Aula Magna del Dipartimento
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When Will the Cancer Start?

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Abstract: Cancer is a genetic disease that results from accumulation of unfavorable mutations. As soon as genetic and epigenetic modifications associated with these mutations become strong enough, the uncontrolled tumor cell growth is initiated, eventually spreading through healthy tissues. Clarifying the dynamics of initiation is critically important for understanding the mechanisms of the cancer appearance. Here we present a new theoretical approach, stimulated by analogy with chemical reactions and other stochastic processes in physics, to evaluate the dynamic processes associated with the cancer initiation. It is based on a discrete-state stochastic description of the formation of tumors as a fixation of unfavorable mutations. Using a first-passage analysis, the probabilities for the cancer to appear and the average times before it happens are explicitly calculated. It is predicted that the slowest cancer initiation dynamics is observed for neutral mutations, while it is fast for both advantageous and, surprisingly, disadvantageous mutations. The method is applied for estimating the initiation times from clinical data for 28 different types of cancer. It is found, surprisingly, that the higher probability of the cancer to occur does not necessary lead to fast times of starting the cancer. This suggests that both lifetime risks and cancer initiation times must be used to evaluate the possibility of appearance of the cancer tumor. The relations of the cancer initiation processes with dynamics of chemical reactions is discussed. Our view of cancer initiation as a motion in the effective free-energy landscape provides new insights on the mechanisms of these complex processes.