

Patient-oriented gene-set analysis of cancer mutation data

Simina M. Boca, Kenneth Kinzler, Victor E. Velculescu,
Bert Vogelstein, Giovanni Parmigiani

Johns Hopkins University, Baltimore, MD

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Stages of cancer

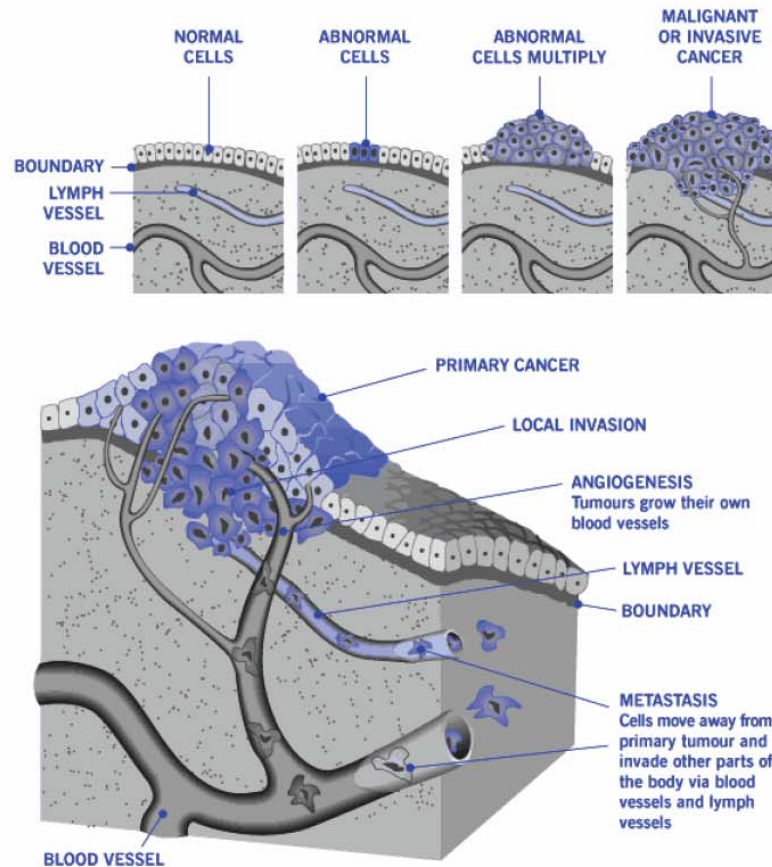


Figure: From <http://www.cancervic.org.au/>

DNA alterations in cancer

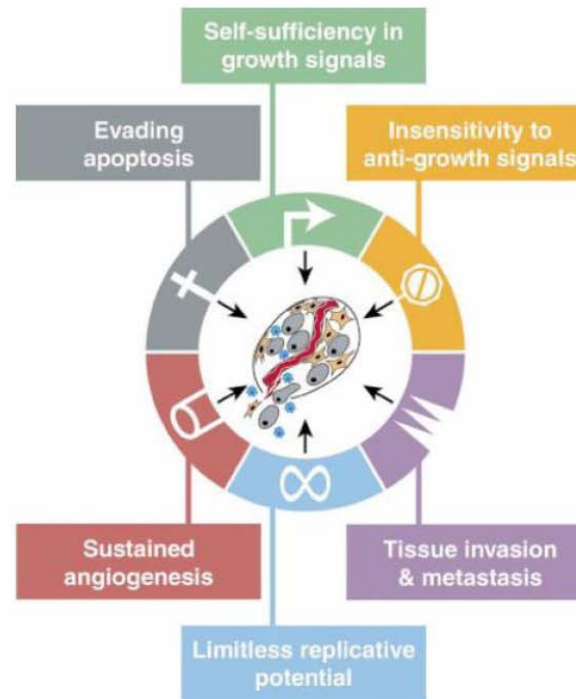


Figure 1. Acquired Capabilities of Cancer

We suggest that most if not all cancers have acquired the same set of functional capabilities during their development, albeit through various mechanistic strategies.

Figure: From Hanahan and Weinberg (2000).

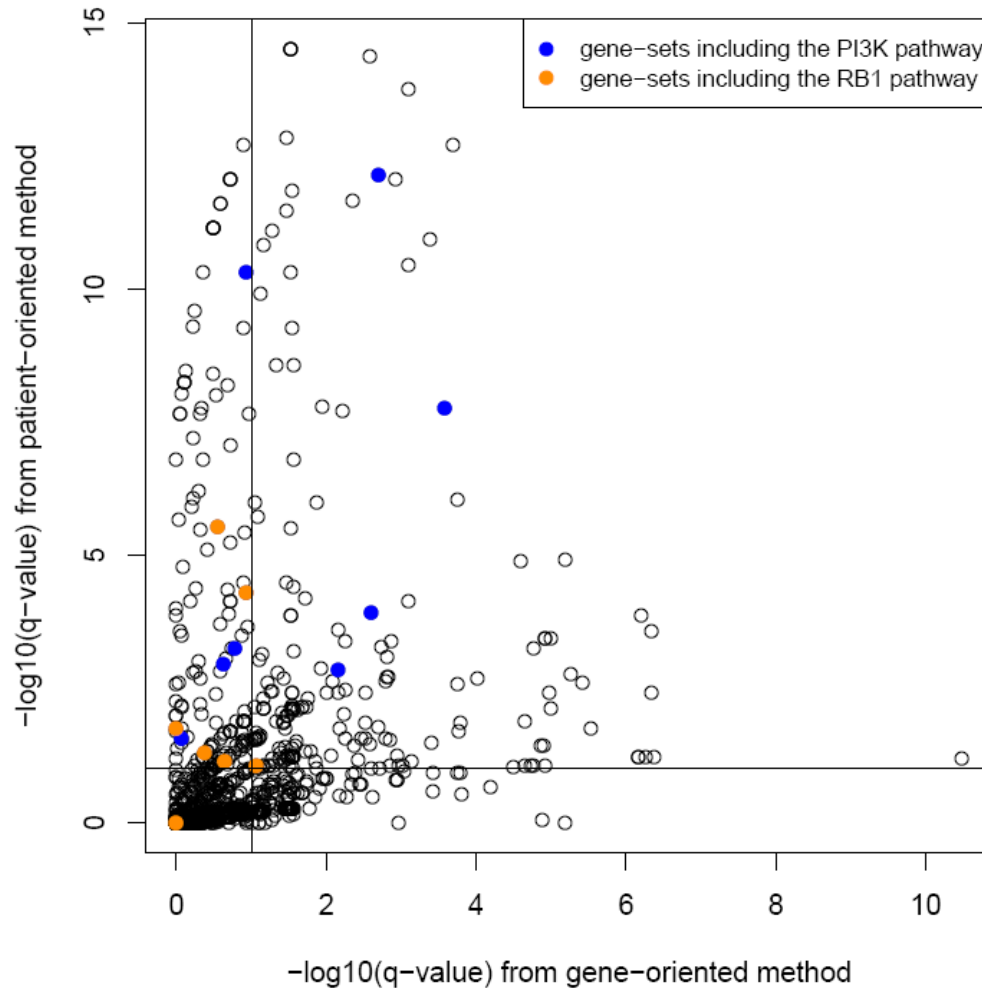
Gene-sets in cancer

- Genetic mutations tend to occur preferentially in a core group of pathways and biological processes.
- It is thus more relevant to consider an analysis at the *gene-set level* instead of at the *gene level*.
- Mutations within the same gene-set often obey the *exclusivity principle* (Vogelstein and Kinzler (2004))

Proposed method

- We propose a *patient-oriented* approach to gene-set analysis for cancer mutation data, which:
 - Incorporates the fact that most gene-sets obey the exclusivity principle.
 - First calculates sample (patient) gene-set scores, then combines them across samples.
- We compare our approach to a standard *gene-oriented approach*, which first scores the genes across all samples, then combines these scores into gene-set scores.

Comparison of methods



Comparison of gene-oriented and subject-oriented methods for the dataset in Parsons et al. (2008).