What does not kill me makes me stronger - dynamic instability and non-genetic plasticity in Tumor Progression

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The spate of tumor genome sequencing data in the past years has begun to shine light on the cracks of the paradigm that cancer is a genetic (mutation-riven) disease. It is increasingly difficult to maintain the concept that cancer progression is driven by a somatic Darwinian evolution of cells that accumulate mutations and undergo selection. In the same time period, systems biologists have learned to view a nominal cell phenotype as a an attractor state - the state at the bottom of the valleys in Waddington's "epigenetic landscape". This picture is more than a metaphor because it explains phenotypic variability ("plasticity") in terms of mathematical principles of gene regulatory network dynamics. But this same framework of non-genetic plasticity should also be applied to cancer progression. In this talk I will propose how principles stabilities and instabilities of cell states (independent of genetic alterations) prompts us to rethink the idea of somatic evolution in the development of therapy resistance. Theory and experiments suggest that treatment either kills the cell, or if not, will induce a stemness state in the non-killed (but stressed) cells and make them more resilient - manifesting Nietzsche's idea of "What does not kill me makes me stronger". I will also present the theory that explain why such behavior is fundamentally inevitable, and show experimental and clinical data in support of it.