1086-60-964 **Cristian Tomasetti*** (cristian@jimmy.harvard.edu), 450 Brookline Ave, Mail Location: CLS11007, Boston, MA 02215, and **Bert Vogelstein** and **Giovanni Parmigiani**. *Stochastic modeling of the accumulation of somatic mutations in cancer.*

One useful approach for better understanding the process of cancer evolution is given by the integration of mathematical modeling with the ever growing amount of sequencing data of cancer tissues.

While it has been hypothesized that some of the somatic mutations found in tumors may occur prior to tumor initiation, there is little experimental or conceptual data on this topic. To gain insights into this fundamental issue, we formulated a new mathematical model for the evolution of somatic mutations in which all relevant phases of a tissue's history are considered. The model provides a way to estimate the in-vivo tissue-specific somatic mutation rates in normal tissues directly from the sequencing data of tumors. The model also makes novel predictions, validated by our empirical findings, on the expected number of somatic mutations found in tumors of self-renewing tissues. Furthermore, a general principle for improving the detection of driver mutations by reducing the amount of "noise" caused by the passenger mutations will be introduced.

Our results have substantial implications for the interpretation of the large number of genome-wide cancer studies now being undertaken. (Received September 17, 2012)