Single cell analysis of resistance to targeted therapies in cancer

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Cancer is a disease of single cells behaving badly, with mutations to certain proteins causing uncontrolled cellular proliferation. This has led to the development of therapies targeting those proteins, such as vemurafenib for melanoma. Yet while most cells will respond to drug, some do not, ultimately repopulating the tumors and causing relapse. This process is often thought to be Darwinian with genetic origins as well. Here, we show that the acquisition of resistance may have in fact have non-genetic origins, and we decompose the resistance process into an early, transient priming phase before the addition of drug, following by a later reprogramming phase consisting of a stepwise epigenetic progression. We discuss some implications for cancer treatment as well as cell fate plasticity.