TCGA PanCanAtlas data analysis suggests multiple possibilities for personalized cancer therapy

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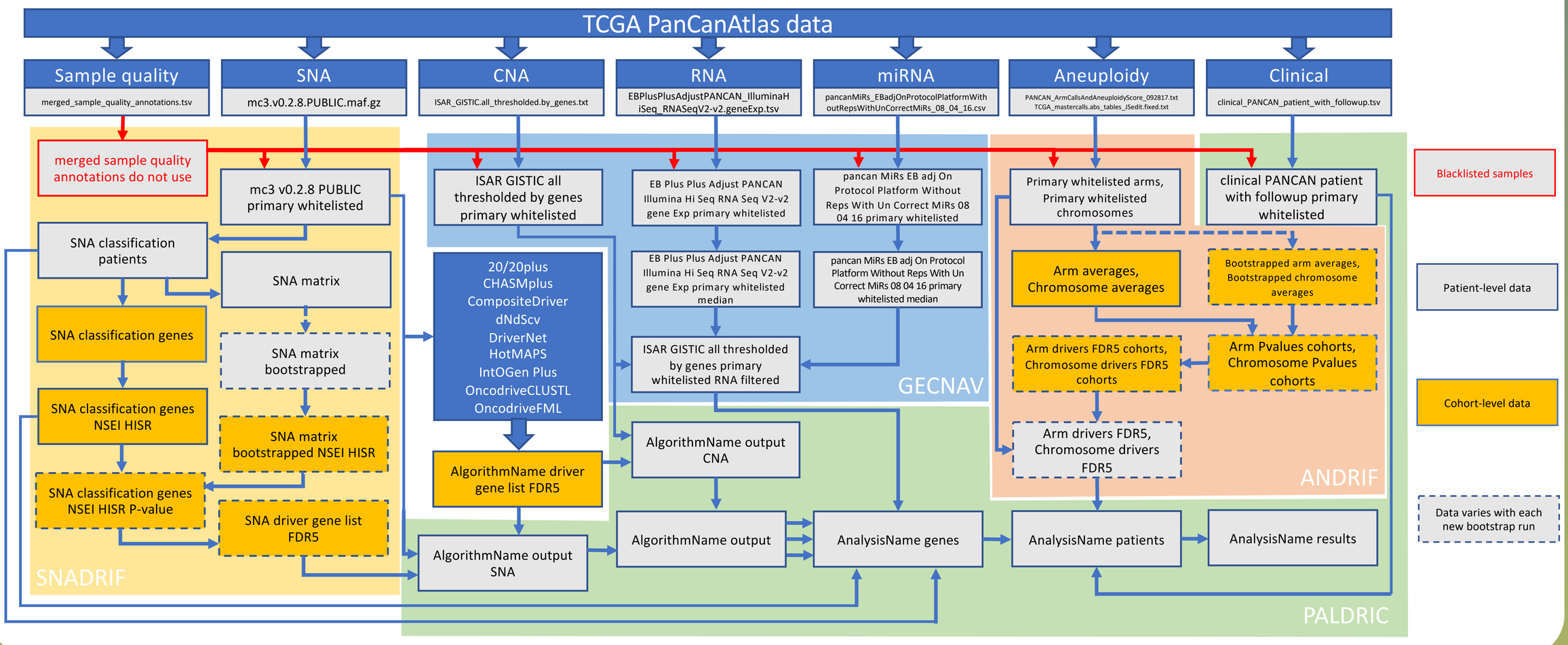
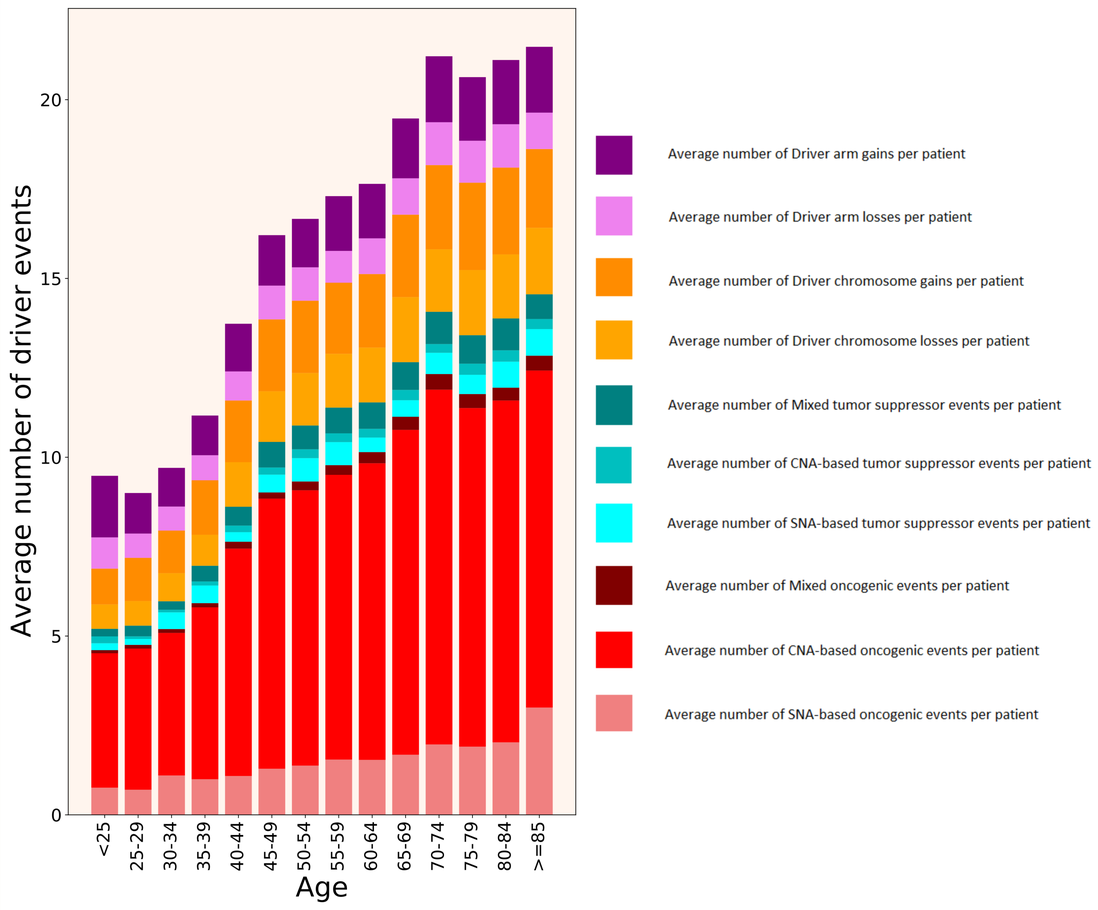
Abstract

Personalized cancer medicine holds promise for the future of cancer treatment. The key to success is the knowledge of exact molecular alterations that drive tumorigenesis in a given patient, so that a suitable targeted therapy can be selected. However, the extent of such alterations, i.e. number of various kinds of driver mutations per patient, is still 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 17.4 driver mutations per patient's tumor, of which 1.6 are hyperactivating point mutations in oncogenes, 8 are amplifications of oncogenes, 0.3 have both in the same oncogene, 0.5 are homozygous inactivating point mutations in tumor suppressors, 0.2 are homozygous deletions in tumor suppressors, 0.7 have inactivating point mutation in one allele and 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 gradually increased with age, from 9.5 for <25 y.o. to 21.5 for >85 y.o. There was no big difference between genders (17.35 in males vs 17.42 in females). The number of driver mutations per tumor varied strongly between cancer types, from 1.4 in thyroid carcinoma to 38.4 in lung squamous cell carcinoma. Overall, our results provide valuable insights into the extent of driver alterations in tumors and suggest that multiple possibilities to choose a suitable targeted therapy exist in each patient.

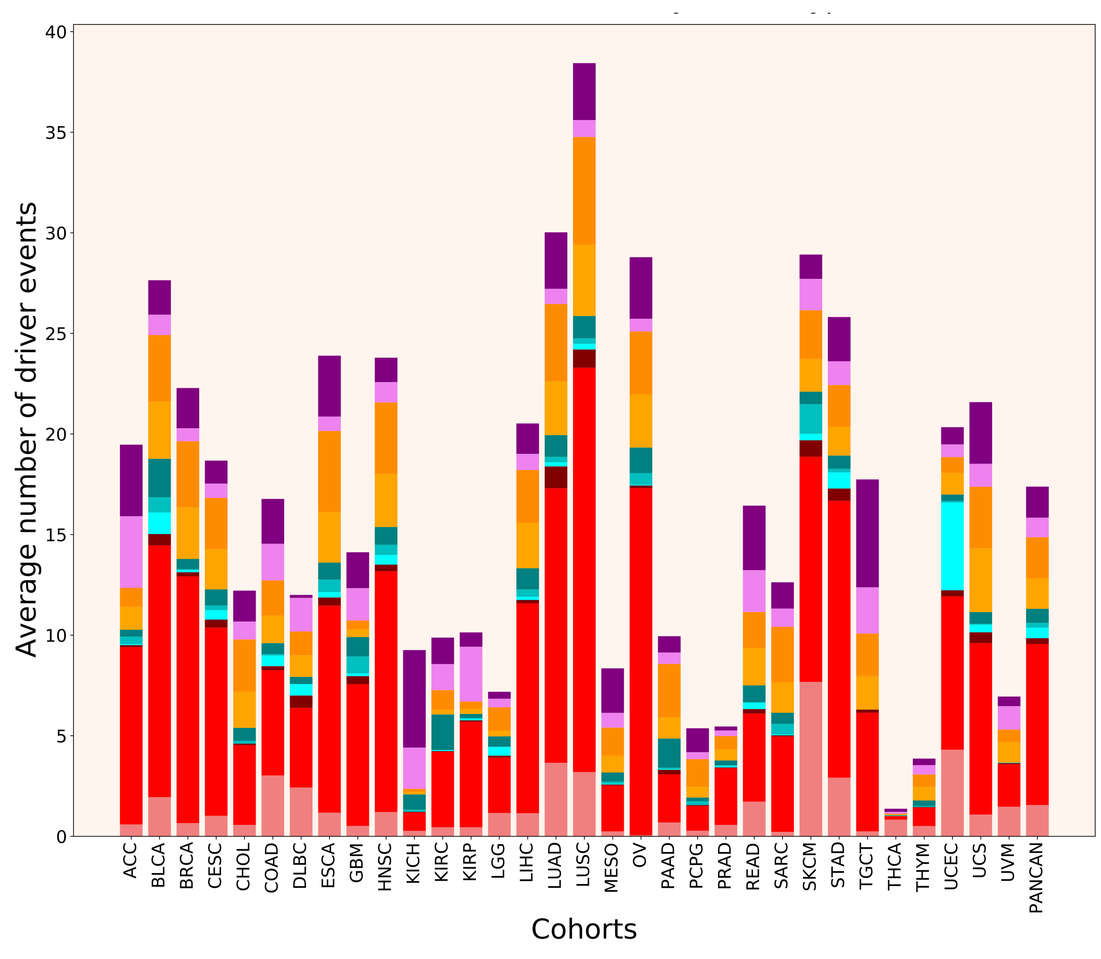
Our pipeline for driver event quantification and analysis



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.