Whole Genome Sequencing (WGS) of Brazilian Melanoma Patients as part of the International Cancer Genome Consortium.

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BACKGROUND: Melanoma is the most aggressive form of skin cancer with increasing prevalence in Brazil. The comprehensive molecular profiling of these tumors and the recent genomic classification has improved the knowledge of melanoma biology and foster the identification of potential clinical biomarkers.

HYPHOTHESIS: The aim of this project is to perform a genomic profile by whole genome sequencing (WGS) of Brazilian melanomas patients.

METHODS: We reported the WGS using Illumina paired-end sequencing strategy (>30 X-fold coverage) of 66 cases (45% primary and 55% metastatic) and respective matched normal.

RESULTS: Overall we observed an average of 46K mutations/genome. The most frequent type of substitutions identified were: C>T (22.5%), T>C (6.4%), T>G (4.4%), T>A (2.9%), C>A (2.8%) and C>G (1.7%). A significative difference between frequency of C>T substitutions was observed among histological subtypes, i.e., acral lentiginous (11.3%), nodular (31.2%) and superficial spreading (25.9%). Among the classic genes involved in melanoma biology, we found that 31.8% of patients had *BRAF* mutations, being the V600E the most frequent (82.6%). A total of 6.1% of patients had *NRAS*, 3.0% showed *KRAS*, one case (1.5%) showed *HRAS*, and 12.1% showed *NF1* mutations. *TERT* promoter mutation (C250T) was found in 28.8% of patients. *TP53* mutations found 4.5% and *RB1* in 1.5% of cases. Oncogenic *KIT* and *PDGFRA* mutations were observed in 6.1%and 1.5%, respectively. *BRAF, NRAS, HRAS, KRAS* and *NF1* mutation were mutually exclusive. *BRAF* and *TERT* mutations were significantly more frequent in superficial than acral lentiginous melanomas.
In conclusion, we showed that Brazilian melanoma patients exhibit a similar mutation profile to the one reported in other populations. Acral/lentiginous melanoma subtype, which is a common subtype in our setting, showed a distinct mutation frequency. Further analysis will extend to other relevant genes and will also include the study of additional genomes to reach the goal of genomic landscape of 100 Brazilian melanomas cases.