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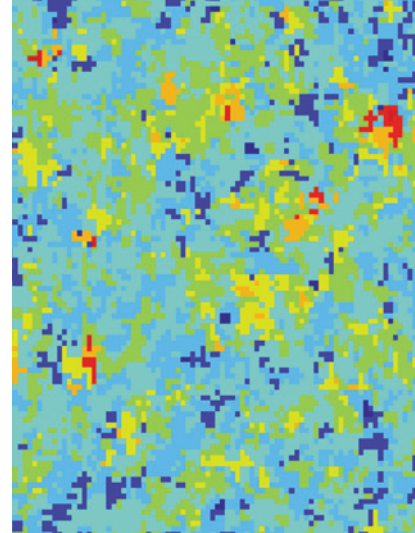
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ABOUT THE COVER

Cancer risk in premalignant diseases, such as Barrett's Esophagus or Inflammatory Bowel Disease, is frequently over-diagnosed and leads to the over-treatment of patients. These problems are a consequence of the lack of *biomarkers* that are able to accurately determine cancer risk in premalignant disease. A biomarker is an assayable property of the disease that correlates with the risk of cancer development; examples of potential biomarkers include the proportion of proliferating cells in a biopsy or the amount of a secreted protein. The study by Dhawan and colleagues (page 283) sort to address a major challenge to biomarker development: how to select the best candidate biomarker from the near-limitless list of candidates. The authors did this by constructing a computational model of cancer development, and using the computer to perform a wide-ranging *in silico* search of biomarker candidates. The cover image shows a snapshot from the simulation: each colored square represents a cell, and the color of the square indicates how many advantageous (driver) mutations that cell has acquired (red=many, dark blue=few). At each step in the simulation, a cell is chosen to replace a neighbor at a rate proportional to the differential number of advantageous mutations between the two cells. This process leads to 'clonal expansions' of patches of neighboring cells with similar genotypes (patches of identically colored cells in the image). The study illustrates how a computational model can provide a high-throughput and low-cost platform for the preliminary assessment of candidates biomarkers, and in so doing diminish the empirical constraints on biomarker development.



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