Predicting outcomes of primary and metastatic pancreatic cancer with principles of mass transport

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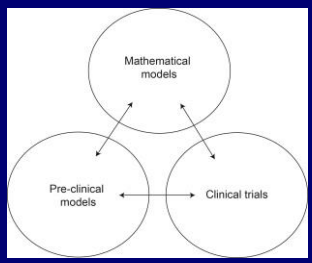
Connecting biology and physics of cancer



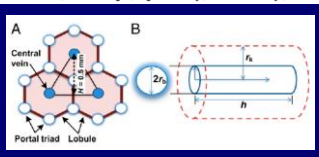
THEORY OF CELL KILL FROM THERAPY

Mass transport in liver metastasis and GBM

Mechanistic patient-specific predictive correlation of tumor drug response with microenvironment and perfusion measurements

Jennifer Pascal[a,1], Elaine L. Bearer[a,b,1], Zhihui Wang[a,1], Eugene J. Koay[c], Steven A. Curley[d], and Vittorio Cristini[a,e,2]

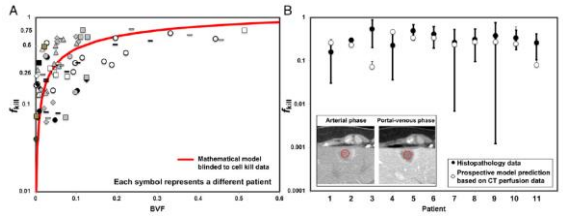
PNAS, 2013



$$f_{kill} = f_{kill}^{max}(r_0) \cdot BVF \cdot \frac{2Lr_b \cdot K_1(r_b/L) - 2Lr_k \cdot K_1(r_k/L) - (r_b^2 - r_k^2) \cdot K_0(r_k/L)}{r_b^2 \cdot (K_0(r_b/L) - K_0(r_k/L))} \quad [1a]$$

$$\frac{r_k}{r_0} = \frac{K_0(r_k/L)}{K_0(r_b/L)} \quad [1b]$$

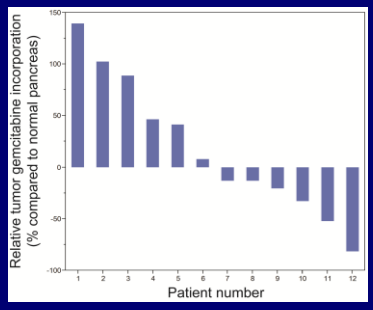
Mathematical prediction of response and correspondence with enhancement



Model applies to colorectal liver metastases and glioblastoma multiforme

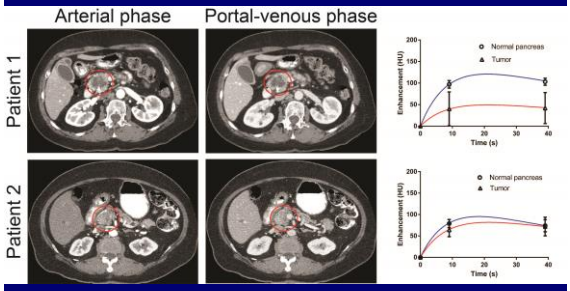
MEASURING AND MODELING DRUG DISTRIBUTION

Marked variability in tumor gemcitabine incorporation



Koay, et al. JCI 2014

Deriving physical properties from imaging

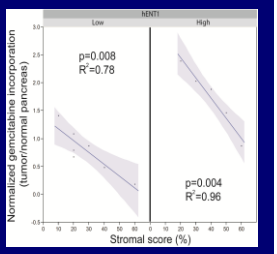


Koay et al., JCI 2014

Transport Oncophysics in human PDAC

Mass transport correlations:

- Delivery

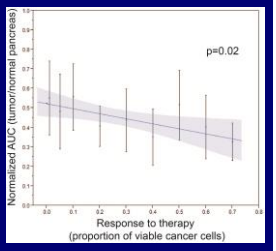


Mutli-scale transport!

Transport Oncophysics in human PDAC

Mass transport correlations:

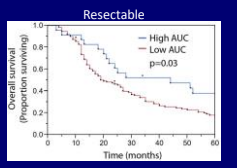
- Delivery
- Response

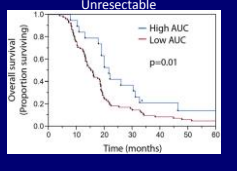


Transport Oncophysics in human PDAC

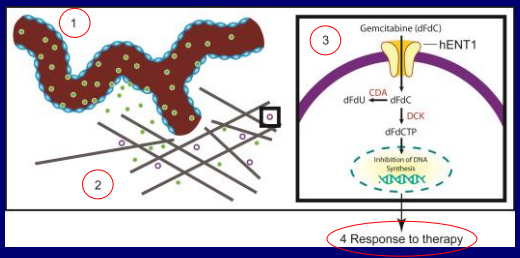
Mass transport correlations:

- Delivery
- Response
- Outcome





From the IV to the cell: Multiple physical barriers to overcome

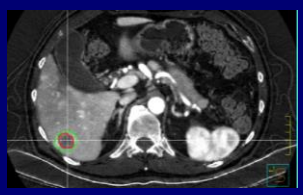


1. Vascular transport
2. Extracellular transport
3. Cellular transport
4. Therapeutic response

Koay, et al. JCI 2014

APPLICATION TO PANCREATIC CANCER LIVER METASTASES

Mass transport of liver metastases



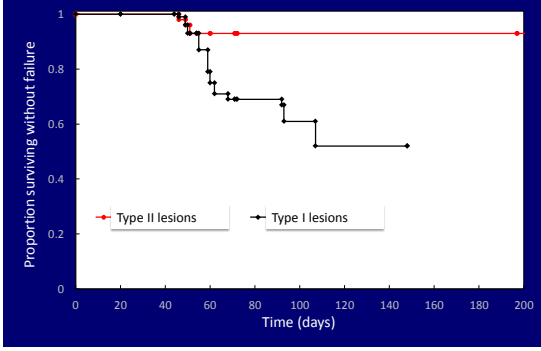
Based on characteristics of metastasis and surrounding liver:
Type I
Type II

Differential responses based on transport characteristic

153 liver metastases:

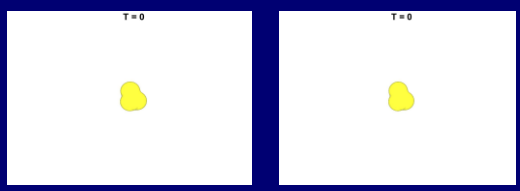
- Partial response (PR)
  - Type I: 23 of 98
  - Type II: 17 of 55
- Progressive disease (PD)
  - Type I: 26 of 98
  - Type II: 3 of 55
- Stable disease (SD)
  - Type I: 35 of 98
  - Type II: 22 of 55
- Complete remission (CR)
  - Type I: 3 of 98
  - Type II: 1 of 55

Time to failure differs significantly



MODELING TUMOR GROWTH AND BEHAVIOR

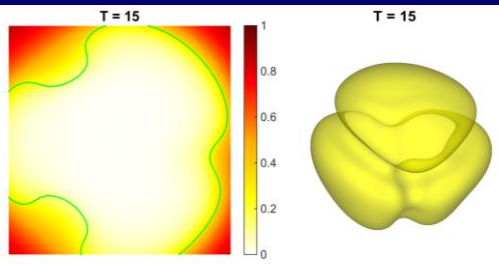
Theory of tumor morphology: Balance of mitosis and relaxation mechanisms



Cristini et al, JMB 2003

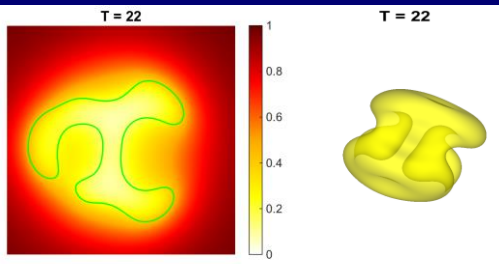
Vittorio Cristini
John Lowengrub

Fast growth rate of cancer cells relative to relaxation ($\lambda_M = 1.5$)



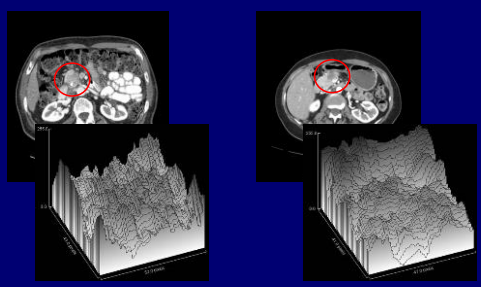
Vittorio Cristini
John Lowengrub

Slow growth rate of cancer cells relative to relaxation ($\lambda_M = 0.5$)



Vittorio Cristini
John Lowengrub

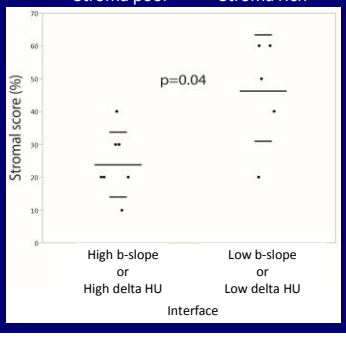
Different imaging characteristics of PDAC



Do these features correlate with outcome?

Differences in stroma by imaging feature

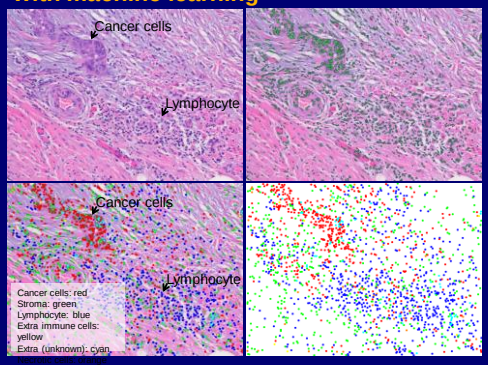
Stroma poor Stroma rich



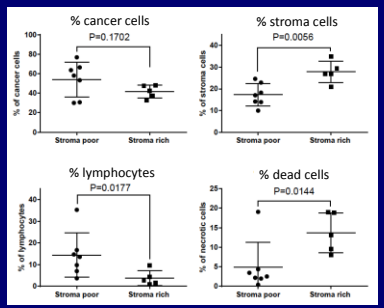
12 patients on prospective "Phase 0" protocol

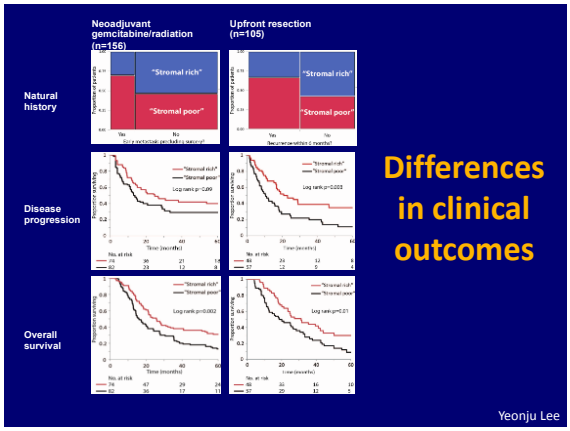
Deyali Chatterjee and Yeonju Lee

Identifying cellular subtypes with machine learning



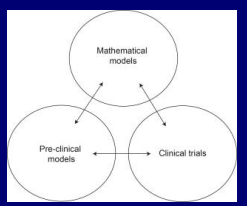
Intrinsic differences in tumor microenvironment





Translating mathematical and physical oncology to patients with pancreatic cancer

- Math models inform clinical studies, vice versa
- Mass transport properties reflect the underlying biology of disease
- Approach enables stratification and possibly selection for therapy
- Prospective trials open and accruing



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