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 thought 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
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...
• ‘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

PARP binds rapidly and directly to single-strand breaks

NAD+

nicotinamide + pADPr

PARP recruits repair enzymes

Once bound to damaged DNA, PARP modifies itself producing large branched chains of Poly (ADP-ribose)

Repaired DNA
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.
ICAM, Angiogenesis and Avemar

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