***Please read and be prepared to discuss the following on Wednesday:***

**https://en.wikipedia.org/wiki/Warburg\_hypothesis**

**https://en.wikipedia.org/wiki/Chemotherapy**

New York Times Article MAY 12, 2016:

**http://www.nytimes.com/2016/05/15/magazine/warburg-effect-an-old-idea-revived-starve-cancer-to-death.html**

Quote from this New York Times article:

'Even James Watson, one of the fathers of molecular biology, is convinced that targeting metabolism is a more promising avenue in current cancer research than gene-centered approaches. At his office at the Cold Spring Harbor Laboratory in Long Island, Watson, 88, sat beneath one of the original sketches of the DNA molecule and told me that locating the genes that cause cancer has been “remarkably unhelpful” — the belief that sequencing your DNA is going to extend your life “a cruel illusion.” If he were going into cancer research today, Watson said, he would study biochemistry rather than molecular biology.'

**Cancer chemotherapy focuses on damaging DNA synthesis and mitotic spindles**

* Cyclophosphamide         cross-links DNA strands.
* Daunorubicin         intercalates between DNA base pairs
* *DNA base analogs          get covalently incorporated into DNA*
* Vincristine         Binds to tubulin; prevents microtubule formation
* *Taxol         Binds to tubulin; stimulates abnormal microtubule polymerization*
* Rituximab         A monoclonal antibody against all B-lymphocytes
* *Gleevec         Inhibits an over-active tyrosine phosphokinase*
* QUOTE: "*A new study finds that a year's supply of Gleevec (imatinib), a leukemia drug, costs about* ***$159 to make [a year's supply, including a profit margin]*** *, but the yearly price tag is* ***$106,322 in the U.S. and $31,867 in the U.K.*** *A generic version costs about* ***$8,000 in Brazil****.* ...more than a million cancer patients around the world meet criteria for taking the five TKI pills. "Very few of them are being treated now," he says, because the drugs are so expensive. And the implications stretch way beyond these specific cancer drugs. Overall prices for cancer medications have been going up at a fast clip. Dr. Peter B. Bach of Memorial Sloan Kettering Cancer Center in New York has documented a nearly 100-fold increase in cancer drug prices since 1965 after adjusting for inflation." (QUOTED)  <http://commonhealth.wbur.org/2015/09/cancer-drug-cost> **(which is no longer posted)**

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1) What is the reason for anti-cancer selectivity of anti-DNA and anti-tubulin chemicals?

If cancer cells' have defective checkpoint controls? (Instead of excess growth rates, per se.) then normal cells would detect damaged DNA and abnormal mitotic spindles, and respond by delaying growth; But cancer cells would continue growth & division, thereby killing themselves.   Improved understanding of how treatments actually work will help improve effectiveness.

2) Invent a chemical that **becomes poisonous at acidic pH**. (using the Warburg Effect)

3) Invent a tyrosine analog that gets **converted into a poison when phosphorylated**.

4) How to kill cells with an under-active Ras enzyme? (One fifth of human cancer deaths?)