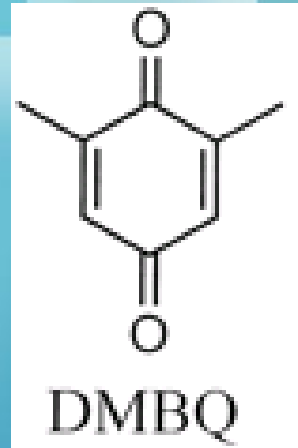


DCA and Avemar

A theoretical protocol for Cancer

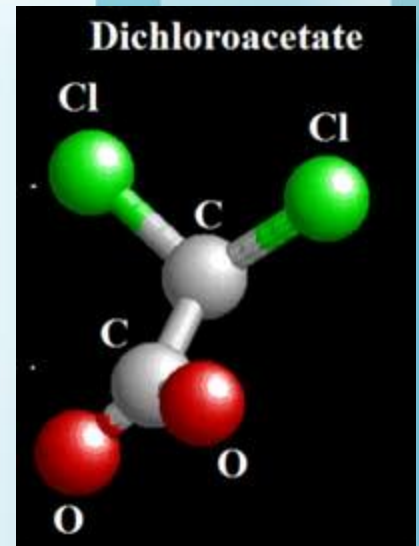
What is Avemar?

- 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?

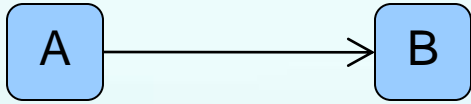
- **DCA is a small, simple chemical, similar to vinegar**
- **It has been used for years in a rare condition known as Congenital Lactic Acidosis**
- **Demonstrated action against a wide variety of cancers in mice in 2007 with a limited follow up study in humans in 2010.**



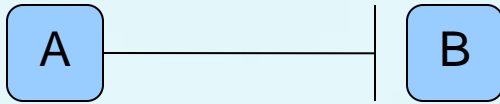
Why Avemar and DCA?

- **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)**

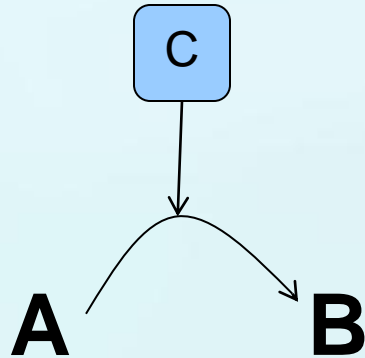
A word on biology pathway diagrams



'A' promotes 'B'



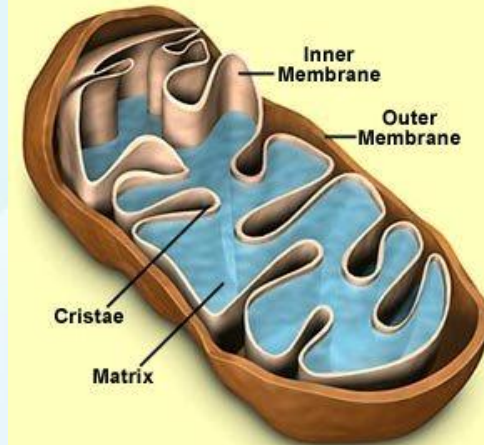
'A' inhibits 'B'



Reactant 'A' reacts to produce product 'B'
under the influence of catalyst/enzyme 'C'

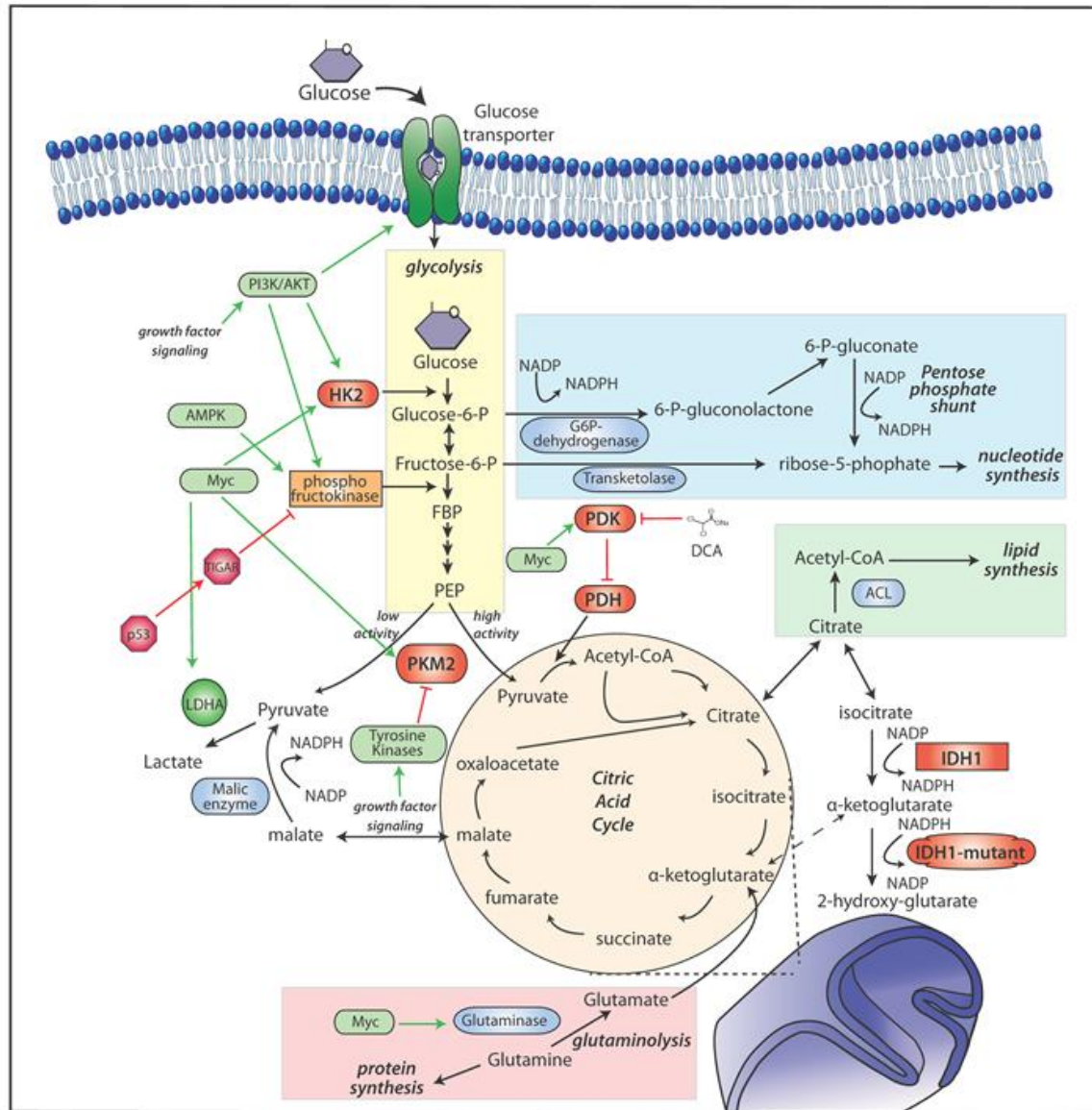
What are the Mitochondria?

- 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)

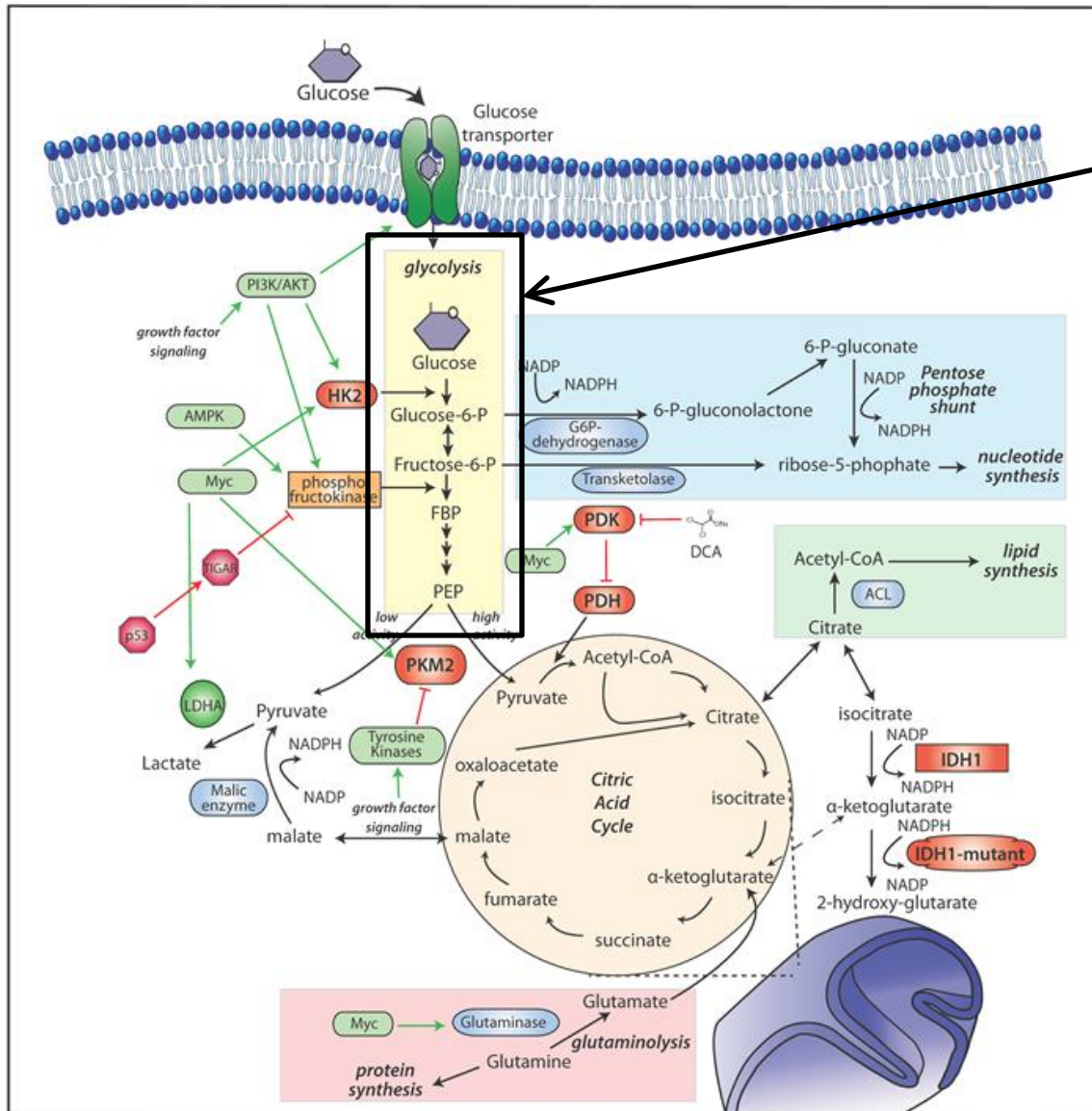


Mitochondrion

Examining Cellular Metabolism

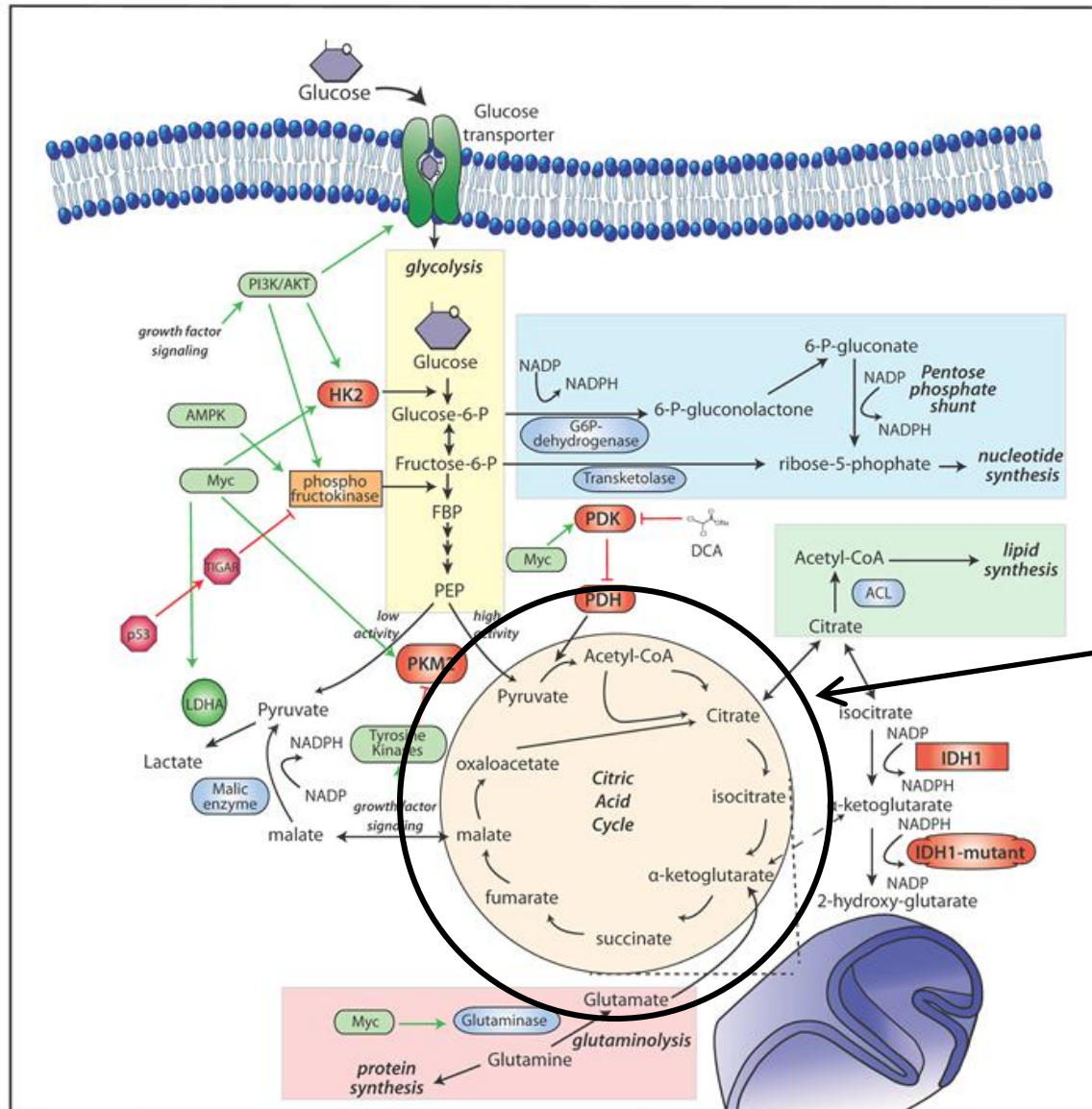


Glycolysis



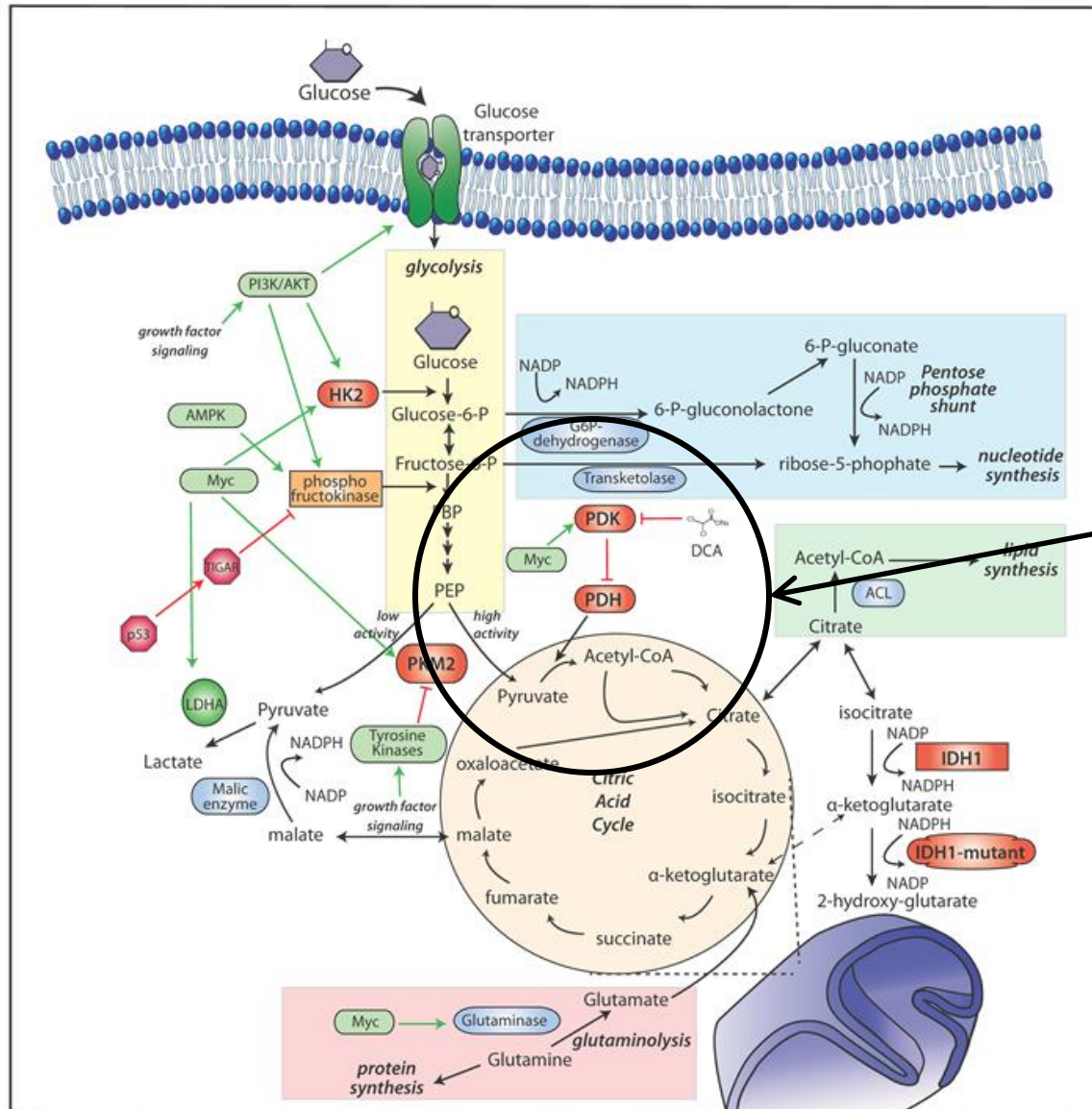
- Glycolysis does not require oxygen
- Produces 2 units of energy (ATP)

Aerobic Respiration (Mitochondria)



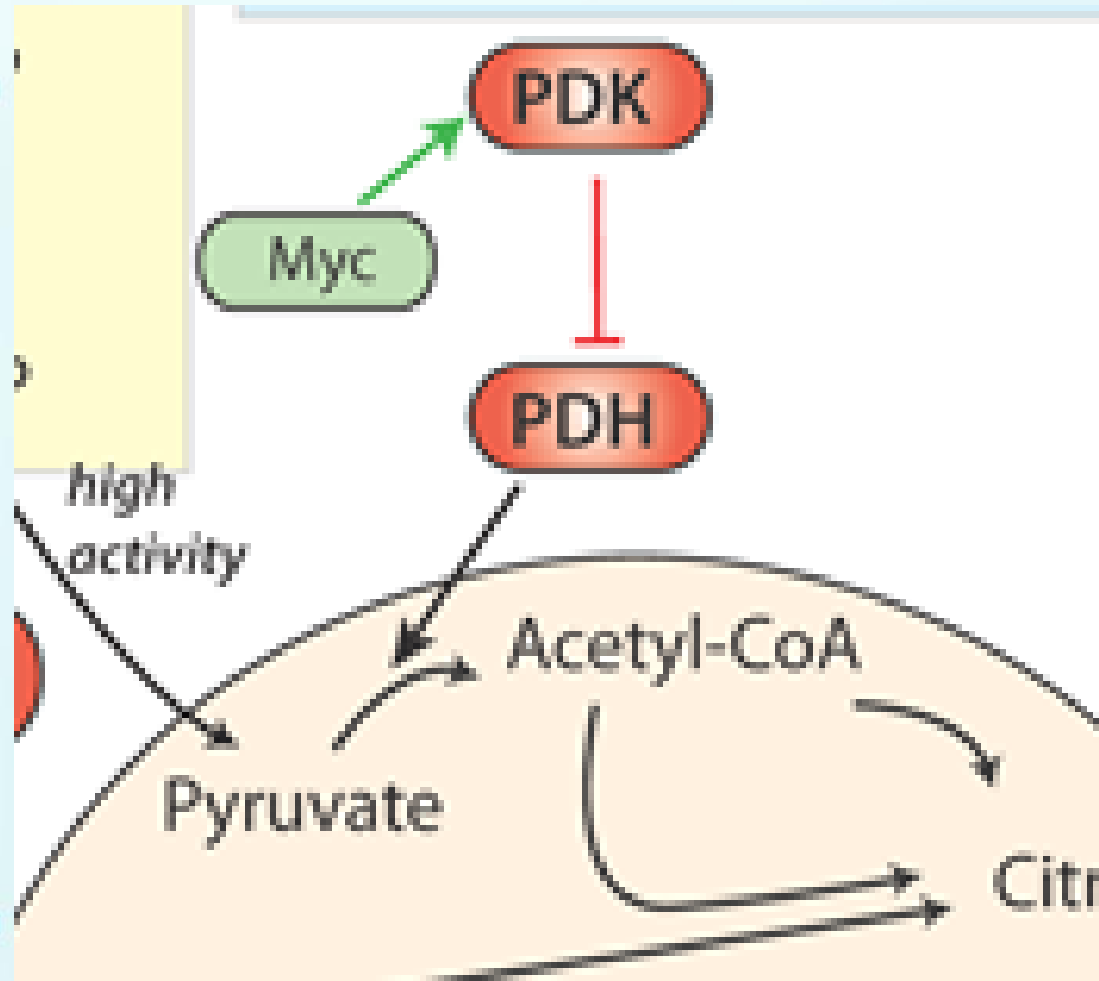
- Aerobic metabolism occurs in the mitochondria
- Also known as the Citric Acid Cycle
- Produces 36-38 energy units (ATP)
- 19X more efficient
- Analogous to a cellular afterburner

Derailed Aerobic Respiration



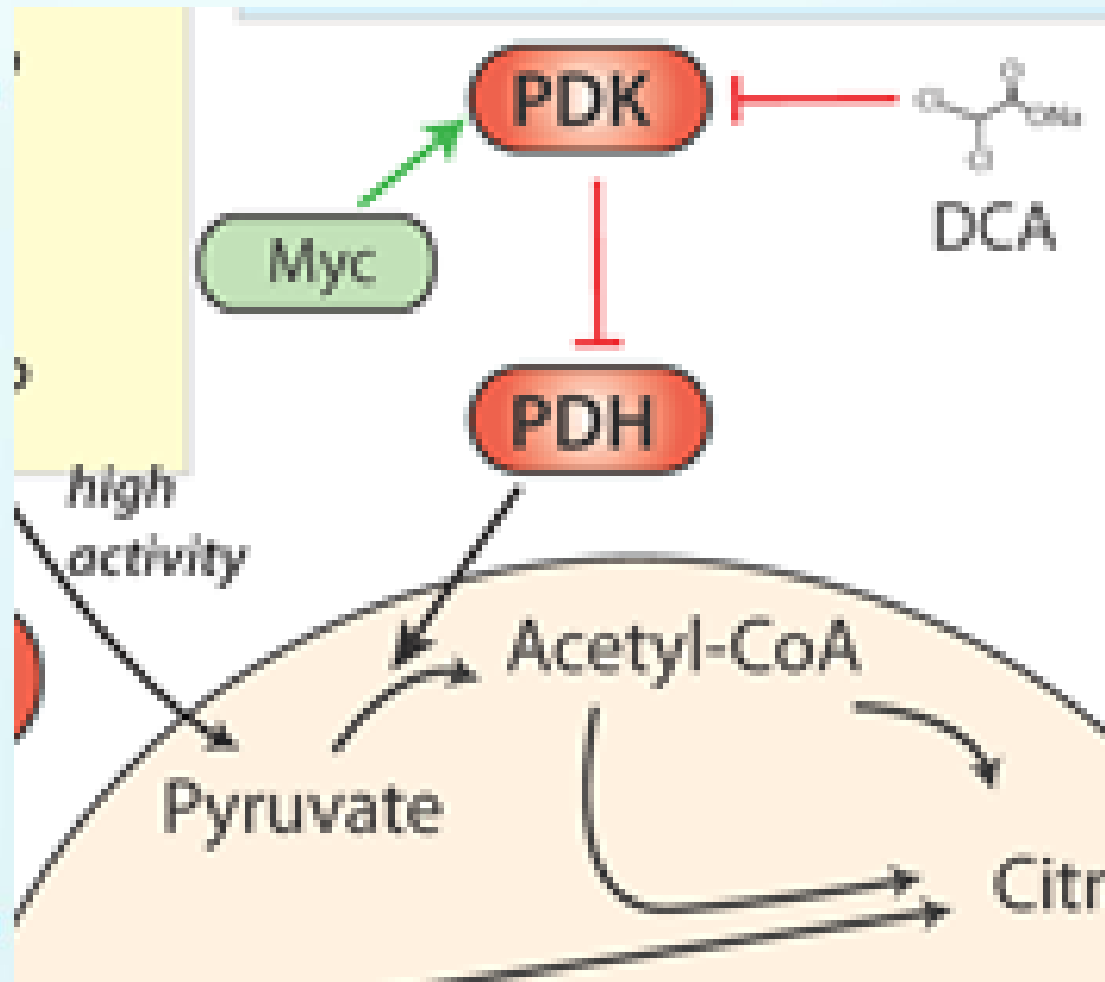
• In cancer cells, aerobic respiration is derailed
 • We'll be looking at the encircled area, the entrance to the Citric Acid Cycle, to see how

Derailed Aerobic Respiration



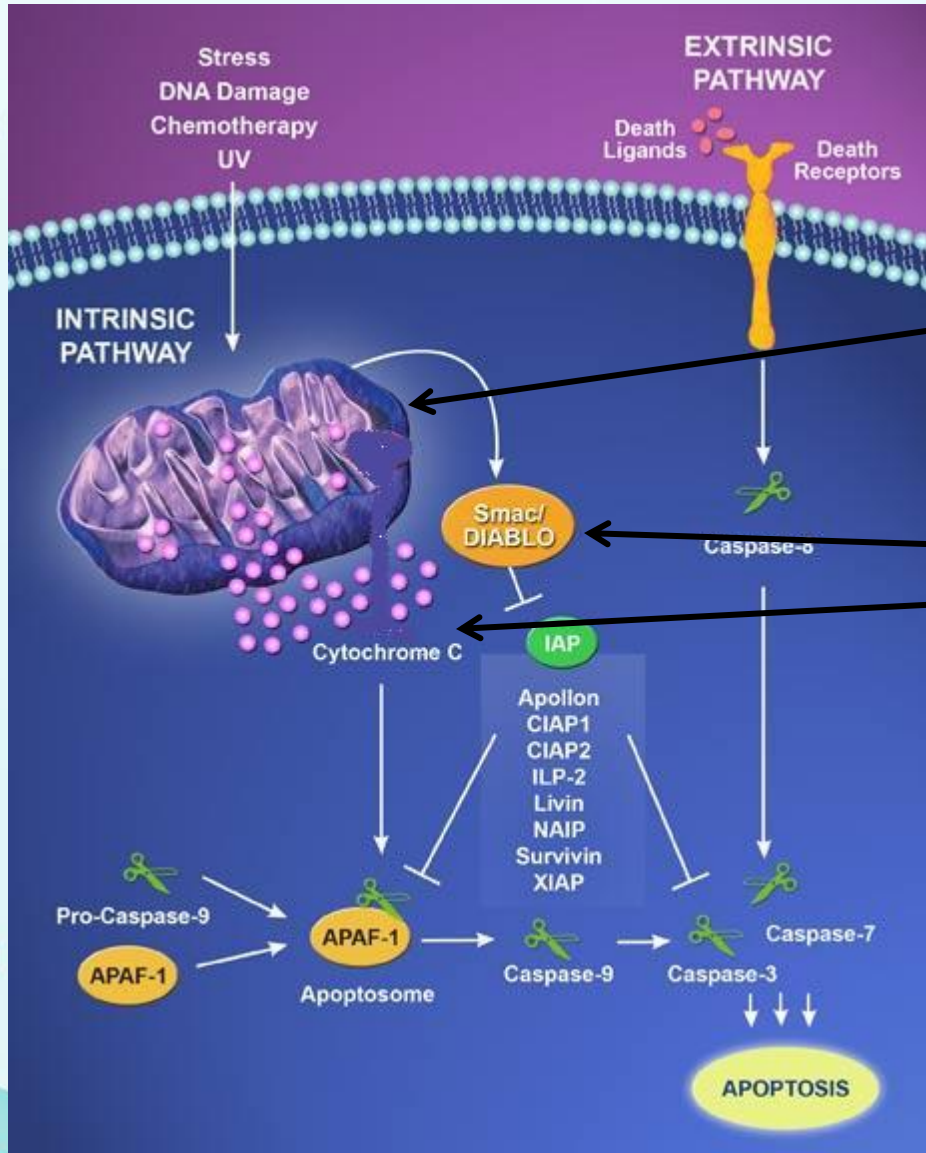
- 'Myc' is an oncoprotein (cancer promoting protein)
- It stimulates the enzyme PDK.
- PDK, in turn, antagonizes (inhibits, slows down) PDH
- With PDH inhibited, the reaction of Pyruvate to Acetyl-CoA cannot proceed
- Aerobic metabolism is derailed

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

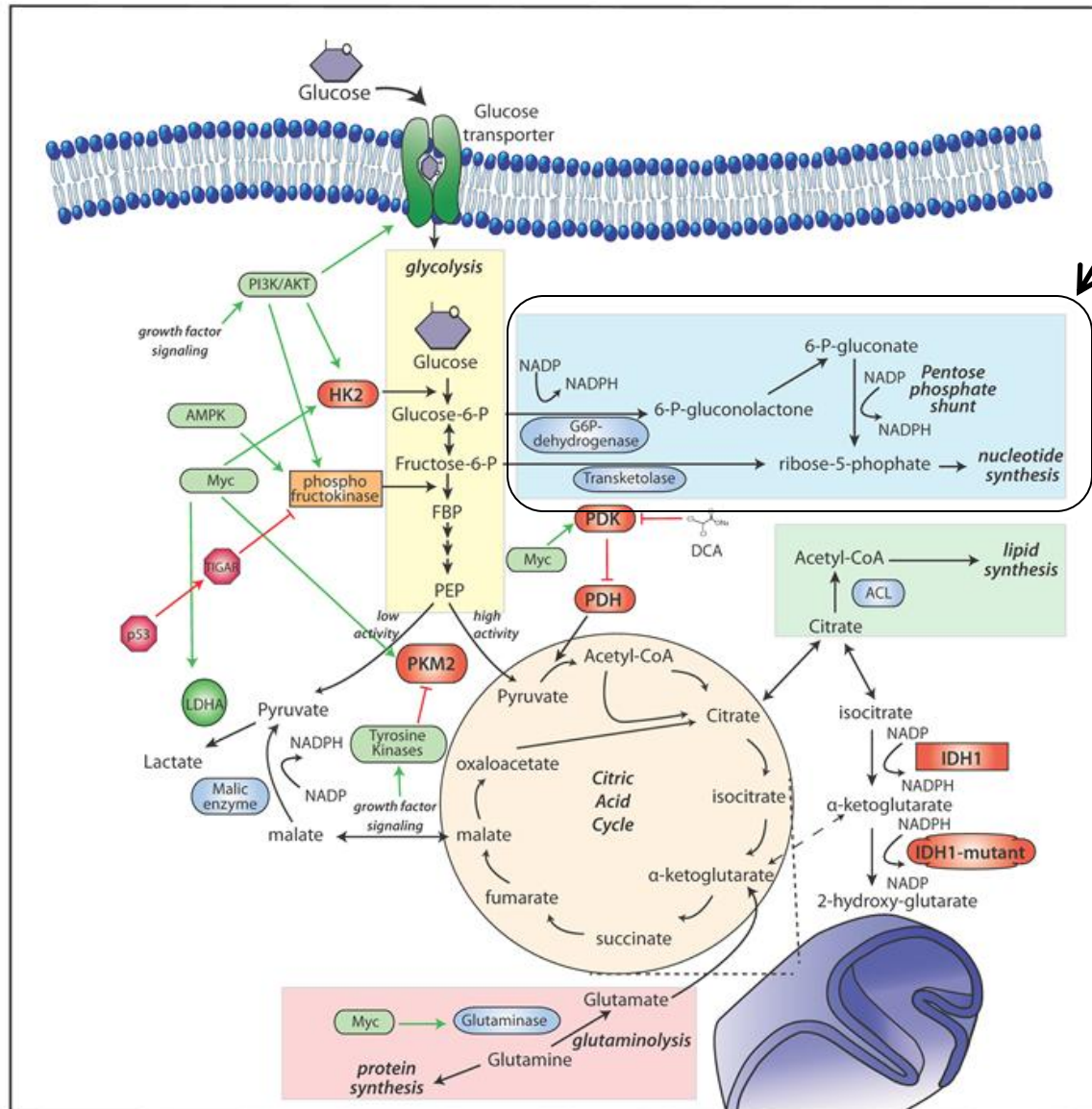
So why isn't DCA the end of the story?

- **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?

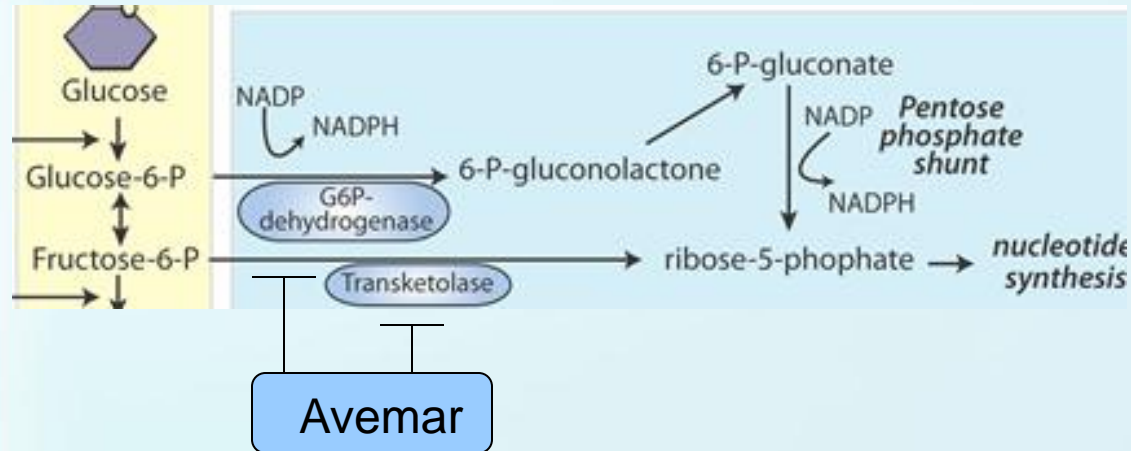
- **Tumors are constantly multiplying requiring the construction of DNA.**
- **DNA is made largely of sugar.**
- **Since anaerobic respiration is considerably less efficient, the cancer cell must compensate by overdriving glycolysis and a glycolysis alternative called the 'Pentose Phosphate Shunt'**
- **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

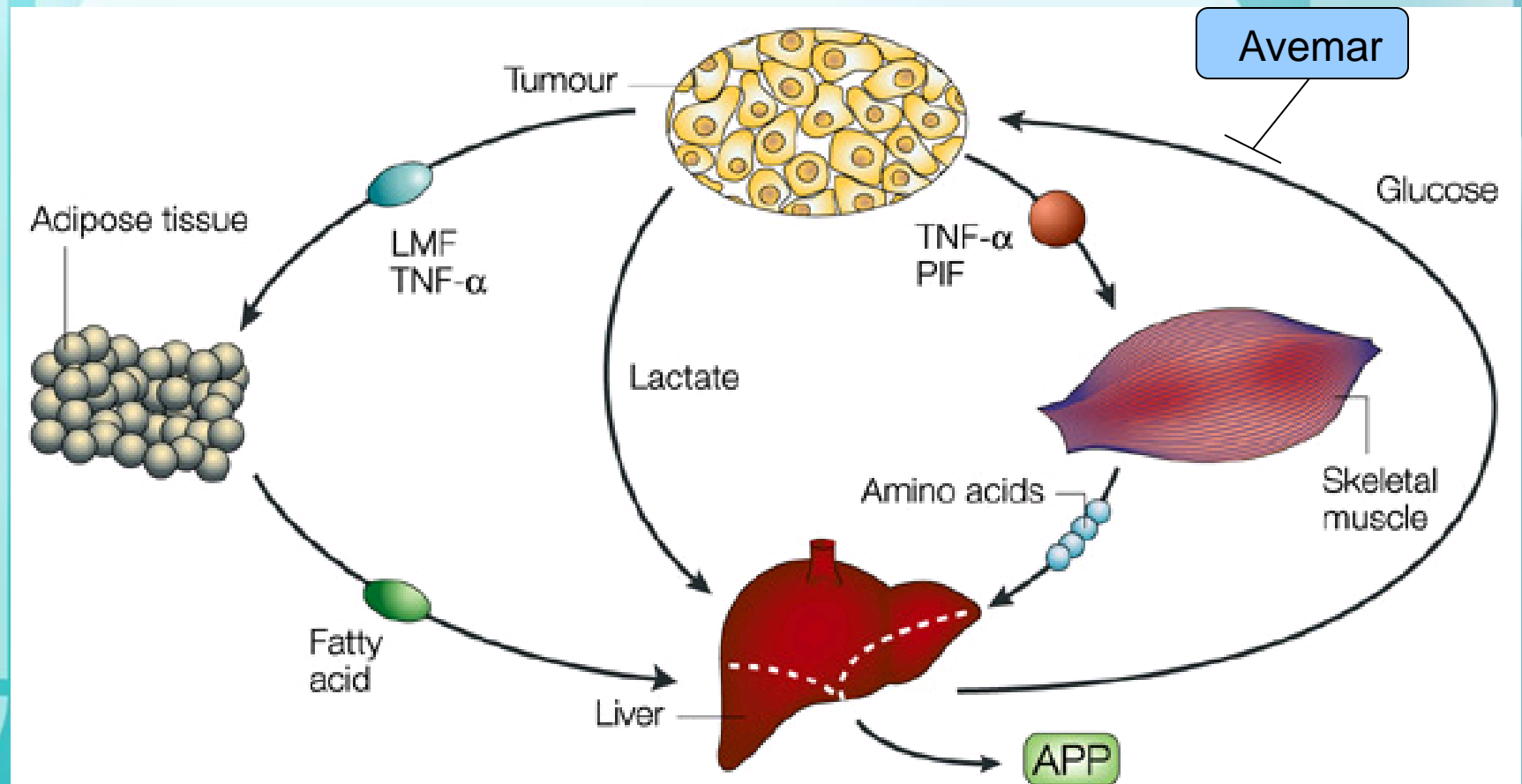


- Avemar selectively inhibits G6P-Dehydrogenase and Transketolase which are key to the pathway
- ‘Selective’ means that it would take 50x the prescribed dose to inhibit the pathway in normal cells
- With the pathway now restored to normal balance (no longer in overdrive) sugars can reach the Citric Acid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

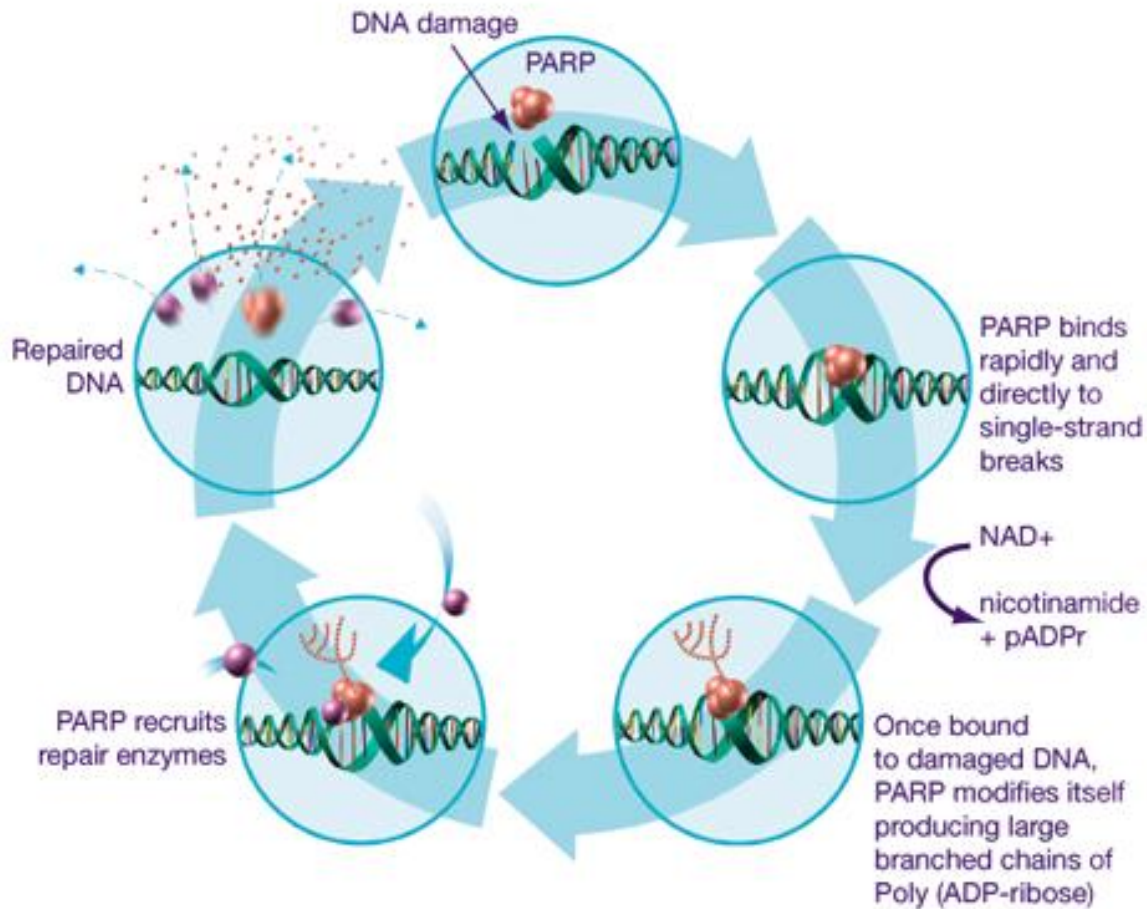
Cachexia



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**

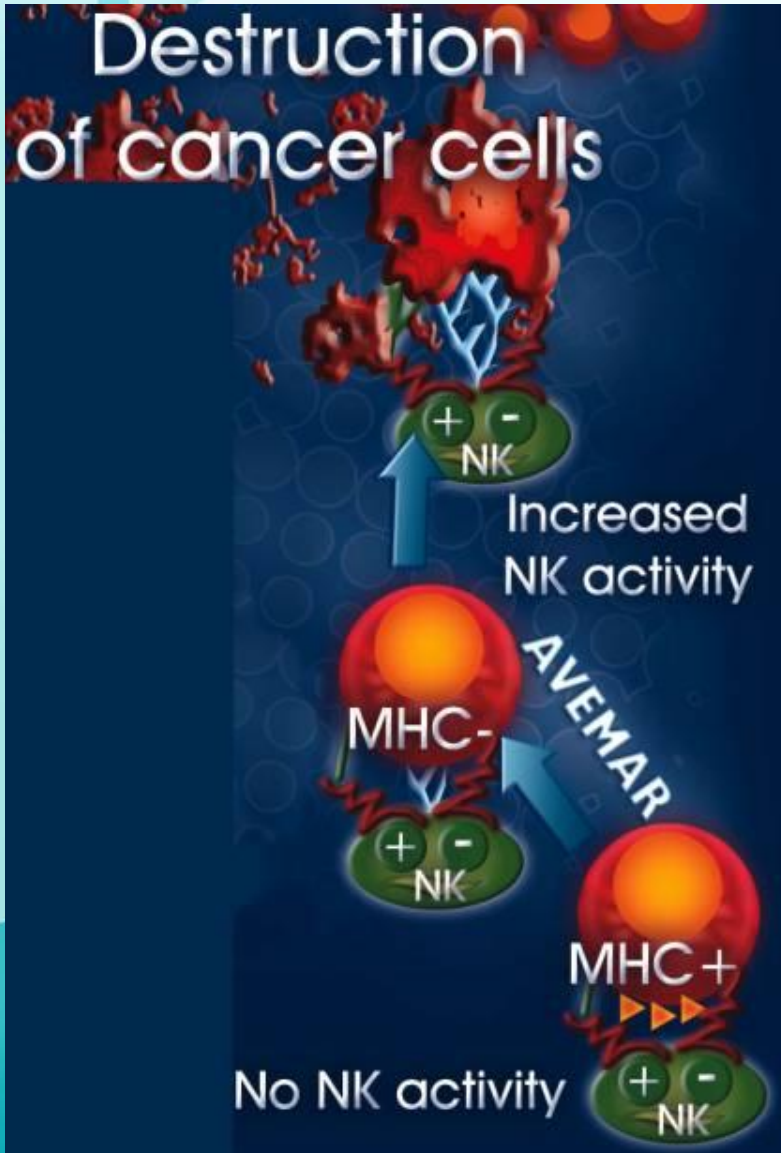
PARP Mechanism of Action



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

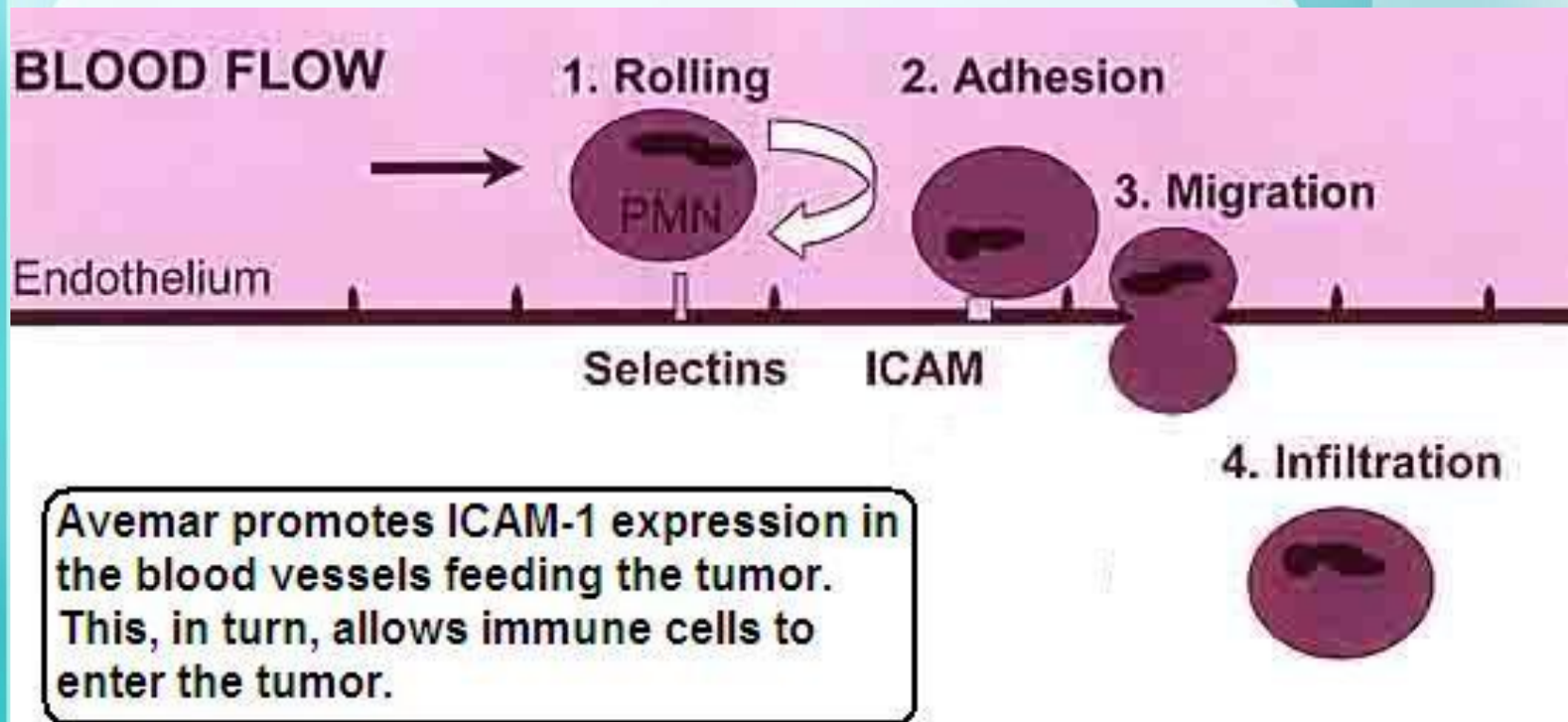


- With the downregulation (prevention) of MHC-1 expression (display on the cell surface) the NK (Natural Killer) cells can target the cancer cells
- This unmasks the cancer cells to the immune system
- This prevents metastasis**

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 and ICAM



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:**
- **<http://www.mskcc.org/mskcc/html/69418.cfm>**

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:
- http://en.wikipedia.org/wiki/Dichloroacetic_acid#Side_effects

Where to get Avemar?

- <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/>**

DO NOT SELF MEDICATE: Consult your physician

Further Reading

- <http://www.dca.med.ualberta.ca/Home/index.cfm>
- <http://medicorcancer.com/dca-therapy.html>
- <http://www.avemar.com/>
- <http://www.martincwiner.com/dca>

Scholarly Papers: Avemar

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Scholarly Papers: DCA

- <http://www.sciencedirect.com/science/article/pii/S1535610806003722#sec1>
- [http://www.thedcasite.com/Library/Dichloroacetate induces apoptosis in endometrial cancer cells.pdf](http://www.thedcasite.com/Library/Dichloroacetate%20induces%20apoptosis%20in%20endometrial%20cancer%20cells.pdf)
- <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>
- <http://dca-information.pbworks.com/f/Metabolic%20Modulation%20of%20Glioblastoma%20with%20Dichloroacetate.pdf>

www.martincwiner.com/dca