Passenger mutations as a target for the personalized therapy of cancer

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The American FDA approved the first comprehensive NGS diagnostic assay for cancer at the end of 2017, leading the way to personalised therapy of cancer and the massive employ of bioinformatics (https://www.fda.gov/downloads/medicaldevices/productsandmedicalprocedures/invitrodiagnostics/ucm584603.pdf).

In NGS-detected genes from cancer patients, driver and passenger mutations can be distinguished. The former provides a proliferative advantage to cancer cells and are commonly found, the latter do not provide proliferative fitness and are different in different patients. However, some passenger mutations might occur in genes involved in metabolism and could be mildly deleterious for cancer cells. Such deleteriousness could be increased using a specific inhibitor of the mutated protein product. A personalized therapy of cancer could address both driver and passenger mutations.

To evaluate to which extent it is possible to address passenger mutations for the cure of cancers, we built a gene/ inhibitor list, crossing DrugBank, a database that combines detailed drug data with comprehensive drug target information, with COSMIC, the catalogue of somatic mutations in cancer. First, we obtained the approved drugs annotated as inhibitors from DrugBank, and the genes encoding their target proteins. We then looked for these genes in COSMIC, to check how many missense mutations have been detected in cancer patient genomes.