

Mitokondriaalne metabolism ja vähk

Eesti Keemiaselts 100

Tuuli Käämbre

KBFI



Nobel Prize in Physiology or Medicine (1931)

O T T O W A R B U R G

The oxygen-transferring ferment of respiration
Nobel Lecture, December 10, 1931

Otto Heinrich Warburg

1883-1970

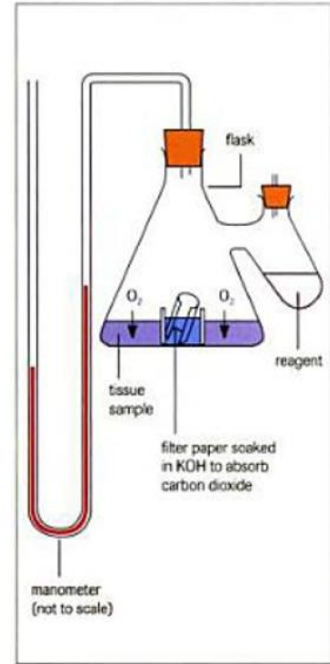
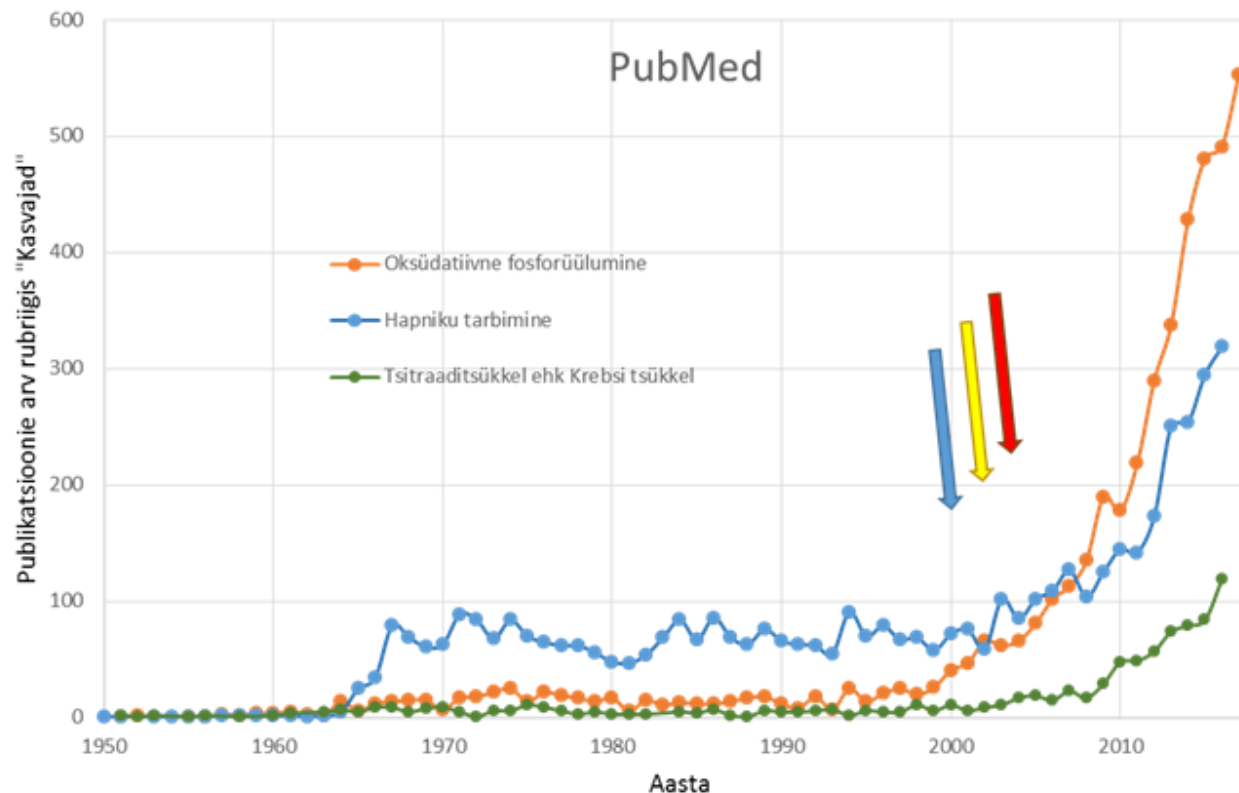
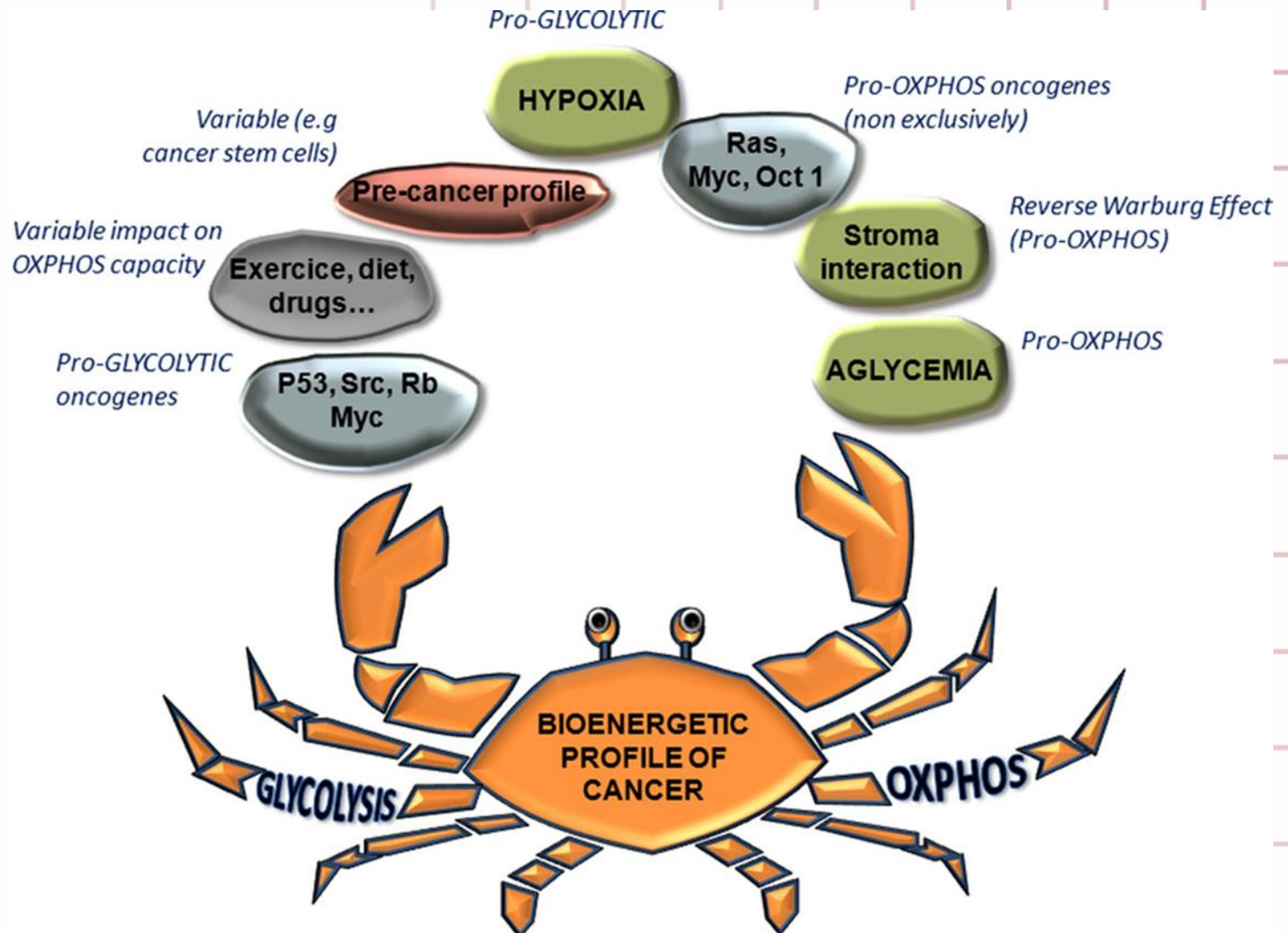


Illustration 1 Warburg flask used for measuring oxygen uptake by small samples of tissue.

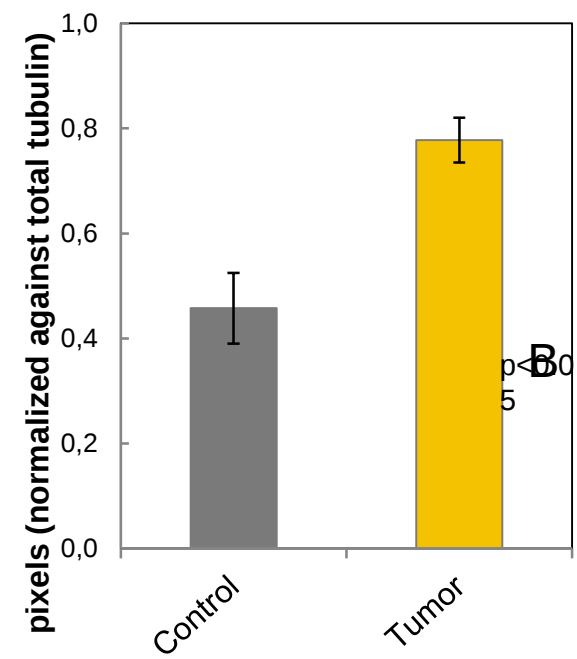
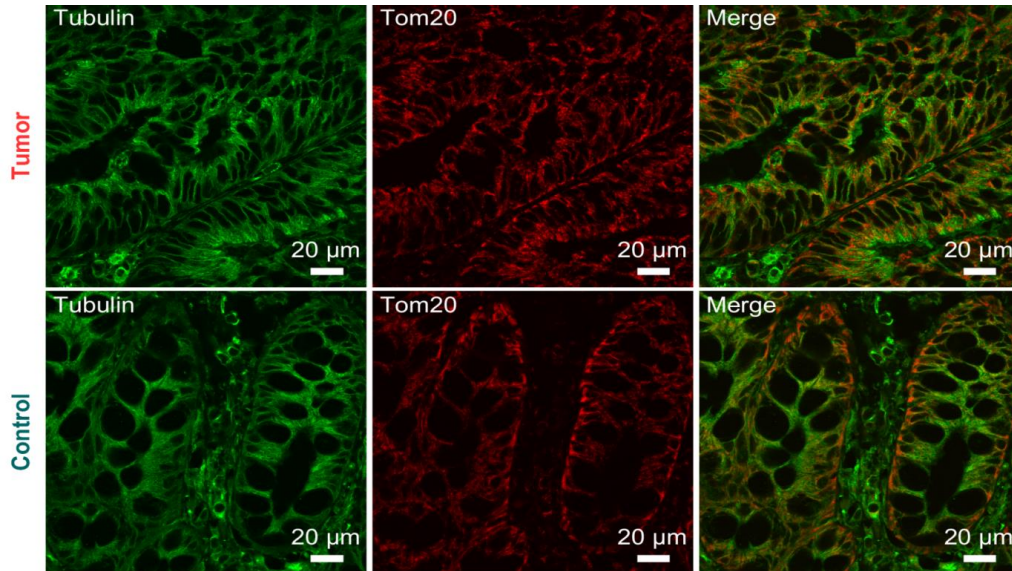
***"Cancer, above all other diseases, has countless secondary causes. But, even for cancer, there is only one prime cause. Summarized in a few words, the prime cause of cancer is the replacement of the respiration of oxygen in normal body cells by a fermentation of sugar."* -- Dr. Otto H. Warburg**

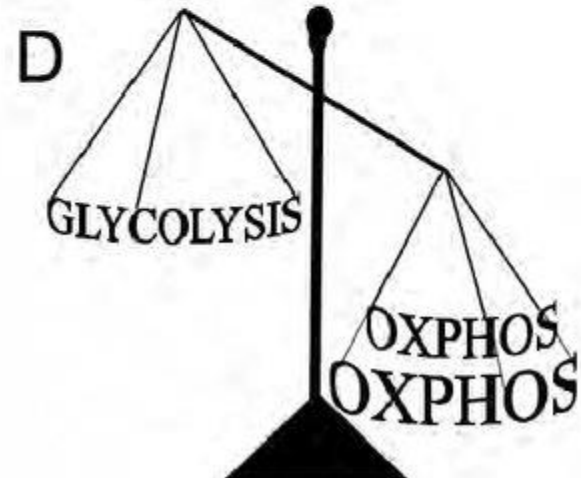
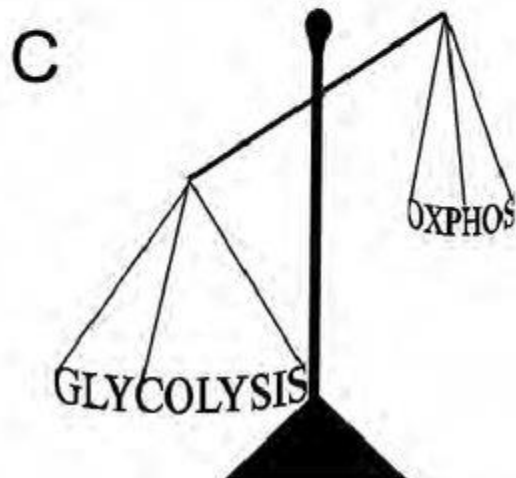
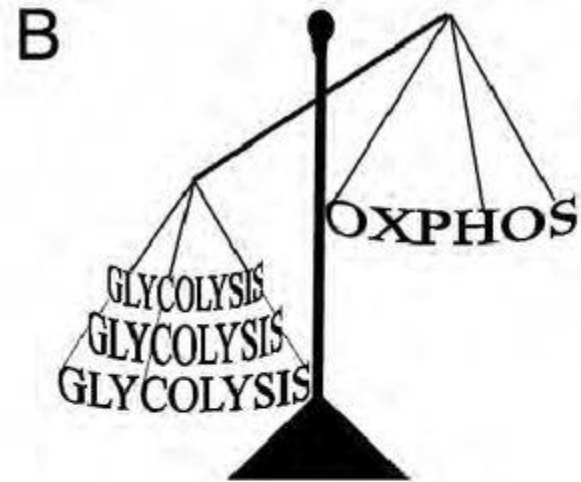
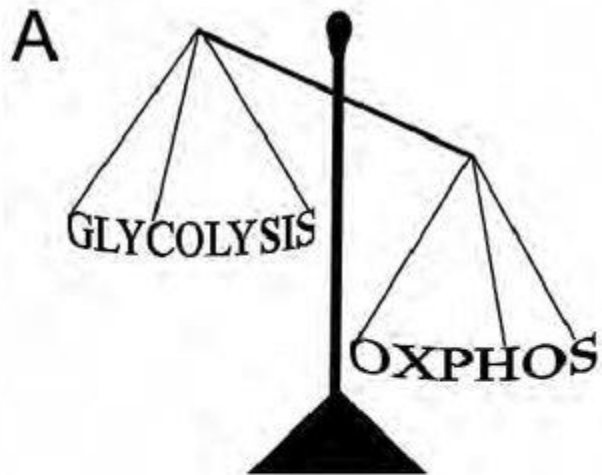


Punane nool osutab Zu ja Guppy artikli ilmumise aega, kus näidati esmakordselt, et oksüdatiivne fosforüülumine domineerib ATP tootmise protsessides väga paljude kasvaja paikmete puhul. Kollane ja sinine nool näitavad esimesi töid, mis puudutasid oksüdatiivse fosforüleerimise funktsionaalsust st. oligomütsiinitundlikku hapnikutarbimise olemasolu ja kõrget mitokondri membraanpotentsiaali kasvajakududes.

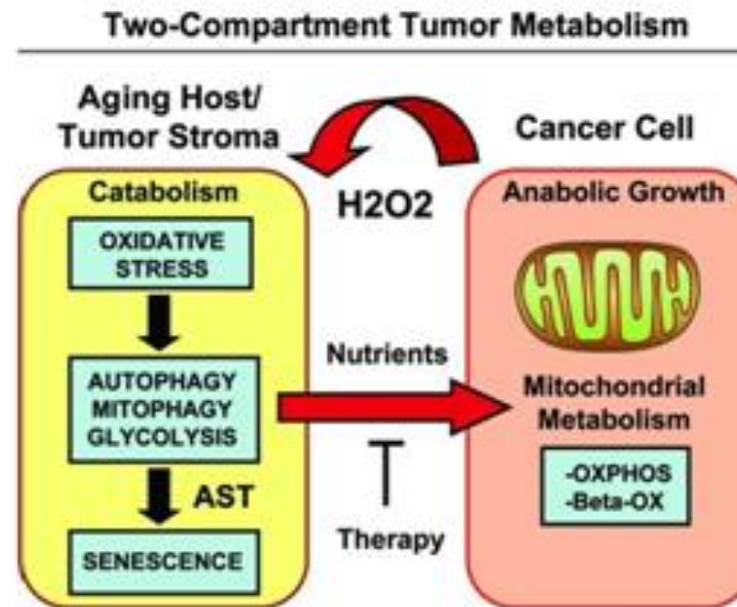


Tumor and mitochondria

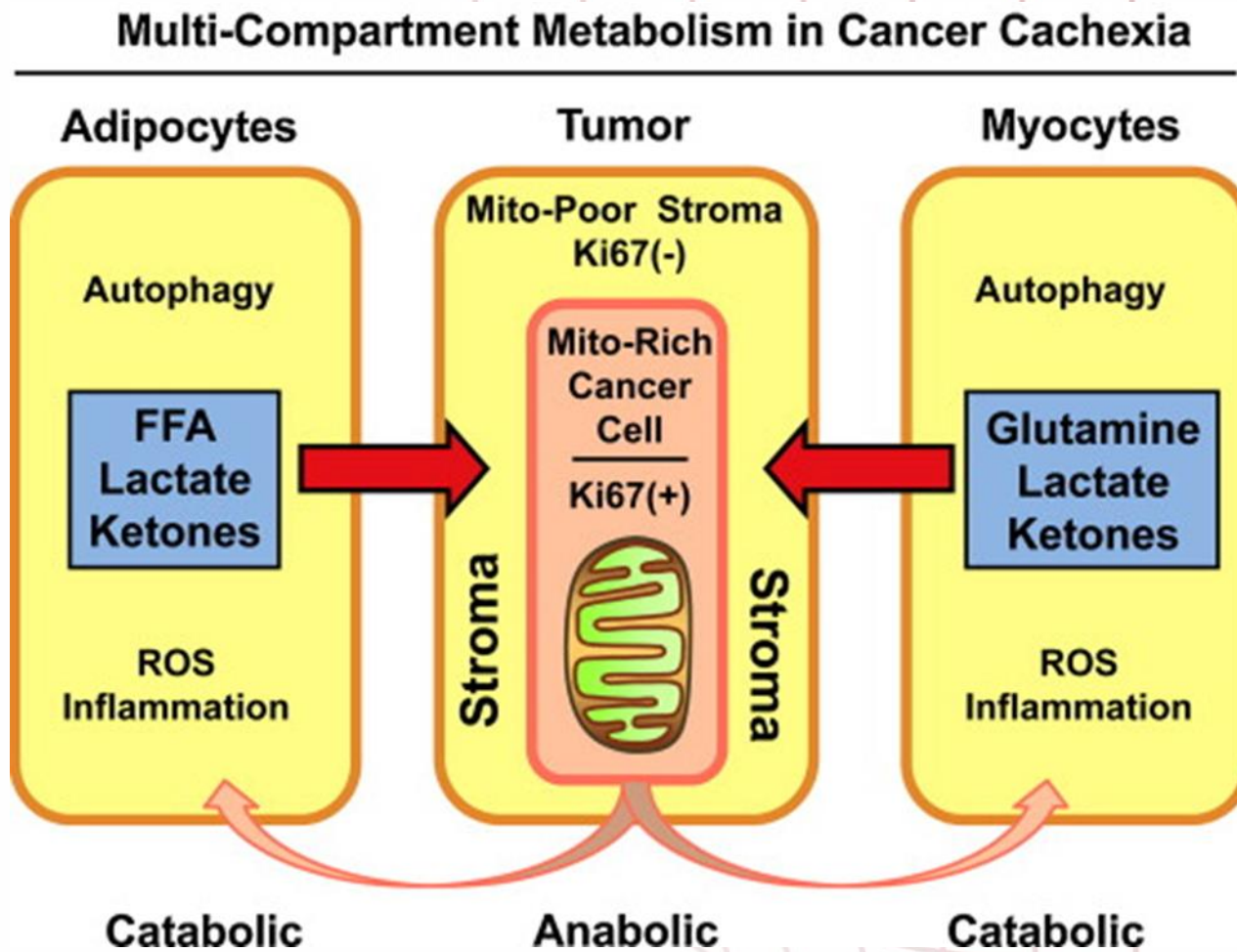




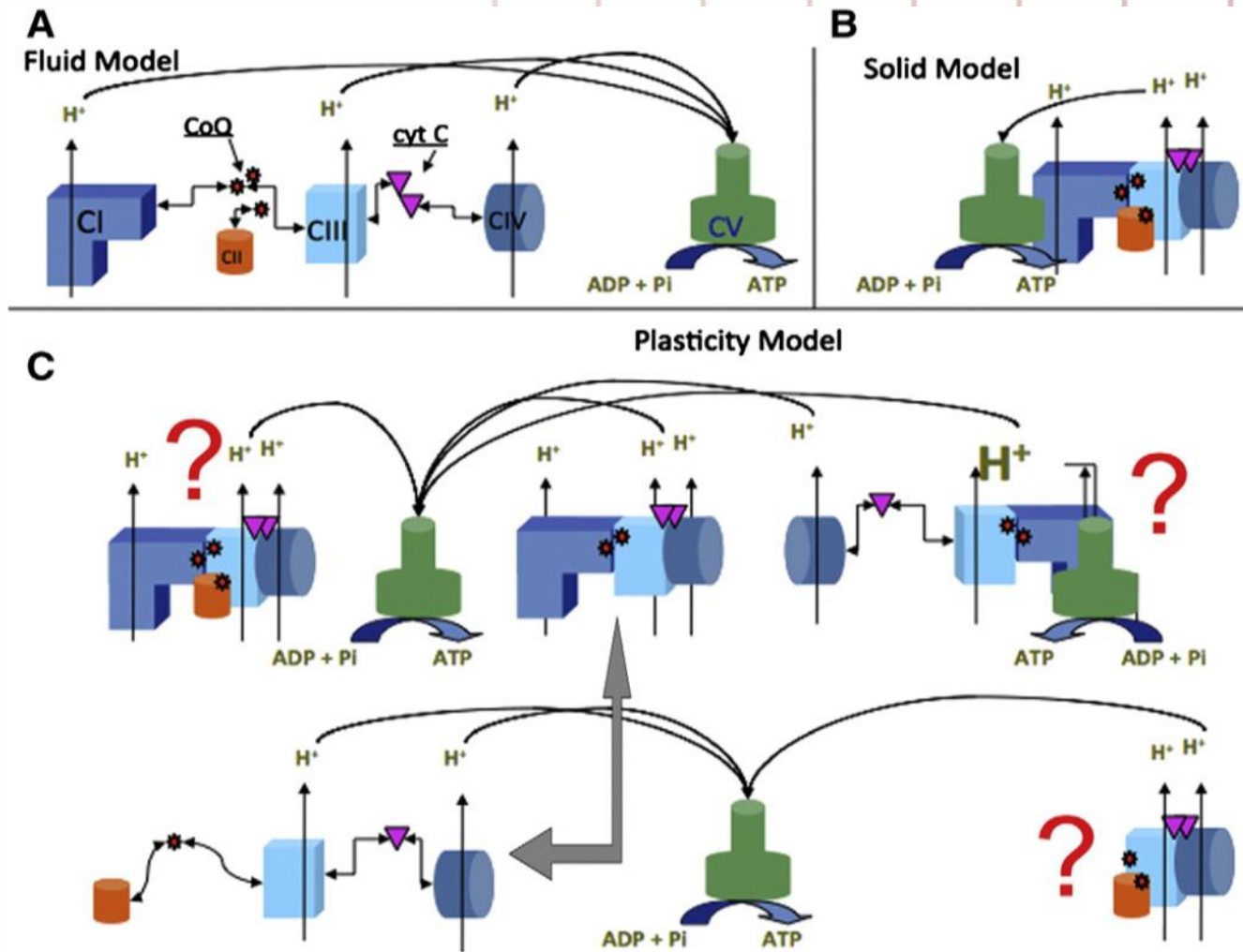
Kahekompartmendiline mudel

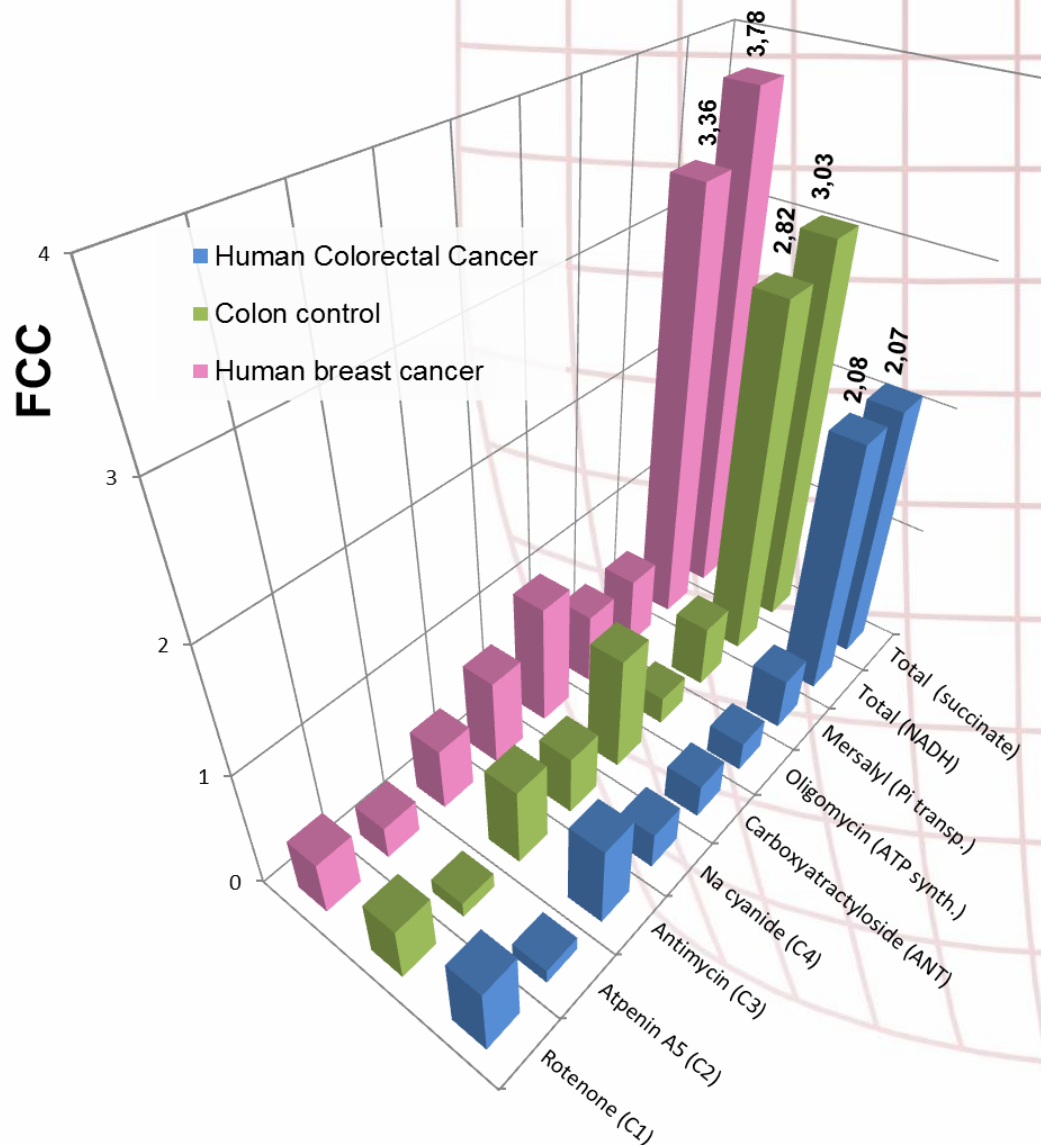


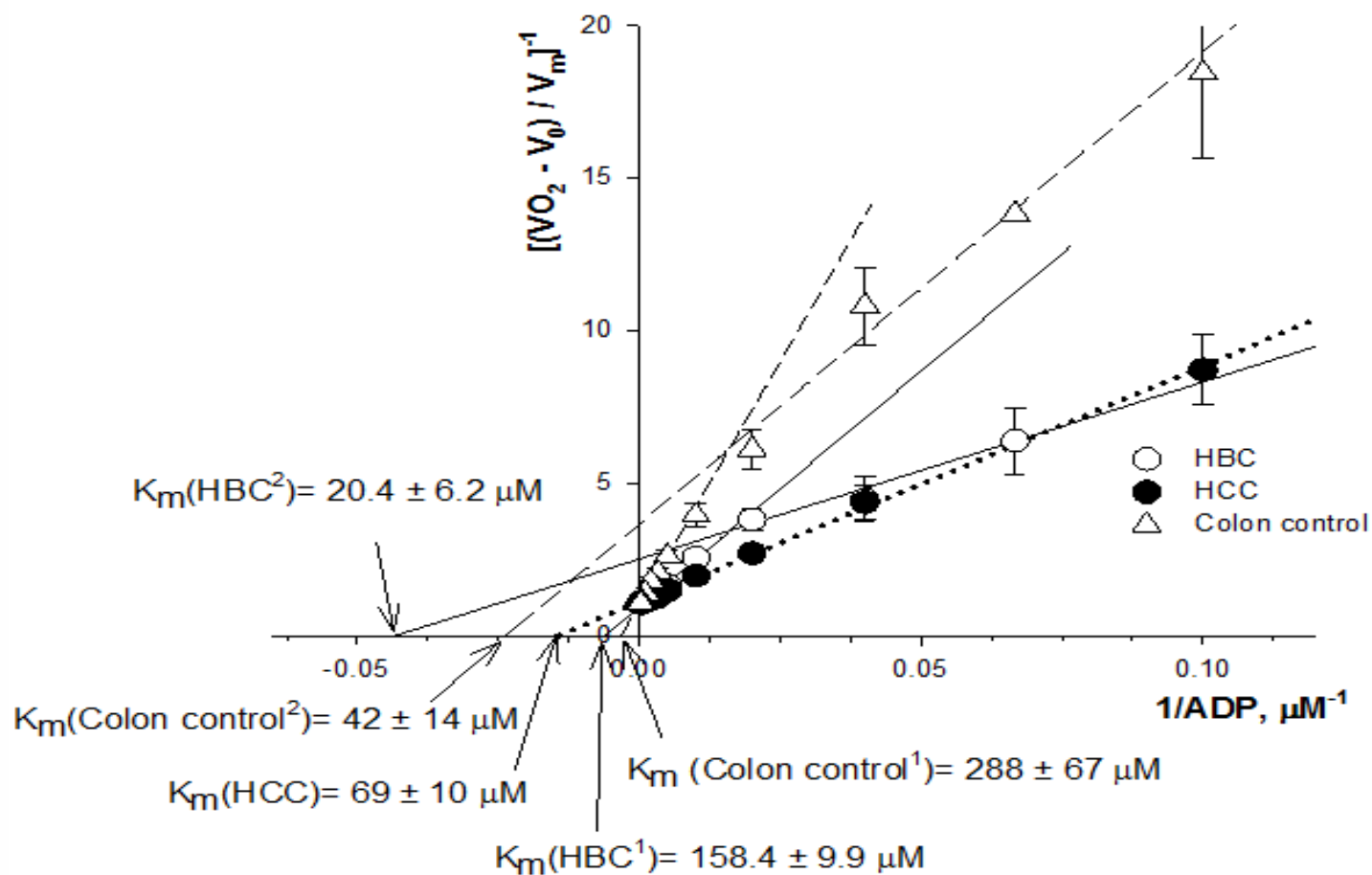
Martinez-Outschoorn, U.E., et al., Hereditary ovarian cancer and two-compartment tumor metabolism: epithelial loss of BRCA1 induces hydrogen peroxide production, driving oxidative stress and NFκB activation in the tumor stroma. *Cell Cycle*, 2012. 11(22): p. 4152-66.



Martinez-Outschoorn, U., F. Sotgia, and M.P. Lisanti, Tumor microenvironment and metabolic synergy in breast cancers: critical importance of mitochondrial fuels and function. *Semin Oncol*, 2014. 41(2): p. 195-216.

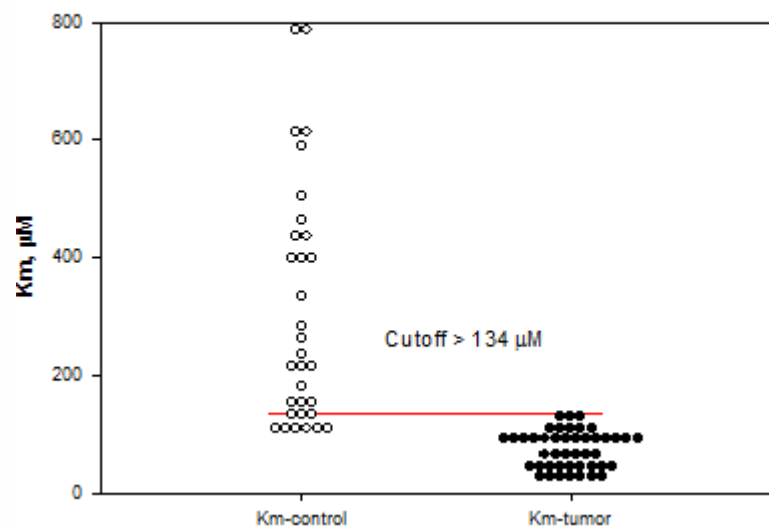






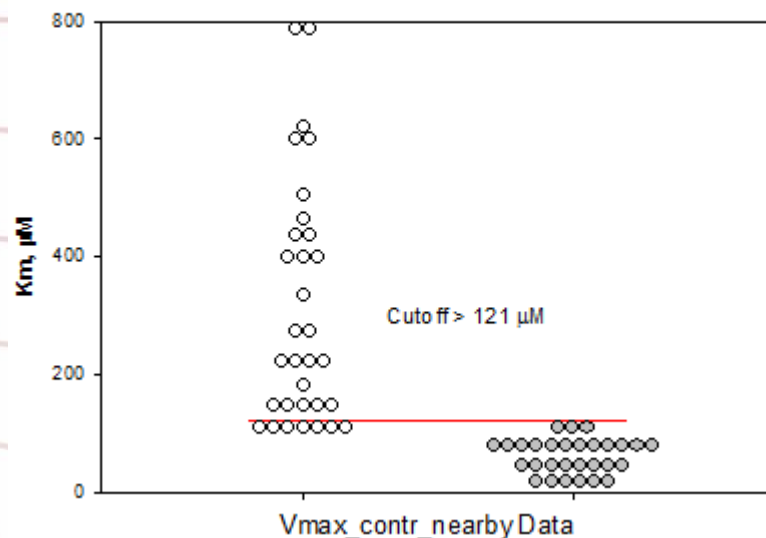
Km_contr_tumor Data

Dot Histogram



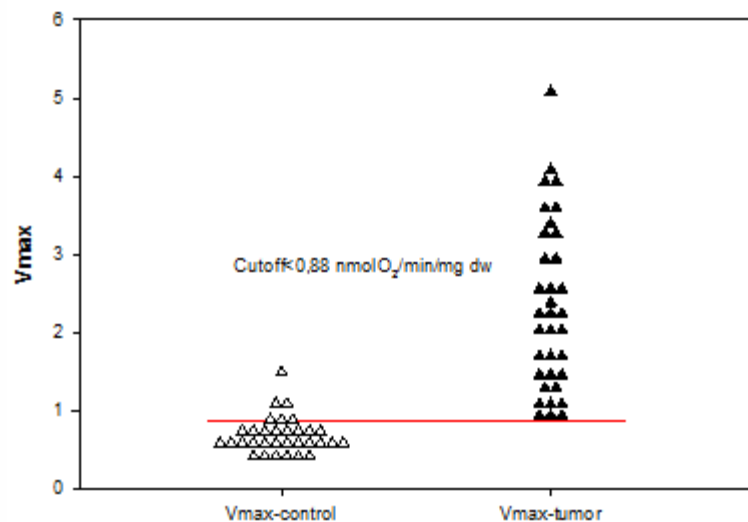
Km_control_Nearby Data

Dot Histogram - 2

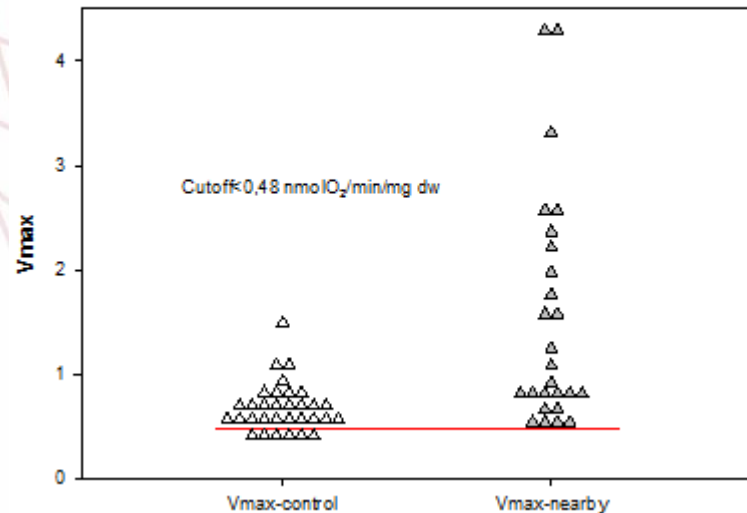


Vmax_contr_tumor Data

Dot Histogram - 5



Dot Histogram - 6



Inimese rinnavähk

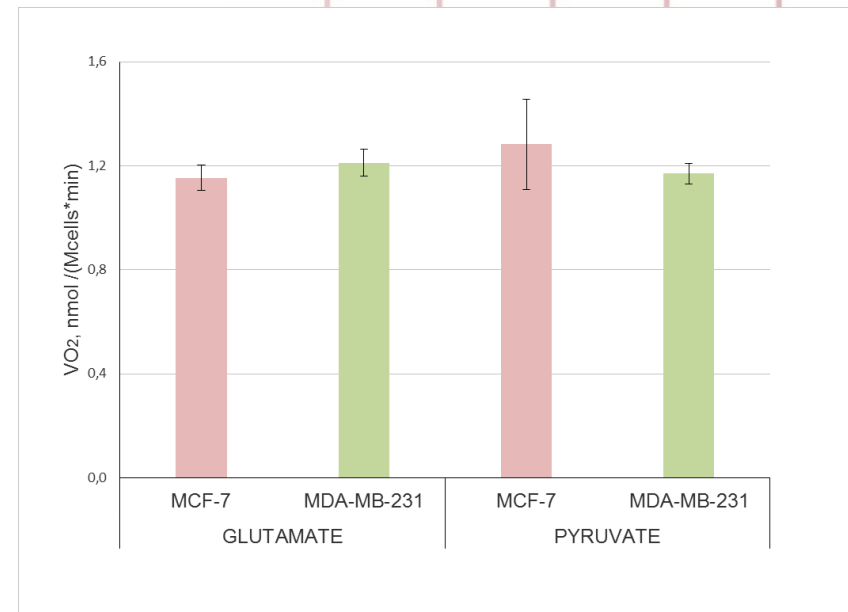
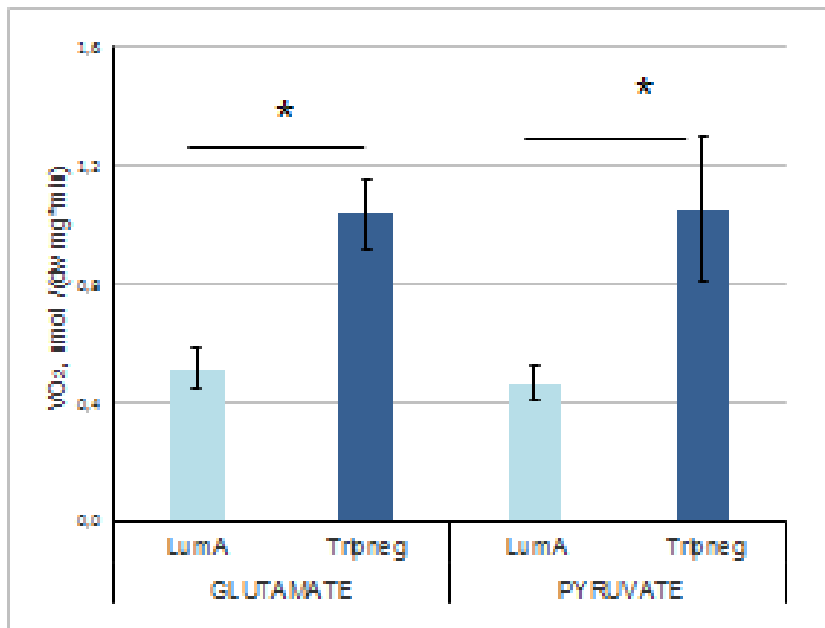
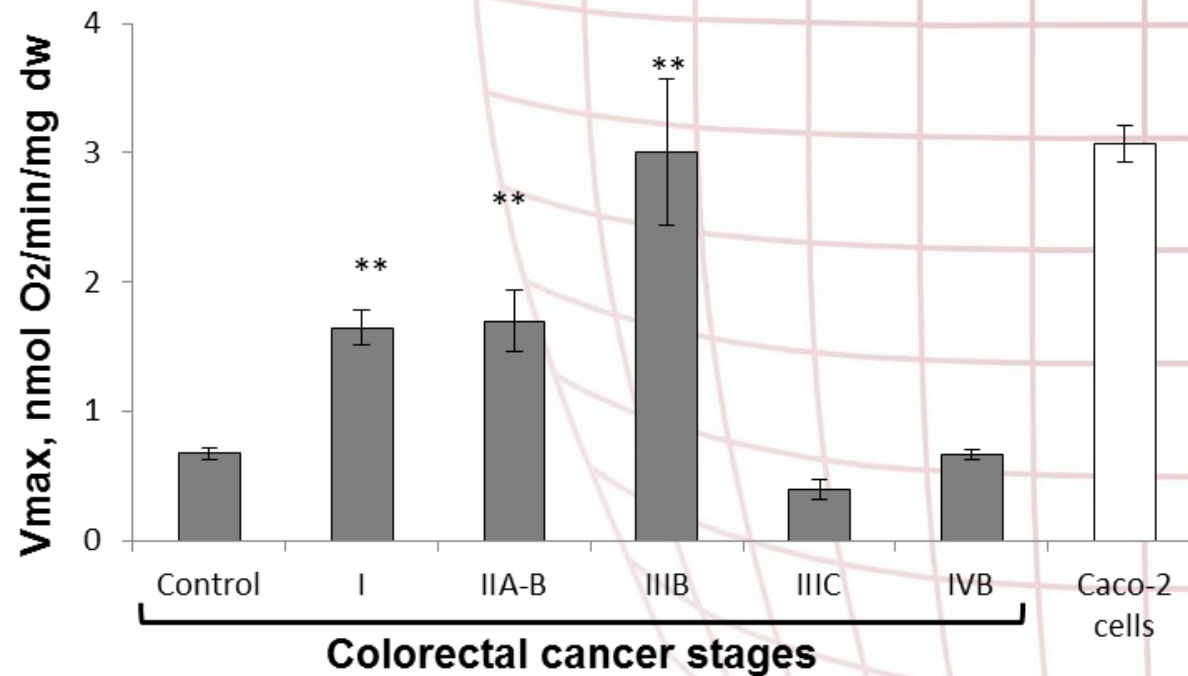


Fig. 5A

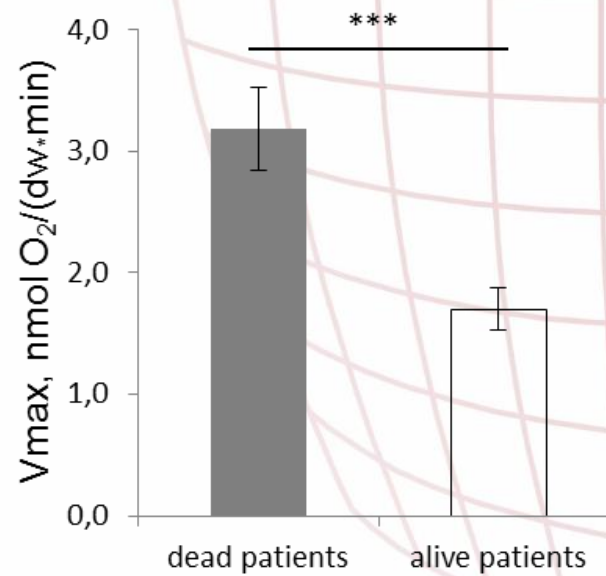
Kliiniline materjal

Rakukultuurid

Inimese soolevähk

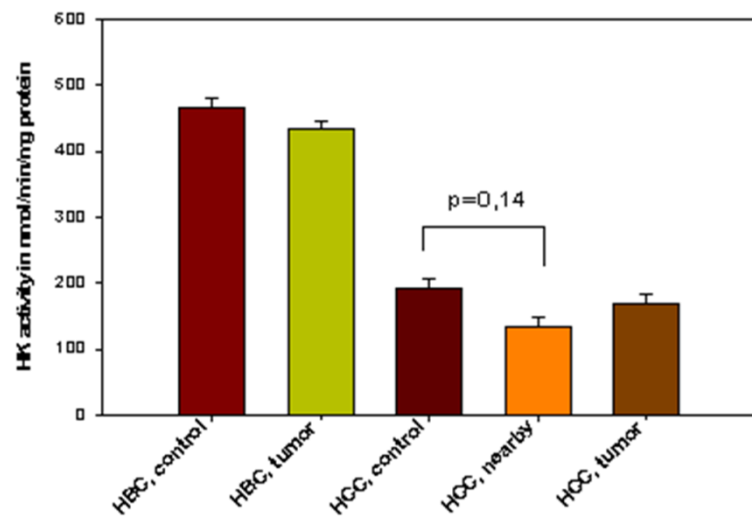


Haiguse pahaloomulus sõltub ATP sünteesi kiirusest?

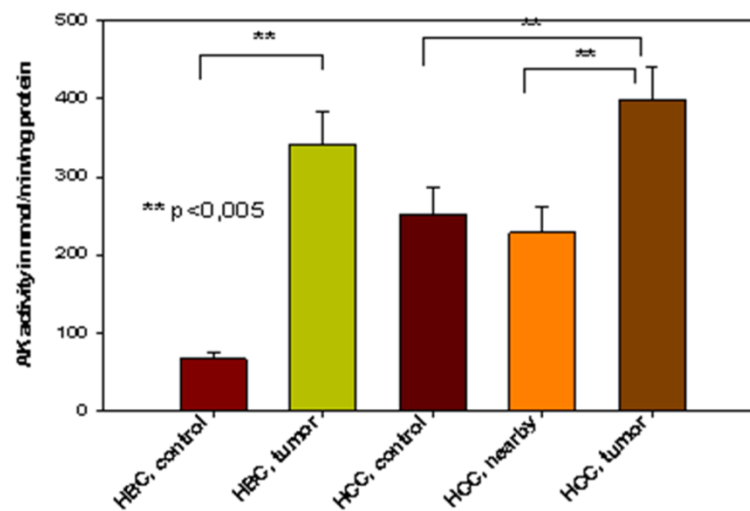




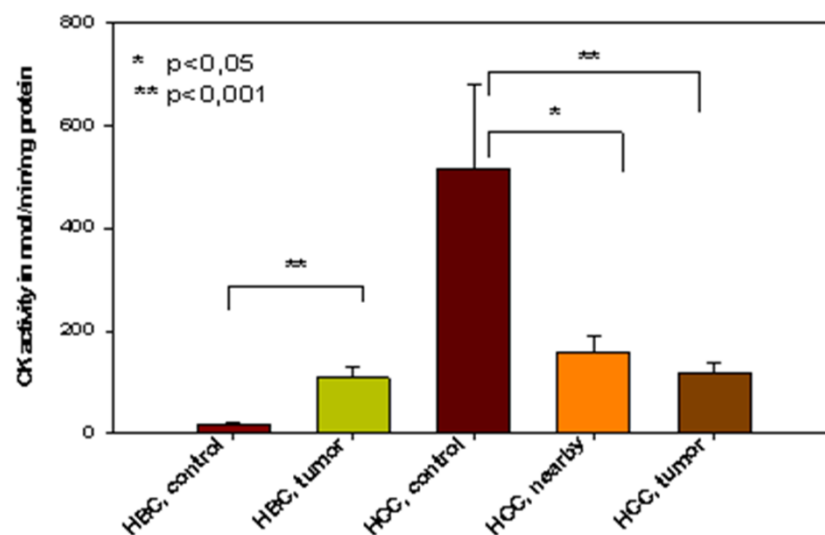
Hexokinase



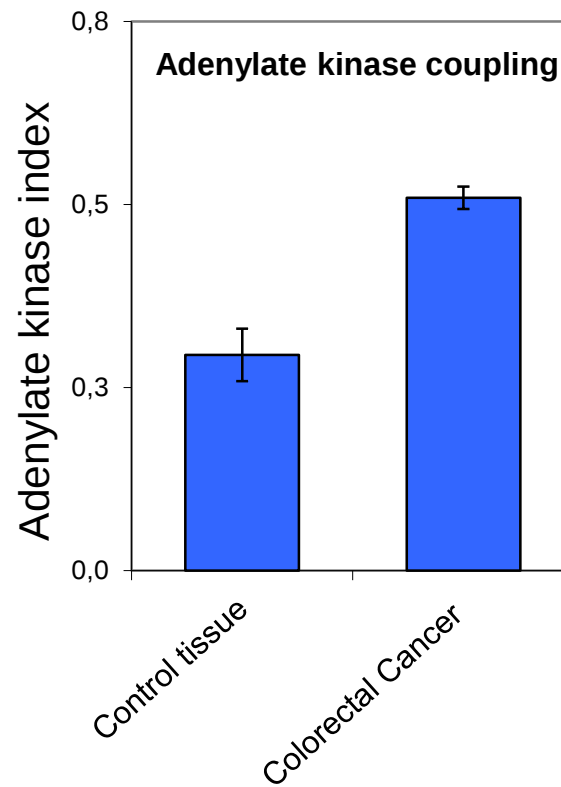
Adenylate kinase



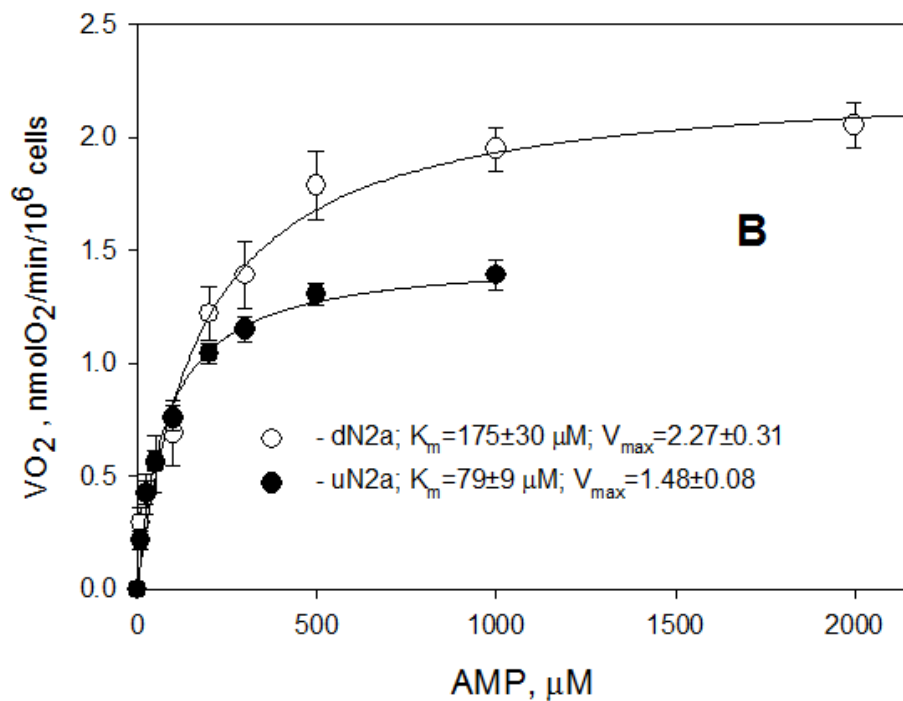
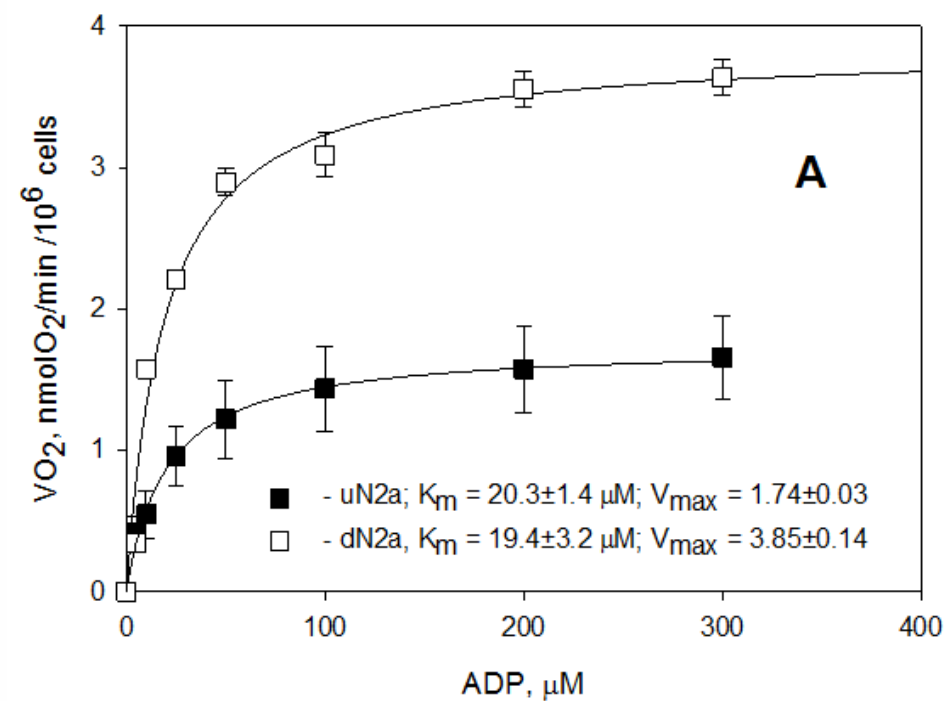
Creatine kinase



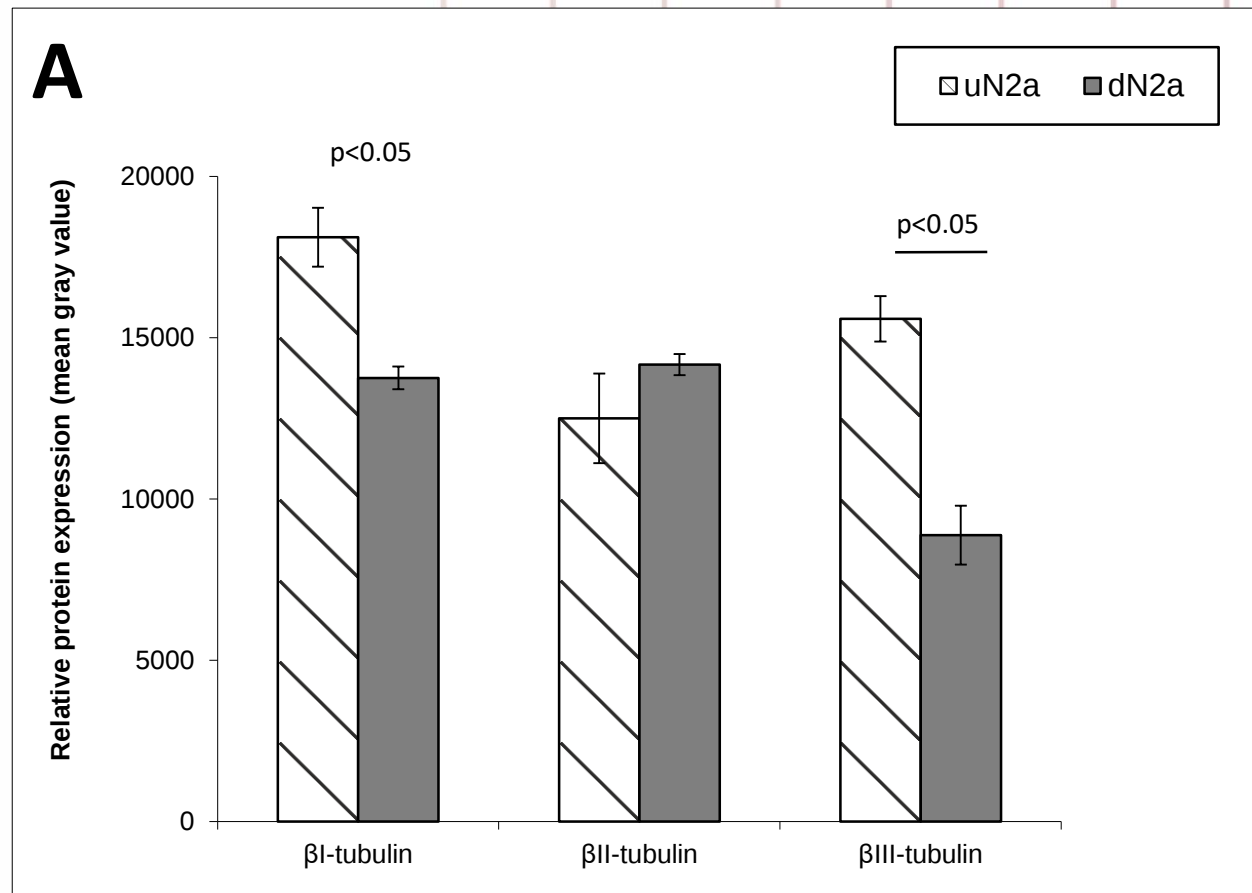
Adenülaatkinaasi süsteem

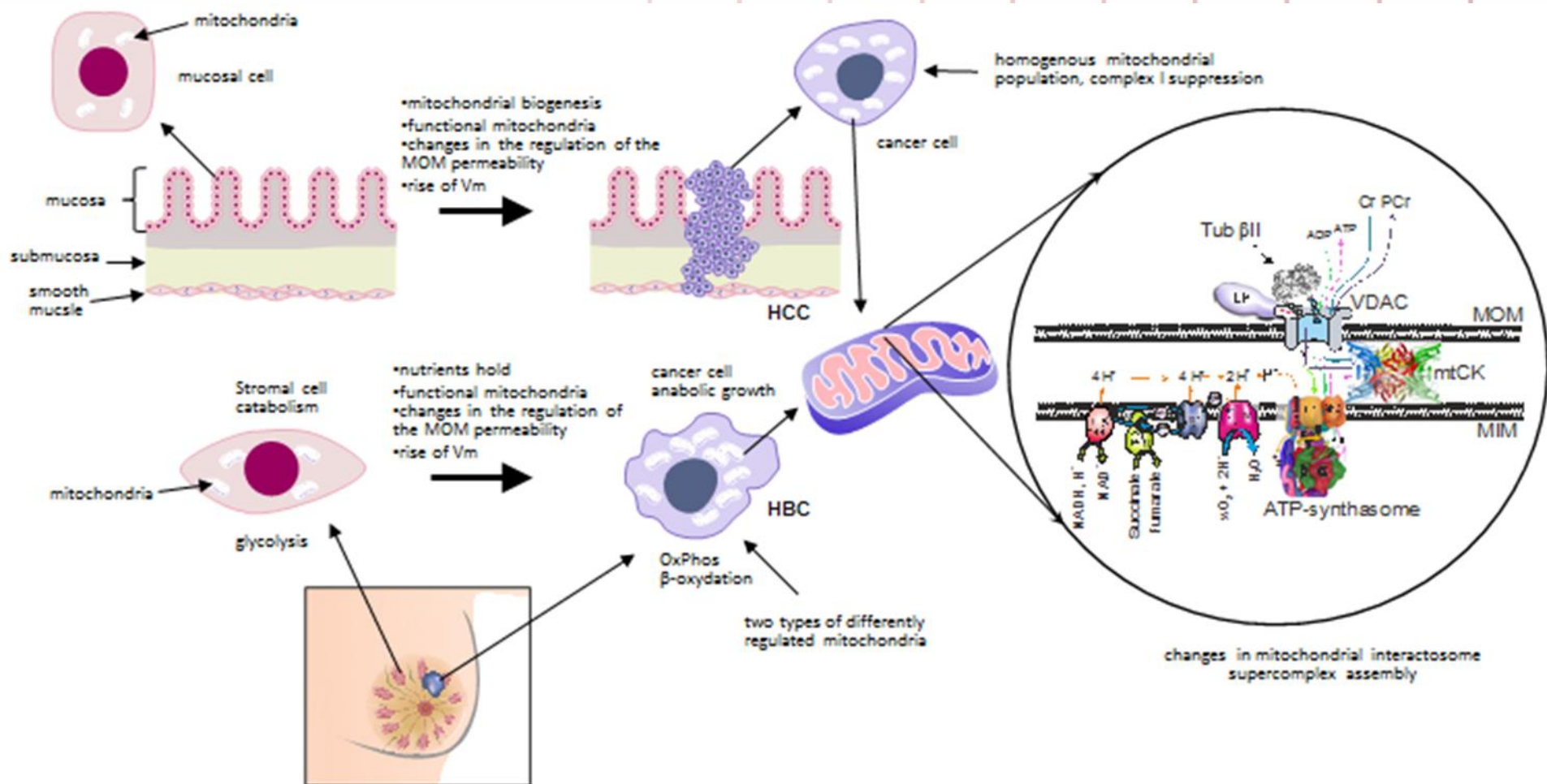


$$I_{AKtotal} = (V_{AMP} - V_{AP5A}) / V_{AP5A}$$

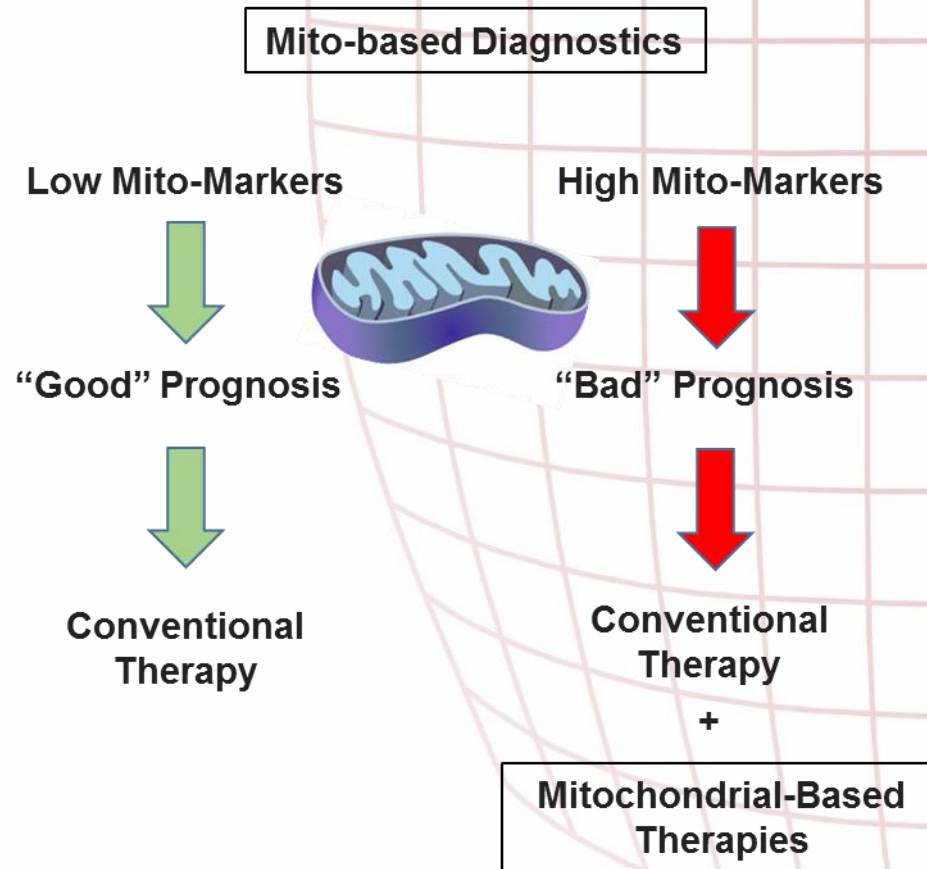


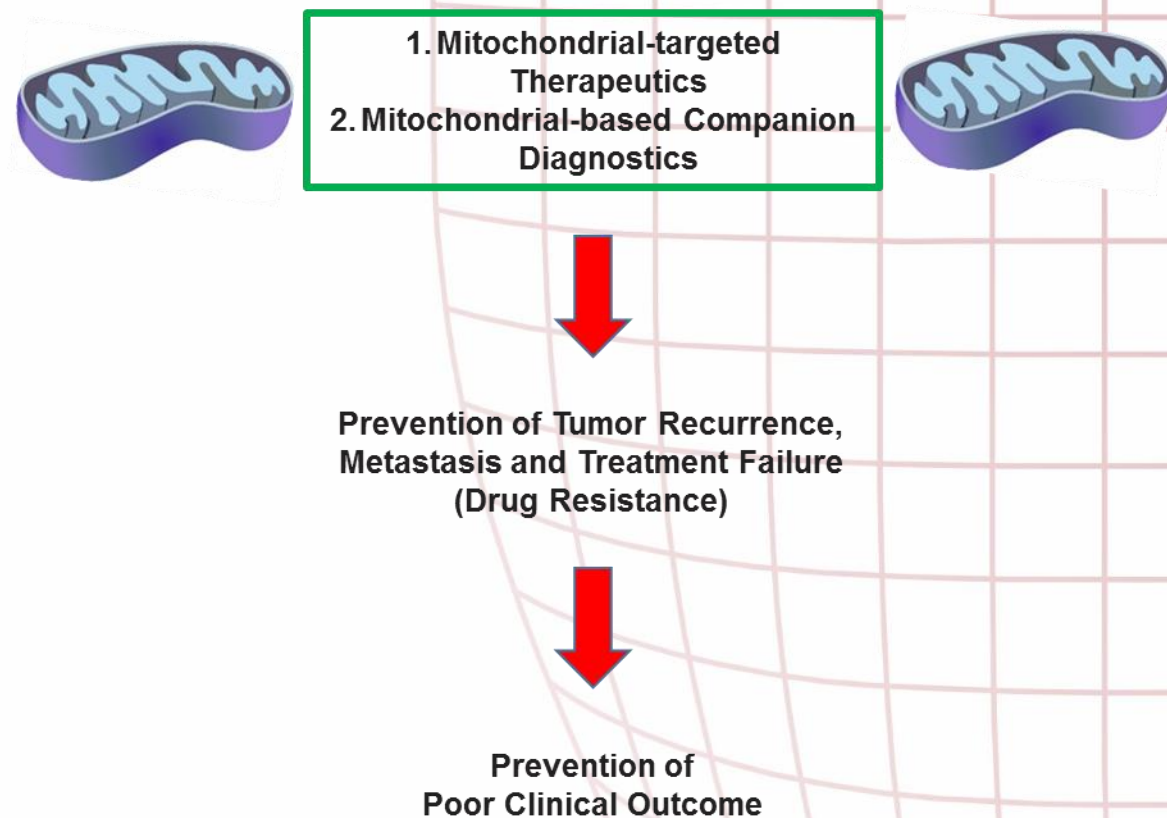
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Personalized Cancer Diagnosis and Treatment





Tänan kuulamast!

