

300P Differential molecular signature in patients from African origin with triple-negative breast cancer

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Background: Breast cancer (BC) is more aggressive in pre-menopausal women of Black race (BW). These women usually have worse prognosis and higher mortality rate when compared with patients of other races, even when socioeconomic factors are accounted for. Triple-negative BC (TNBC), the most aggressive and less treatable BC, due to the lack of therapeutic targets, such as oestrogen and progesterone receptor or HER2, is more frequently diagnosed in these young BW.

Methods: To identify the driving biological factors of this racial disparity we performed a comprehensive differential gene expression (DGE) analysis using the R package edgeR and RNA-sequencing BC data from The Cancer Genome Atlas, which has specifically USA data. In a total of 1097 BC patients, 183 are BW, 32 with TNBC (17.5% of all BW); 757 are White, 69 with TNBC (9.1%); and 61 are Asian, 8 with TNBC (13.1%).

Results: DGE between BW with TNBC and TNBC patients of other races revealed 251 up- and 269 downregulated genes (adjusted p-value ≤ 0.05 , $|\log_2(\text{Fold Change})| \geq 1$, applied in all the analysis). To remove genes associated with race alone and not with TNBC in BW per se, we performed a DGE analysis between all non-TNBC cases in BW and all non-TNBCs in the other races, resulting in 315 up- and 139 downregulated genes in non-TNBCs of BW. Common genes between the two analyses were identified and extracted from the first list, resulting in 198 up- and 250 downregulated genes exclusively differentially expressed in TNBC of BW. Our candidates include genes related to insulin-resistance and obesity (e.g. FBXO2 [p-adj = 2.07E-04, $\log_2\text{FC} = 1.58$], POU2AF1 [p-adj = 1.80E-03, $\log_2\text{FC} = 1.43$]), and epithelial-mesenchymal transition and metastasis (e.g. FOXF2 [p-adj = 9.51E-05, $\log_2\text{FC} = 1.39$], NOTCH3 [p-adj = 9.51E-05, $\log_2\text{FC} = 1.35$]). These genes are being validated using formalin-fixed paraffin-embedded TNBC tissues from BW, collected from different Portuguese hospitals and from a Mozambican hospital, where tumour tissue is compared to normal adjacent tissue by qRT-PCR, immunohistochemistry and Western blot.

Conclusions: Our work will unveil the molecular signature(s) that characterise and define molecularly TNBC in BW and, ultimately, will guide the development of new therapeutics for this unmet medical problem.

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