Clonal selection of tumors and its consequences in personalized medicine

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Molecular evidence supports the view that all types of cancer arise from defects in the structure and / or regulation of genes. Accumulation of mutations is key for progression from dysplasia to invasive tumor. The gradual dominance of mutated cells with accumulated mutations and epigenetic changes is significantly exacerbated by clonal selection, which takes place against the background of intra-tumor heterogeneity. Clonal selection is the process by which fast-growing or resistant tumor clones suppress those slow-growing and predominantly spread in the body. This process is thus behind the gradual weakening of the response of most progressive oncological diseases to treatment. This is because chemotherapy and targeted treatment select and propagate clonal residues with a resistant genotype. Due to the failure of DNA repair mechanisms, the genotype is further fragmented into sub-clones. The data suggest that chemotherapy stimulates metastasis or relapse in almost 20% of patients. Therefore, treatments that better take into account clonal selection are being considered. Geographical genotyping of the tumor over time should be at the forefront of morphological evaluation as an indicator of treatment success. Treatment should be performed by monitoring intra-tumor heterogeneity in order to propagate responsive clones at the expense of resistant ones.