Association between levels of 5-hydroxymethylcytosine and clinical/histopathologic features in locally advanced breast cancer: Results from the biomarkers breast cancer cohort of Mexican women (2012-2015)

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Breast cancer is a leading cause of cancer death in the world. In developing countries, most patients are still diagnosed in locally advanced stages (LABC), which highlight the importance of identifying prognostic and predictive biomarkers. In this study, we determined the level of 5-hydroxymethylation (5hmC) in the biopsy at diagnosis. Then, we determined its association with clinical and histopathologic characteristics in a prospective cohort of LABC patients (N=84), diagnosed between 2012 and 2015; using a semi-quantitative enzyme-linked immunosorbent assay. We found a statistically significant association between low 5hmC levels with histological grade: Mean %5hmC in low grade tumors 0.17%, (95% CI 0.07-0.26%), intermediate-grade tumors 0.15% (95% CI 0.10-0.19%), high grade tumors 0.066% (95% CI 0.05-0.08%; p<0.001). We also observed an association between 5hmC levels with histological type: Invasive ductal carcinoma 0.10% (95% CI 0.07-0.12%) vs. non-ductal invasive carcinoma 0.22% (95% CI 0.07-0.36; p=0.008). Additionally, we found a negative and significant association with Ki67 (β=-0.012, standard error [SE]=0.0061, p=0.047), a known marker for cellular proliferation. Multivariate analysis confirmed the association between lower levels of 5hmC with age (β=-0.066, SE=0.031, p=0.036) and histological grade (β=-1.197, SE=0.589, p=0.042). No association was observed with therapeutic response or free-relapse survival, probably attributed to only 2-3 years of follow-up, and to few deaths (N=2) and relapse (N=7) that have been observed. This is the first report on the association between levels of 5hmC with the histological type and histopathologic grade in a prospective cohort of LABC. Our findings suggest that 5hmC levels may be a potential biomarker for tumor aggressiveness in LABC.

Biography
Diddier Prada graduated as Medical Doctor from the Universidad Industrial de Santander, Colombia. Then, he pursued a PhD in Biomedical Science at the Universidad Nacional Autónoma de México (UNAM). He was a Post-doctoral Fellow at Harvard T.H. Chan School of Public Health, from 2013 to 2016; his stay included one-year and a half as Research Associate in the laboratory of Environmental Epigenetics in the Department of Environmental Health. He is currently working as Associate Researcher at the National Cancer Institute of Mexico, and he is also Associate Professor of Biomedical Informatics in the Faculty of Medicine at the UNAM. He has published papers in highly reputed peer-reviewed journals (e.g. Circulation, Environmental Research, and Environmental Health Perspectives). He has also published one book and five chapters in internationally recognized books, plus one that is currently in press dipradao@incan.edu.mx

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