DCA and Avemar

A theoretical protocol for Cancer
What is Avemar?

- Avemar is a fermented wheat germ product.
- It is approved by the FDA as GRAS (Generally Reported As Safe)
- The active ingredients are 2,6 dimethyl benzoquinone (DMBQ) and 2 methyl benzoquinone (and several others)
What is DCA?

- DCA is a small, simple chemical, similar to vinegar
- It has been used for years in a rare condition known as Congenital Lactic Acidosis
- Demonstrated action against a wide variety of cancers in mice in 2007 with a limited follow up study in humans in 2010.
Why Avemar and DCA?

• Cancer cells revert to an older, less efficient method of metabolism.
• In so doing they employ various methods to prevent their own destruction
• Avemar shuts down the energy pathways cancer draws energy from
• Avemar prevents cancerous cells from evading the immune system
• DCA activates the more efficient aerobic metabolism returning the cell to normal functioning
• (‘Normal functioning’ in this case means the cell will detect it is in an unhealthy state and undergo apoptosis which is cellular suicide)
A word on biology pathway diagrams

‘A’ promotes ‘B’

‘A’ inhibits ‘B’

Reactant ‘A’ reacts to produce product ‘B’ under the influence of catalyst/enzyme ‘C’
What are the Mitochondria?

• Healthy cells use mitochondria to produce energy.
• Mitochondria are organelles (small cellular components with specific functions)
• Mitochondria require oxygen to function
• They are hugely more efficient than the anaerobic (without oxygen) glycolysis
• They have long been though to be damaged beyond repair in the case of cancerous cells
• Recent research (2007) involving DCA reveals that the mitochondria were only dormant and could be revived
• The mitochondria -- not the nucleus -- controls apoptosis (cellular suicide in cancerous or injured states)
Examining Cellular Metabolism
Glycolysis

- Glycolysis does not require oxygen
- Produces 2 units of energy (ATP)
Aerobic Respiration (Mitochondria)

- Aerobic metabolism occurs in the mitochondria
- Also known as the Citric Acid Cycle
- Produces 36-38 energy units (ATP)
- 19X more efficient
- Analogous to a cellular afterburner
Derailed Aerobic Respiration

- In cancer cells, aerobic respiration is derailed
- We'll be looking at the encircled area, the entrance to the Citric Acid Cycle, to see how
Derailed Aerobic Respiration

- ‘Myc’ is an oncoprotein (cancer promoting protein)
- It stimulates the enzyme PDK.
- PDK, in turn, antagonizes (inhibits, slows down) PDH
- With PDH inhibited, the reaction of Pyruvate to Acetyl-CoA cannot proceed
- Aerobic metabolism is derailed
DCA Restores Mitochondrial Function

- DCA antagonizes PDK
- With PDK out of the picture, PDH is free to catalyze (promote, help) the Pyruvate to Acetyl-CoA reaction, restoring the Citric Acid Cycle
- The mitochondria is now up and running
- The mitochondria can now effect apoptosis.
The mitochondria now effects apoptosis.

- The mitochondria releases several agents that trigger apoptosis.
- Most notably: Cytochrome C and Smac/DIABLO.
So why isn’t DCA the end of the story?

• The core of a tumor is extremely anoxic (without oxygen)
• By analogy the mitochondria have the keys in the ignition but no fuel to work with.
• Cancer cells consume huge amounts of sugar starving the mitochondria
• DCA does nothing to help the immune system recognize and consume cancer.
How and Why Do Tumors Consume So Much Sugar?

- Tumors are constantly multiplying requiring the construction of DNA.
- DNA is made largely of sugar.
- Since anaerobic respiration is considerably less efficient, the cancer cell must compensate by overdriving glycolysis and a glycolysis alternative called the ‘Pentose Phosphate Shunt’
- By analogy a car with a less efficient engine must consume far more gasoline to function
The Pentose Phosphate Shunt and Cancer

• The Pentose Phosphate Shunt is used to build DNA in healthy cells
• It produces some energy as well
• In cancerous cells it is rapidly accelerated
• In the diagram you can see how it would siphon off sugars before they could get near the Citric Acid Cycle
• Thus even with DCA restoring the mitochondria, it might still be starved
Avemar Selectively Modulates the Pentose Phosphate Shunt

- Avemar selectively inhibits G6P-Dehydrogenase and Transketolase which are key to the pathway.
- ‘Selective’ means that it would take 50x the prescribed dose to inhibit the pathway in normal cells.
- With the pathway now restored to normal balance (no longer in overdrive), sugars can reach the Citric Acid Cycle in the mitochondria.
Modulating Glucose Uptake Prevents Cachexia

- It’s actually a condition called ‘cachexia’ which typically proves fatal in cancer
- Cancer cells produce a large amount of lactic acid as the result of glycolysis
- Lactic acid is the same acid that causes your muscles to burn after a hard workout
- The liver converts this lactic acid, regrettably, back to sugar
- Avemar prevents cancer cells from building enough DNA to multiply as quickly as they need.
- Sugar consumption is thus reduced and the vicious cycle is broken
Cachexia

Avemar
**PARP Inhibition**

- PARP is an enzyme which repairs DNA.
- Cancer cells duplicate repeatedly which can introduce copy errors in the DNA.
- Without PARP to repair those errors, the DNA becomes fragmented and unreadable leading to cell death.
- Avemar has been shown to selectively disable PARP in cancer cells.
- Again ‘selectively’ means that PARP is not inhibited in healthy cells.
PARP Mechanism of Action

- **DNA damage** is detected by PARP, which binds rapidly and directly to single-strand breaks.
- PARP recruits repair enzymes.
- PARP modifies itself by producing large branched chains of Poly (ADP-ribose) upon binding to damaged DNA.
- Repaired DNA is generated through this process.
Immunological Actions of Avemar

- Avemar sports immunological functions
- Cancer cells display a signal called ‘MHC-1’ which is a deceptive ‘I am healthy’ signal
  - (Cells which are actually healthy also display this signal)
- Cells which fail to display MHC-1 on their surface are consumed by the immune system’s NK (Natural Killer) cells.
MHC-1 Downregulation and Avemar

- With the downregulation (prevention) of MHC-1 expression (display on the cell surface) the NK (Natural Killer) cells can target the cancer cells
- This unmasks the cancer cells to the immune system
- **This prevents metastasis**
In order for a tumor to feed itself, it needs to stimulate the creation of supplying blood vessels.

In cancer, this process is called: angiogenesis.

Blood cells have a lining called an endothelium.

Normal blood vessels have components in their lining called ICAM which facilitates immune cells leaving the blood and entering the tissue.

Cancer blood vessels are almost entirely devoid of ICAM.

Avemar promotes the expression (display on the lining) of ICAM such that the immune cells can enter the tissue (tumor) and destroy it.
Avemar promotes ICAM-1 expression in the blood vessels feeding the tumor. This, in turn, allows immune cells to enter the tumor.
Avemar Safety and Side Effects

- Avemar is FDA approved
- It is already an accepted adjunct therapy to chemotherapy
- Some side effects include:
  - Mild and infrequent side effects may include diarrhea, nausea, flatulence, soft stool, constipation, dizziness
- For more information see:
DCA Safety and Side Effects

- DCA has been used successfully in humans for a rare disease called Congenital Lactic Acidosis
- DCA can be prescribed ‘off label’ by your physician
- Some side effects:
  - peripheral neuropathy (tingling in the fingers)
  - numbness in toes or fingers
  - shaking or tremors in hands
  - weakness in legs
  - mild nausea
  - swollen ankles
  - more urination
  - dizziness
  - anxiety
  - depression
  - sleepy
  - breathing heavier than usual
  - tingling (neuropathy) in the lips
- Note: Side effects are typically rare and dose dependent. They are orders of magnitudes less severe than standard chemo therapy. Consult your physician for more details.
- More information:
Where to get Avemar?

- [http://www.avemar.com/aww](http://www.avemar.com/aww)

**DO NOT SELF MEDICATE:** Consult your physician
Where to get DCA?

- DCA can be obtained from a compounding pharmacy but must be prescribed by a qualified physician.
- Medicor Cancer Centres treats patients internationally
- [http://www.medicorcancer.com/](http://www.medicorcancer.com/)

DO NOT SELF MEDICATE: Consult your physician
Further Reading

- [http://www.dca.med.ualberta.ca/Home/index.cfm](http://www.dca.med.ualberta.ca/Home/index.cfm)
- [http://medicorcancer.com/dca-therapy.html](http://medicorcancer.com/dca-therapy.html)
- [http://www.martincwiner.com/dca](http://www.martincwiner.com/dca)
Scholarly Papers: Avemar

Scholarly Papers: DCA

- https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2567082/
- http://mct.aacrjournals.org/cgi/content/meeting_abstract/8/12_MeetingAbstracts/B97
- http://www.nature.com/bjc/journal/v102/n12/full/6605701a.html