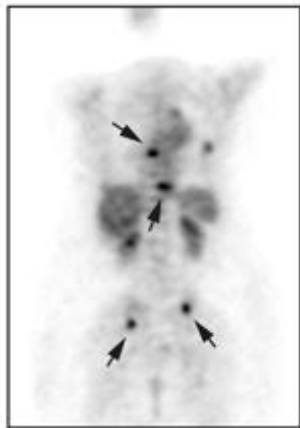
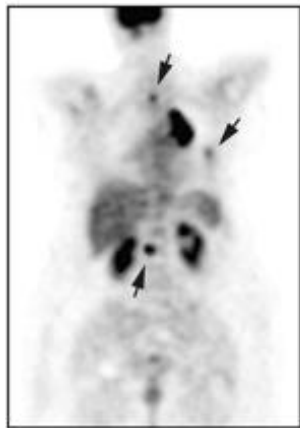
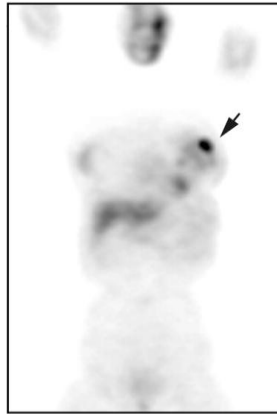
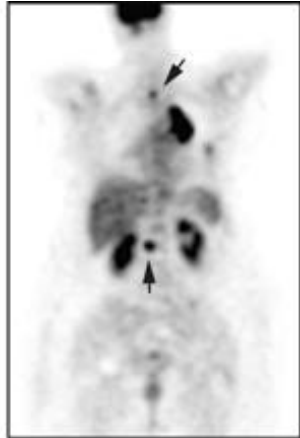


# PET imaging of $^{18}\text{F}$ -deoxyglucose (FDG)



Recurrent Melanoma

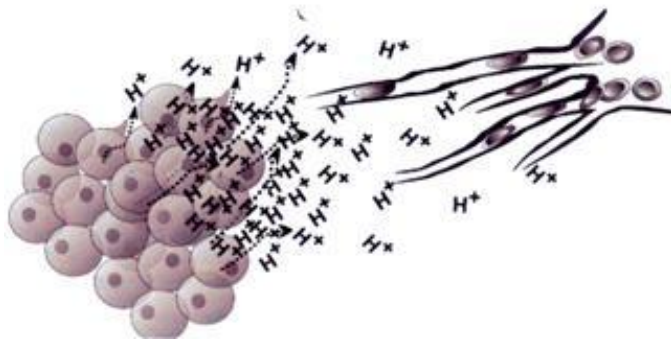
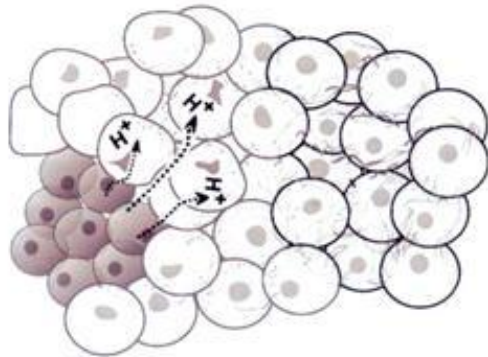
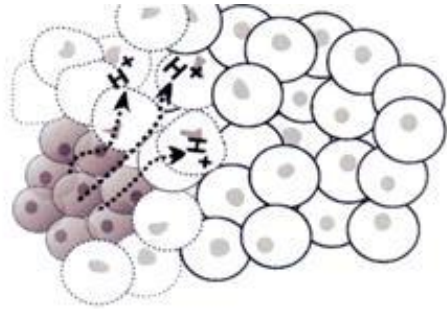
Breast w/ equivocal MRI

Cancers with elevated Fd Glucose uptake:

- Colorectal
- Brain
- Breast
- Melanoma
- Cervical
- Ovarian
- Lung
- Pancreatic
- Esophageal
- Lymphoma
- Leiomyosarcoma
- H&N

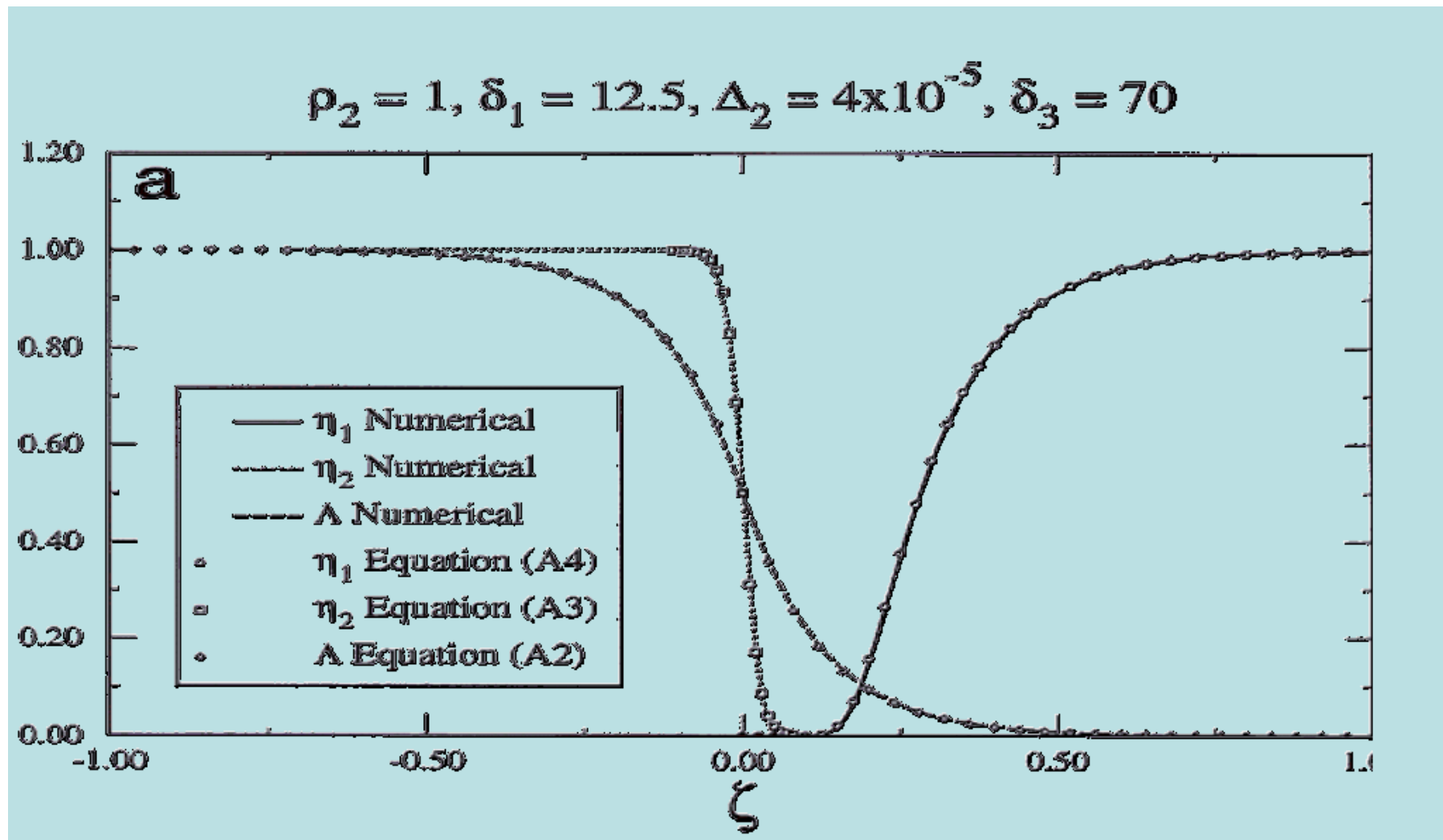
*Anderson & Price (2000) E.J. Cancer*

Cancer as a population biology problem. What are their competitive advantages of increased glucose uptake? acid-mediated tumor invasion hypothesis (Cancer Research 1996, 2001, 2002, 2006, 2009, Nature 2006):

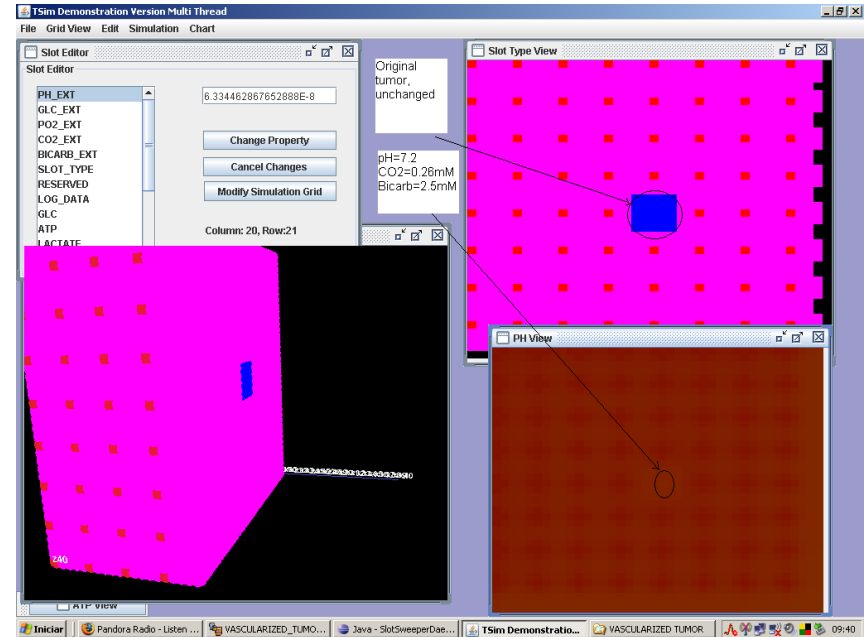
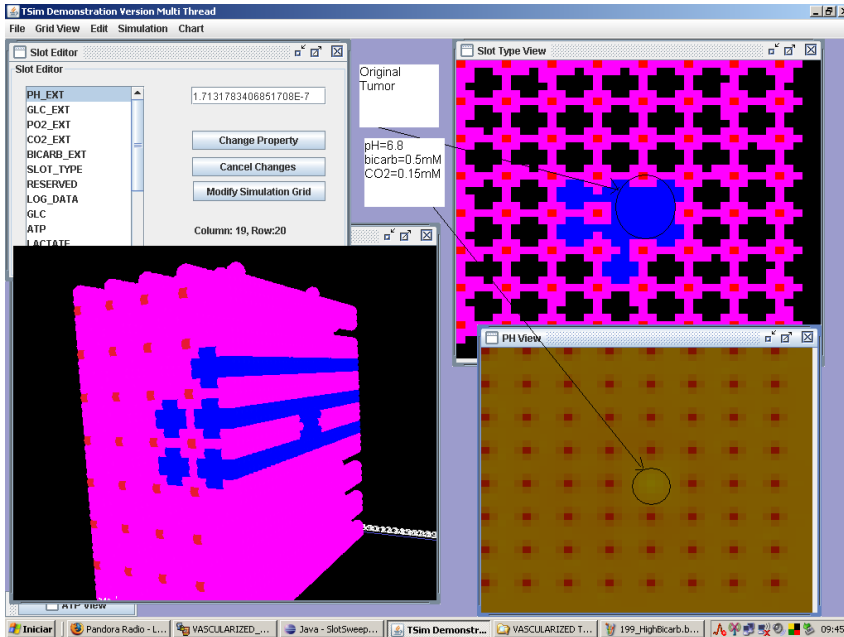


- General concept: Tumor cells use an evolutionary strategy called “spite” by creating a harsh micro-environment more unfavorable to normal tissue than to themselves.
- Specific concept: Altered tumor metabolism results in an acidic  $pH_e$  both in the tumor and in a ring of surrounding normal tissue.
- Tumor cells have an ideal  $pH_e$  (i.e. maximum proliferation) of about 0.5 pH units lower than normal.
- Peri-tumoral acidosis induces normal cell death, ECM breakdown, angiogenesis and blunts the immune response.

The models demonstrated the growing tumor edge would be preceded by a wave of acid

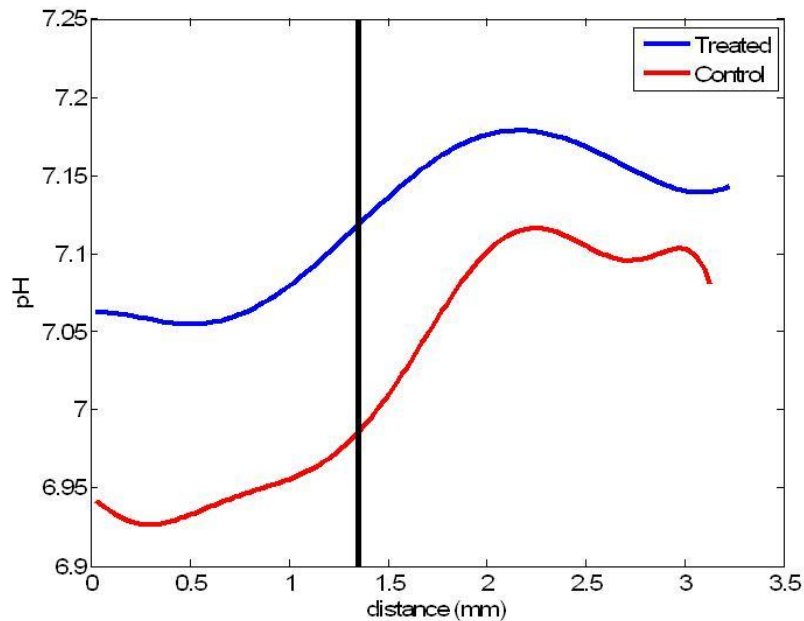
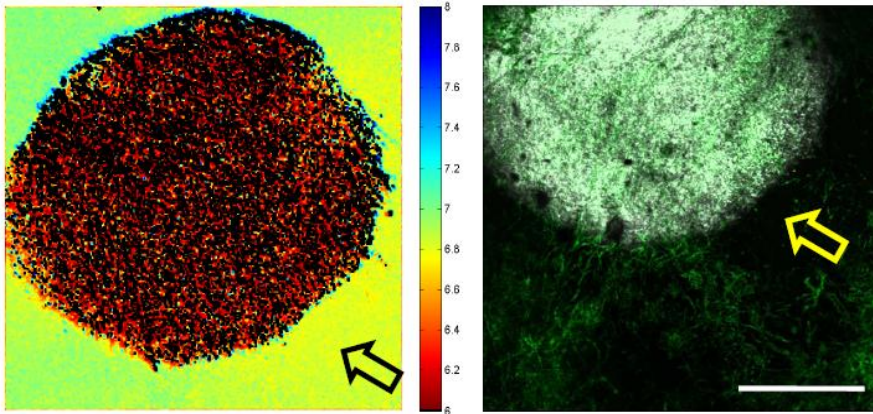


# Hypothesis: Could an increase in serum buffer reduce the gradient and inhibit invasive tumor growth?



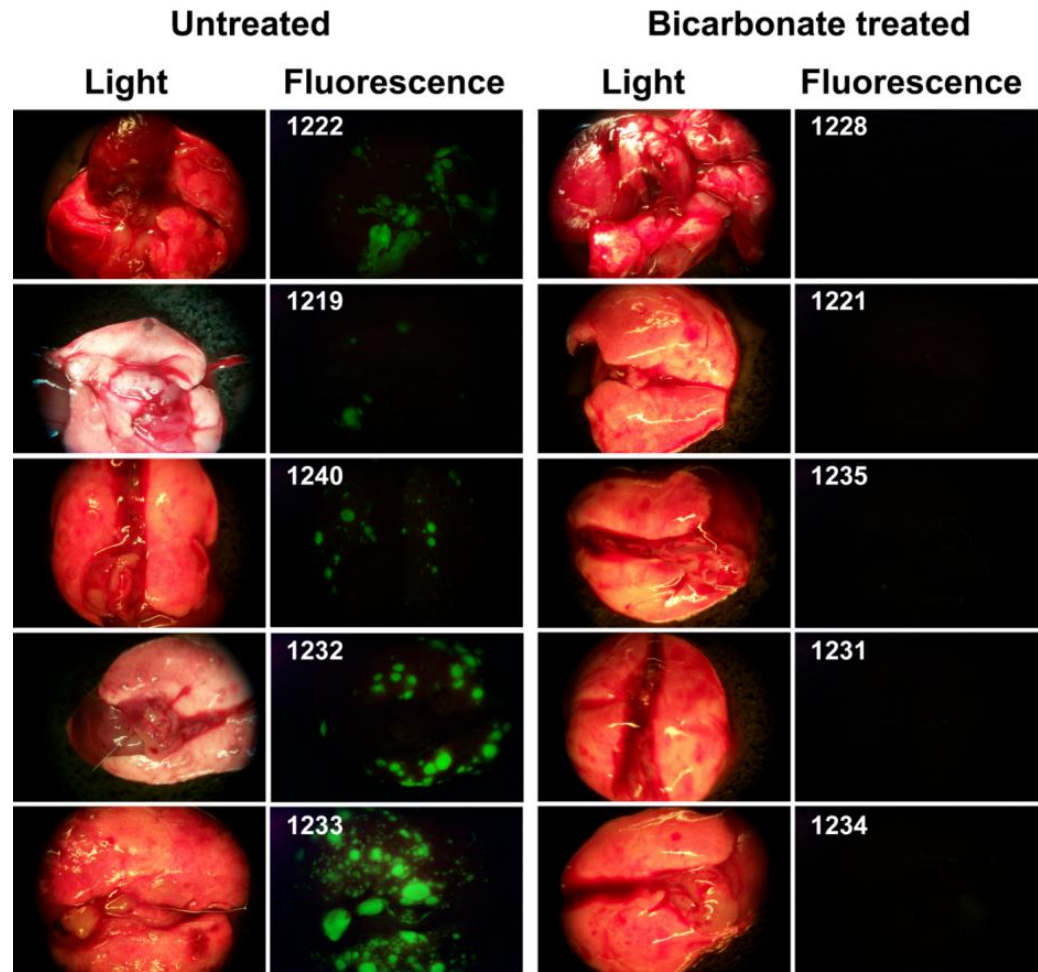
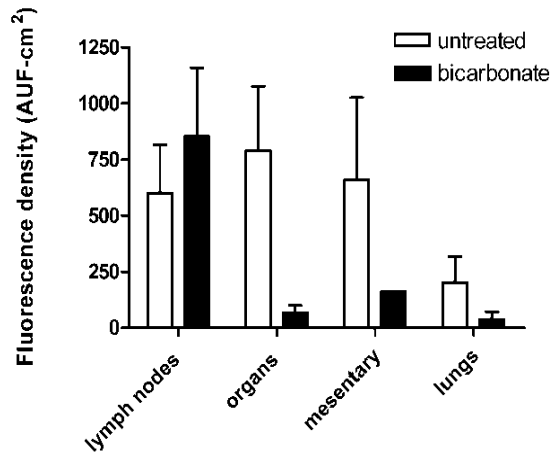
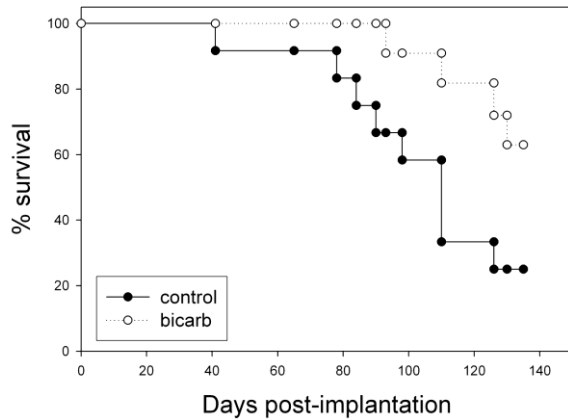
# NaHCO<sub>3</sub> raises Tumor pH

(200 mM ad lib; SCID mice)





# Bicarbonate inhibits metastases and prolongs survival in MDA-mb-231 cells

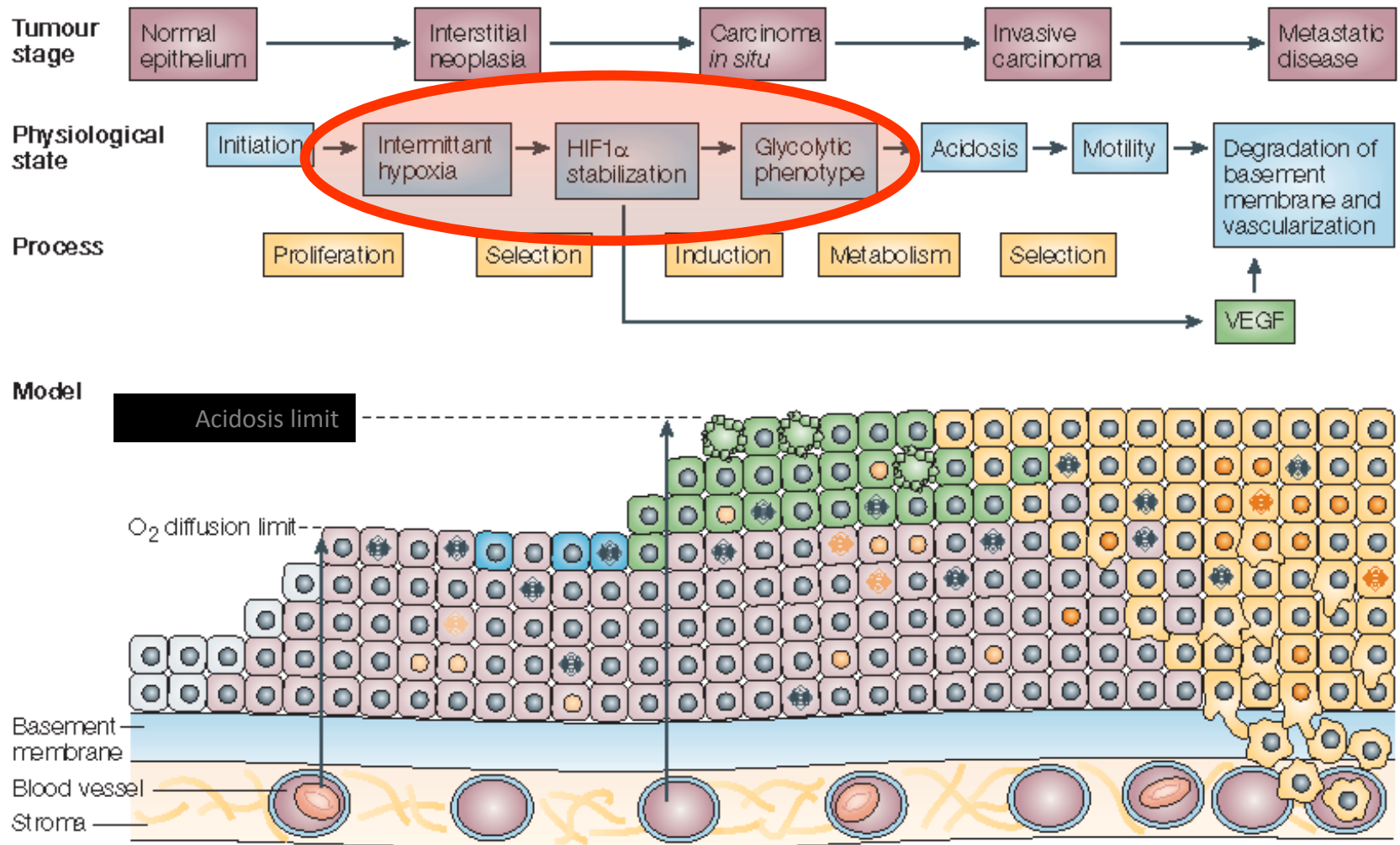


# Moffitt Clinical Trials

- MCC0964: “A phase I/phase II investigation of the effects of oral bicarbonate on bone pain”

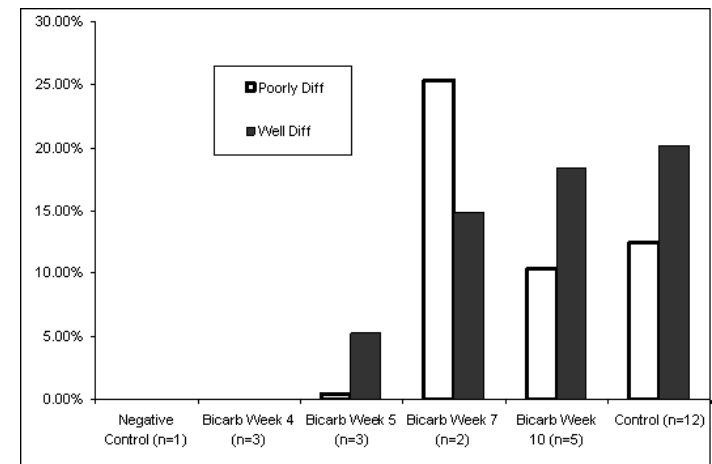
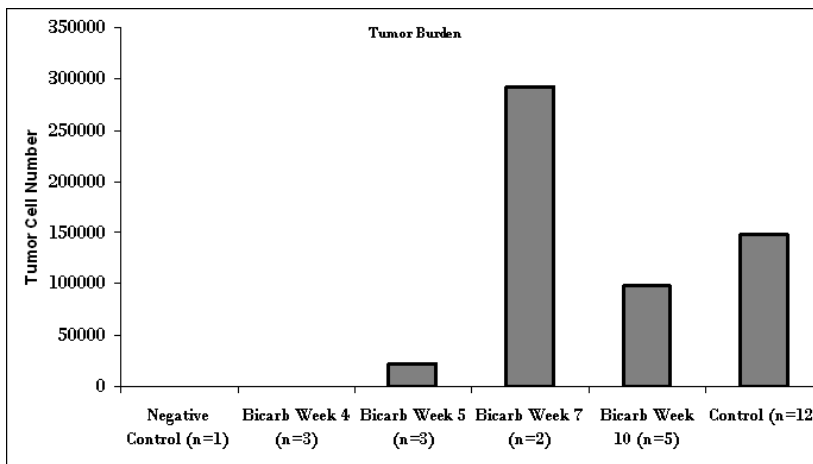
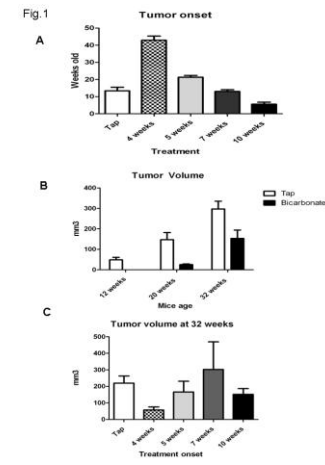
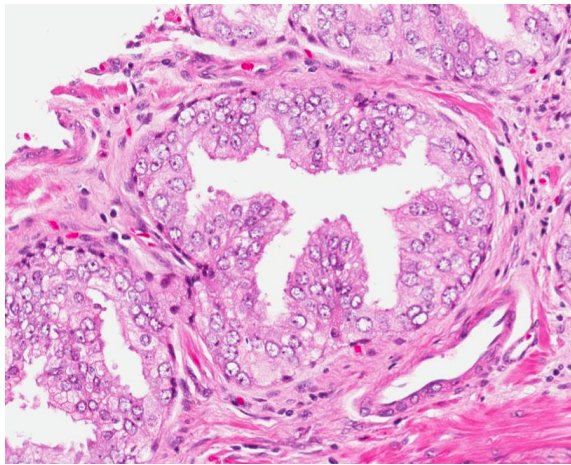
MCC0977: “A phase I/phase II investigating oral sodium bicarbonate with standard Gemcitabine therapy in non-resectable pancreatic cancer”

# Cancer as a complex adaptive system

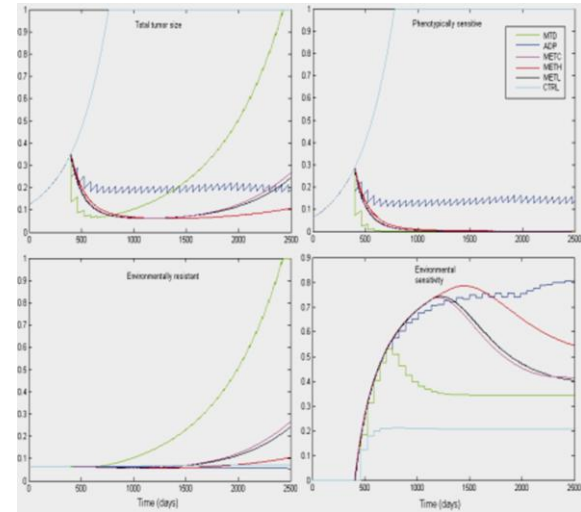




# Preventing Cancer in TRAMP mice



# Evolutionary dynamics in therapy



OPINION

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ESSAY

