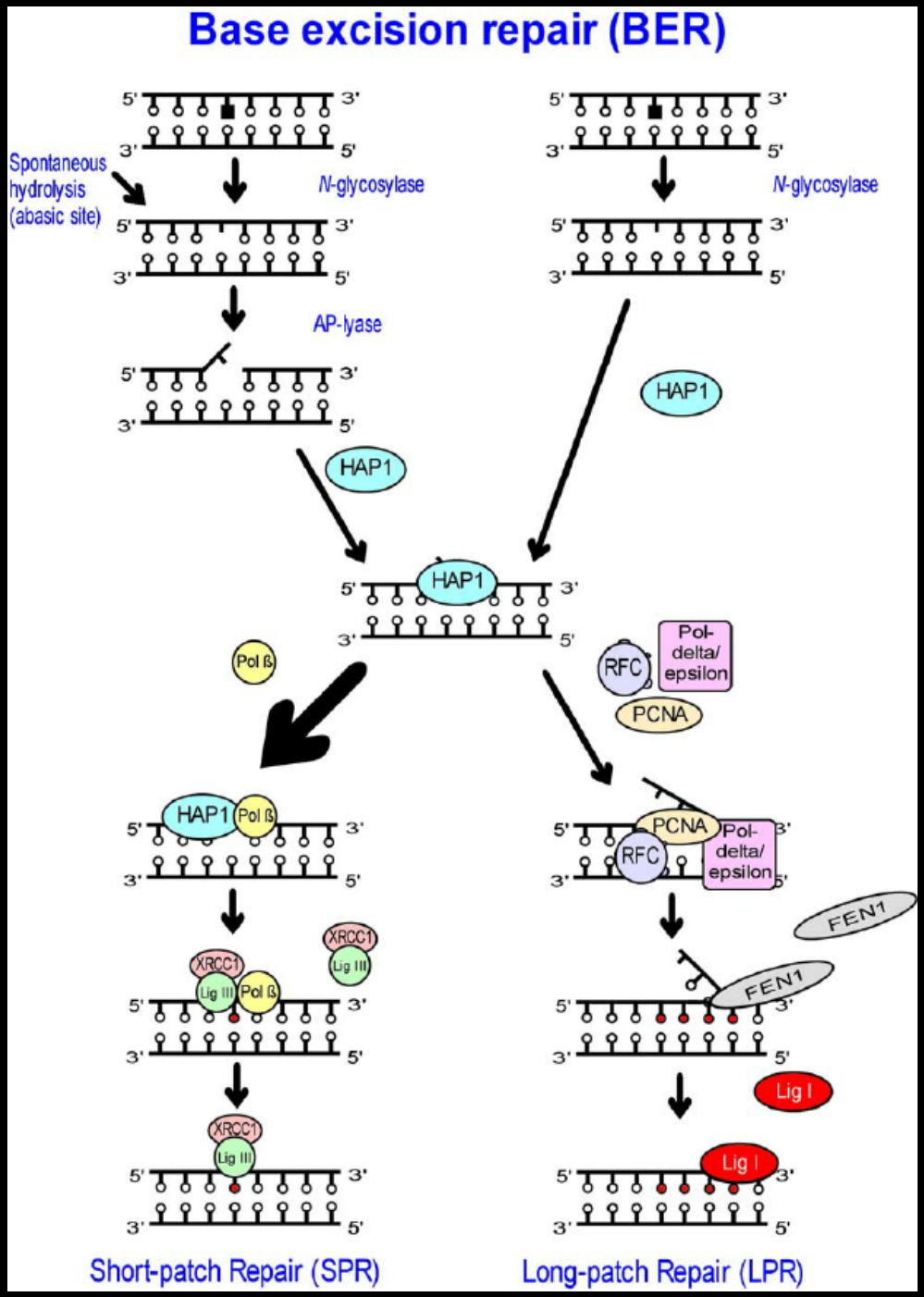

It’s so sad to see him now…
So much better a year ago.
Yes, I know - it's hard for me to see how this has happened to Donald. We're prepared to re-commence intensive treatment

Xeroderma pigmentosum



Xeroderma pigmentosum is a genetic cancer characterized by the inability of cells to repair DNA damages caused by ultraviolet light. The question is how can cannabis reverse the phenotype associated with this genetic mutation?

Xeroderma pigmentosum



Base excision repair is predominantly fixing metabolically created free radicals. Therefore, the reversal of squamous cell carcinoma as on the patients tongue and lips, reversal of melanoma on his head, as well as significant, although partial, restoration of his sight indicate that cannabis is influencing these conditions through its effects on underlying metabolism.

How does the lack of nucleotide excision repair impact cellular metabolism?

The basic observation that must be understood is, “How can cannabis cure this genetic disease?”

From the energetic perspective the question must first be reframed as,

- How does ultraviolet light impact metabolism?
- How do cannabinoids impact metabolism to alter the metabolism of various cancers affecting this young man to promote health?

Cell cycle can be viewed as a series of far from equilibrium phase changes. During G0 a cell his hanging out doing something efficiently when needed (ie create differentiated function such as nerve transmission), or doing nothing but waiting for some environmental change to tell it to do something by becoming something or dividing.

Pathways for change increase flow and free radical production to sustain/build up the metabolic flow in a circumstance specific fashion. The increased flow increases free radical damages to the point that the system must readjust, thus triggering the next phase of cell cycle.

DNA must be ready for replication and hence there is a DNA damage checkpoint prior to the initiation of S-phase.

There is an accumulation of free radical induced systemic damages (to all biomolecules not just DNA) is minimized by turning down the electron transport system as excess free radicals accumulate.

Cells in S-phase that are replicating their DNA, will have turned down the electron transport system (will not apoptosis) and have turned on anaerobic glycolysis for supplying their energy.

Cells trapped in that state, with ongoing excess free radical production yet with survivable flow, will selectively mutates, amplify, etc, the metabolic pathways that are giving survival, Directed Adaptive Evolution

Life/Cancer

When cancers are treated with radiation or chemotherapy, mutations will be ***directed*** to specific targets that can genetically institutionalize successful patterns of metabolic flow.

DNA is the written record of evolving successful metabolism!

Cells turn off the electron transport system when DNA is replicating to avoid apoptosis. Functionally, this metabolic property allows a cell to metabolically survive for years without dividing (senescence).

While surviving, non homologous end joining and associated enzymatic DNA repair related processes, will continue to diversify a cell's genetics to correspond with it's successful metabolism.

Life/Cancer

Different cancers are fueled by diverse energy sources. Different metabolic approaches are necessary to eliminate any particular cancer by free radical overload.

Cancers characterized as being more differentiated might naturally be expected to have enhanced electron transport system activity.

For example:

- a high level of antioxidants would reduce the probability of the electron transport system generating excess free radicals.
- a high level of oxygen availability could accelerate electron transport throughput while minimizing free radical leakage (could explain squamous cell cancers in lungs)
- cells with high levels of UCP2 would have a reduced proton gradient and therefore reduced free radical production.

Life/Cancer

Cancers characterized as less differentiated might naturally have a reduced dependence on the efficient electron transport system activity. Most cancers are characterized by:

- Highly dependent on sugar to meet energy needs
- High lactic acid production despite the presence of oxygen (aerobic glycolysis)
- High levels of glutaminolysis and catabolism of other amino acids
- Excess free radical production

Life/Cancer

Autophagy (fat-burning) shuts down carbohydrate energy sources in favor of recycling.

Associated cancer fueling pathways are shut down

Peroxisome proliferator-activated receptors (PPARs) control cellular fuel supply:

- PPARγ sugar burning-CB1
- PPARα fat burning-CB2
- PPARδ fat burning-CB2

From a thermodynamic perspective, autophagic cells reduced their negentropic transport with the environment. The decreased flow resulted in lower excess free radical production thus decreasing internal entropy while recycling entropic free radical damaged components.

Life/Cancer

Autophagy (fat-burning) shuts down carbohydrate energy sources.

Cells cannot amplify metabolic imbalances that lead to autophagy because they will not produce excess free radicals in the absence of the electron transport system (precisely why the electron transport system is turned off during DNA replication).

Life/Cancer

When carbohydrate metabolism is active, DNA repair mechanisms that maintain genetic fidelity are active

In contrast, DNA repair mechanisms responsible for genetic fidelity are down-regulated when cells burn fat. However, nonhomologous end joining (NHEJ) that promotes genetic changes typical of evolution remain active.

A fat burning stem like cancer cell will adapt its genetics to match its metabolism as long as it does not apoptose or necrose before it is successful.

Fundamental Principles of Metabolism-centric Biology

- Flowing energy and matter natural drives complexity
- Once life evolved, free radicals became global homeostatic regulators of biological complexity.
- Once invertebrates evolved, the endocannabinoid system became the global homeostatic regulator of all biological systems.
- Evolution of species and of cancer is not simply a collection of random accidents.
- Genetic changes are directed towards genes and controlling regions responsible for survival.

For additional information

Email drbobmelamede@me.com
HomePage http://canna-sapiens.com

Monograph In God We Rust: The Beauty of Unintelligent Design
http://canna-sapiens.com/in-god-we-rust-the-beauty.html

Harvard Cancer Lecture 2019
https://www.facebook.com/100003694791385/videos/1551307431669068/

Animation Metabolic Plasticity
https://www.youtube.com/watch?v=8ezjEypHnTA&fbclid=IwAR31zBg8EOOL21rvFY7h3cz-5RydrMGTpreobm1wTlwMqP3gacvNe0oyEak

What If? http://canna-sapiens.com/drbobs-videos/lubjiana-2019.html