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# Predicting cancer outcome

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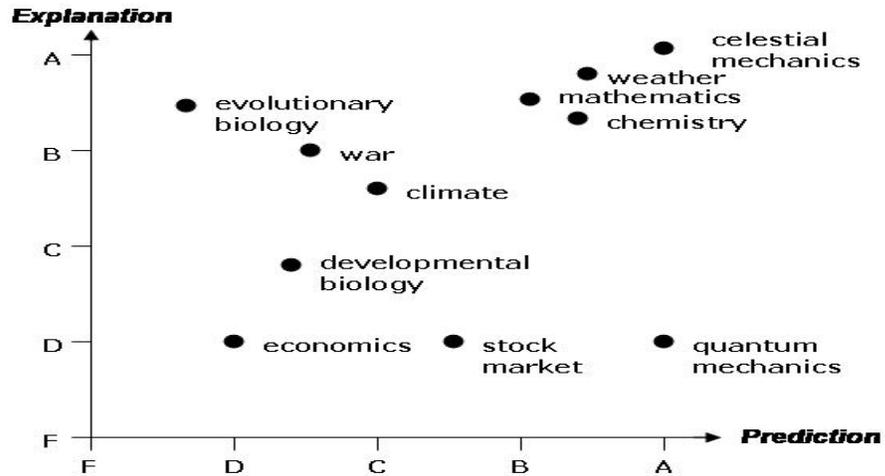
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**Specifications:**

- Word count 177
- References 4
- Figures 1
- Table 1 will be obvious to specialists. It provides context and is optional.

**Correspondence****Predicting cancer outcome**

We read with interest the paper by Michiels et al on the prediction of cancer with microarrays and the commentary by Ioannidis listing the potential as well as the limitations of this approach (February 5, p 488 and 454). Cancer is a disease characterized by complex, heterogeneous mechanisms and studies to define factors that can direct new drug discovery and use should be encouraged. However, this is easier said than done. Casti teaches that a better understanding does not necessarily extrapolate to better prediction, and that useful prediction is possible without complete understanding (1). To attempt both, explanation and prediction, in a single non-mathematical construct, is a tall order (Figure 1).



**Figure 1.** Scientific explainability and predictability. Letters refer to academic grades (1)

At this stage of incomplete knowledge, predictive ability can be enhanced by considering a hybrid approach: computational methods based on known mechanisms of the disease (2, 3, 4), together with microarrays. Multiple initiatives directed to the same objective, namely, the prediction of cancer outcome, may serve to provide validation, a point well made by Ioannidis. A collaborative clinical study utilizing a complementary approach is an appealing possibility (Table 1).

We declare that we have no conflict of interest.

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**Table 1.** Complementary attributes of microarrays and computational models

	<b>Microarrays</b>	<b>Computational models</b>
<b>Objective</b>	Unbiased approach to guiding best-available chemotherapy to individual patients	
<b>Approach</b>	Identify markers of putative gene-based mechanisms	Mechanistic models that incorporate patient-specific cell kinetic parameters to predict heterogeneous outcomes
<b>Technology</b>	Statistical analysis of gene-expression data to create unbiased tumor class predictors and assist in class discovery.	Mechanistic model based on functional data from tumor biopsies.
<b>Methodology</b>	Data mining and exploratory data analysis: Tumors clustered by gene expression Cannot address resistance Cannot address toxicity	Computational Model: cell cycle kinetics, pharmacokinetics and dynamics, drug scheduling. Ability to address genetic and kinetic resistance. Can address toxicity.
<b>Possibilities</b>	Identification of aberrant gene expression profiles across distinct types of cancers. Main value: taxonomy	Deterministic models can generate predictions. Can model combination therapy. Main value: tailored therapeutics
<b>Status</b>	Standards for recording and reporting microarray-based gene expression data not yet established. Incomplete knowledge of gene function	Standards for computational models established. Knowledge of gene function not necessary.
<b>The future</b>	Prospective clinical studies	