The extent of consequential DNA damage in human tumors from TCGA PanCanAtlas

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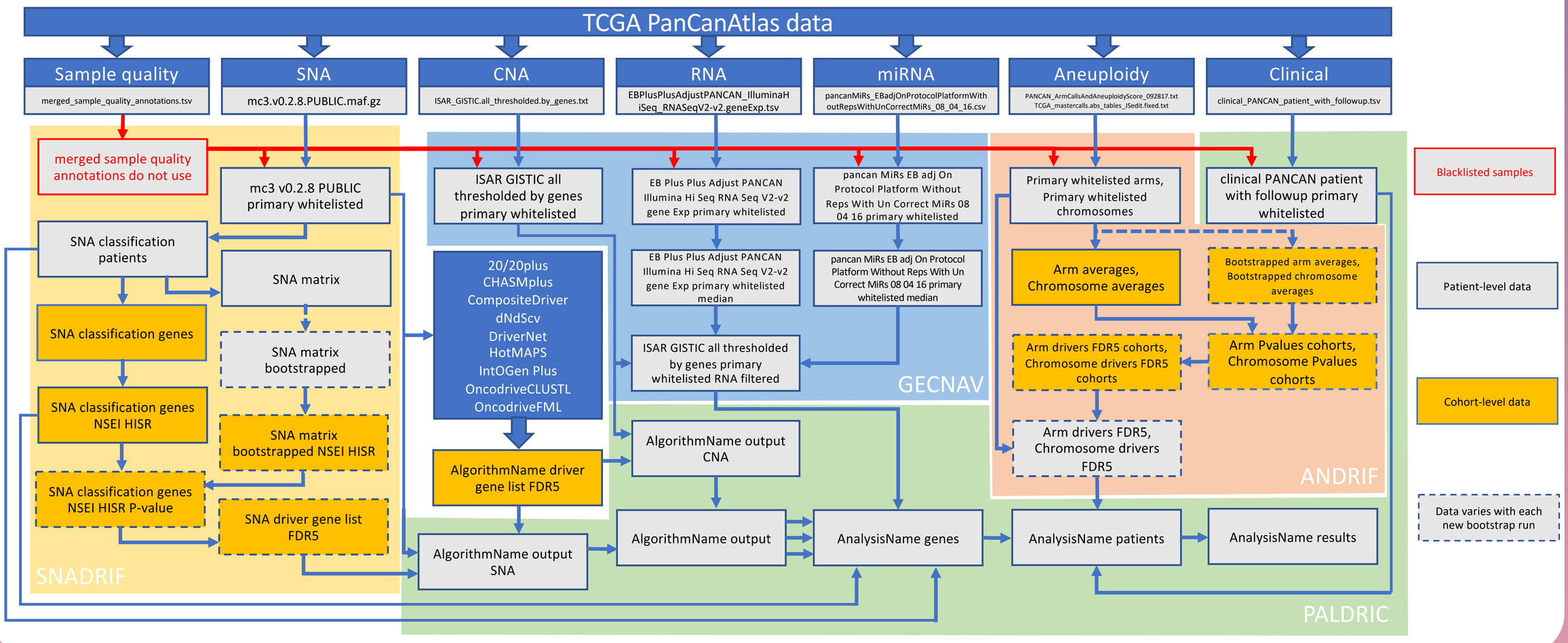
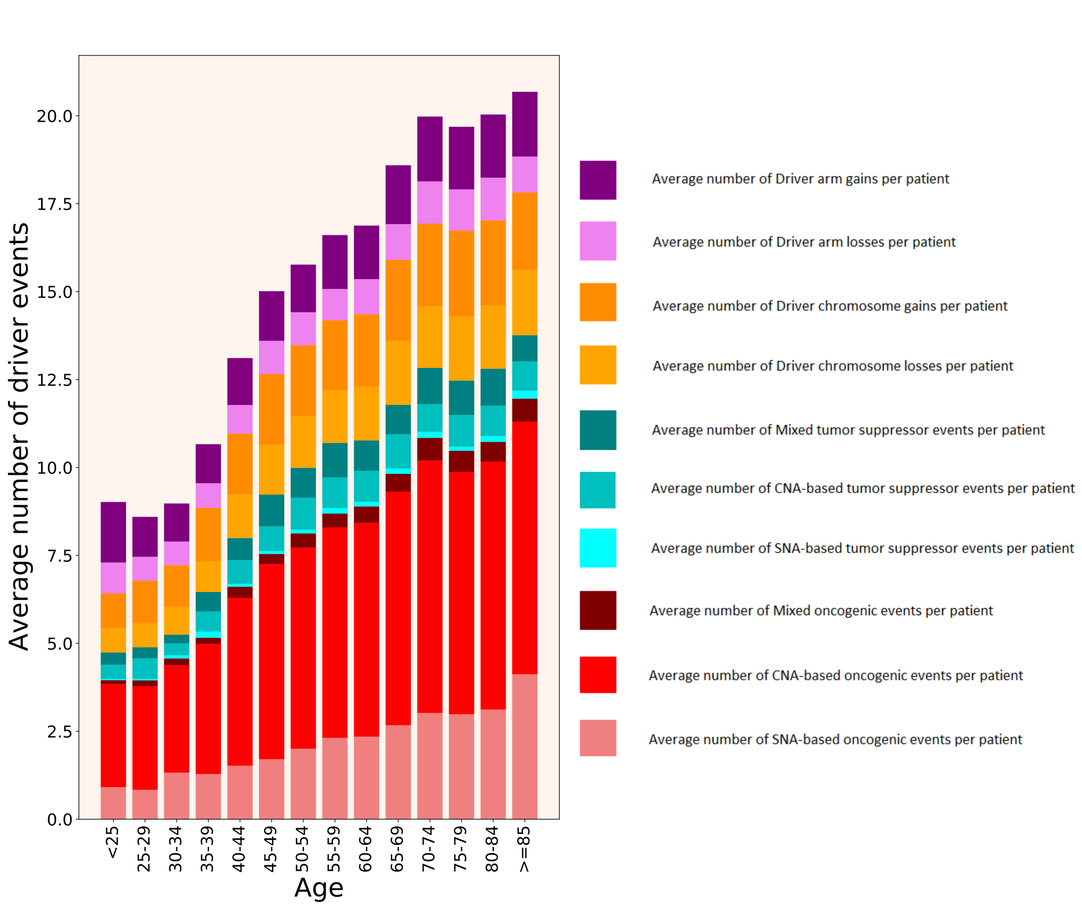
Abstract

The DNA damage is crucial for the emergence of cancer cells. If the DNA damage response is defective, the DNA damage is converted to fixed mutations. Some of these mutations drive tumorigenesis and are called driver mutations. However, the extent of consequential DNA damage per tumor, i.e. the number of various kinds of driver mutations, is not known. We have utilized the largest database of human cancer mutations – TCGA PanCanAtlas, multiple popular algorithms for cancer driver prediction and several custom scripts to estimate the number of various kinds of driver mutations in primary tumors. We have found that there are on average 16.5 driver mutations per patient's tumor, of which 2.3 are hyperactivating SNA mutations in oncogenes, 5.9 are CNA amplifications of oncogenes, 0.4 have both in the same oncogene, 0.1 are homozygous inactivating SNA mutations in tumor suppressors, 0.8 are homozygous CNA deletions in tumor suppressors, 0.8 have inactivating SNA mutation in one allele and CNA deletion in the other allele of a tumor suppressor, 1.5 are driver chromosome losses, 2 are driver chromosome gains, 1 is driver chromosome arm loss, and 1.5 are driver chromosome arm gains. The number of driver mutations per tumor increased with age, from 9 for <25 y.o. to 20.7 for >85 y.o. There was no big difference between genders (16.9 in males vs 16.1 in females). The number of driver mutations per tumor varied strongly between cancer types, from 1.4 in thyroid carcinoma to 37.6 in lung squamous cell carcinoma. Overall, our results provide valuable insights into the extent of functional DNA damage in tumors.

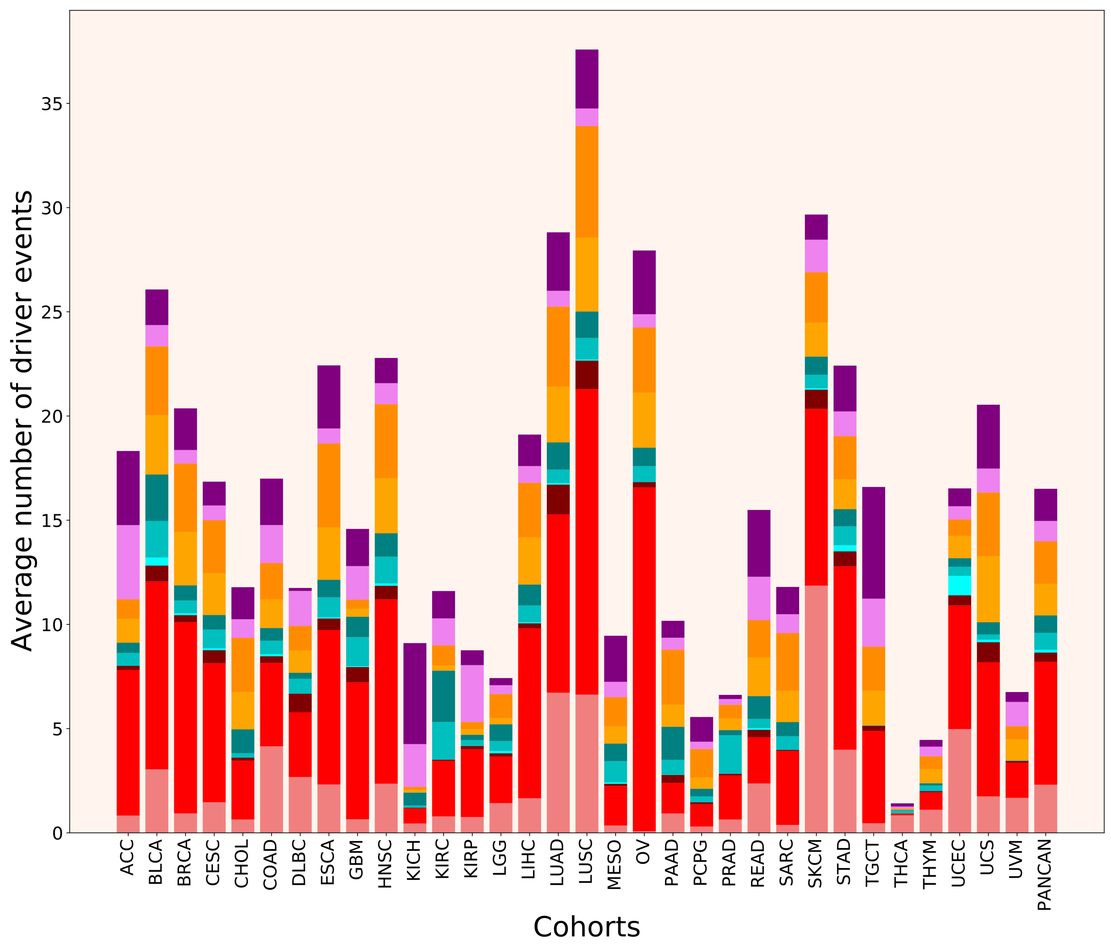
Our pipeline for driver event quantification and analysis



Average number of driver events of various classes in different age groups



Average number of driver events of various classes in different cancer types



Color legend as in the left figure. Standard TCGA cancer type abbreviations are used.