

# Clonal evolution: of which clones?

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Tumors are made up of heterogeneous cells. This heterogeneity makes cancer cells difficult to target and contributes to therapeutic avoidance and relapses. The clonal evolution model describes the dynamical processes of emergence, growth, decline or disappearance of clones constituting a tumor in space and time. Understanding these dynamics helps avoiding certain pitfalls (such as the selection of resistant clones) and lead to innovative therapeutic strategies taking these dynamics into account, such as adaptive therapies. However, the very concept of a clone is more ambiguous than it appears. I will start by showing that the notion of clone is necessarily relative (relating to the choice of traits used to identify and track clones), that its use is polysemous, and that the traditional conception of the clone is no longer in line with the data, nor with the emerging tools available to study clonal evolution. These mismatches might infringe scientific and clinical progress. A conceptual shift is thus needed to overcome these obstacles, and I will propose some solutions to both clarify the concept and make it more operational.