ID: 00763
Type: POSTER
Topic: 1. Epigenomic and cancer

DNA methylation as a predictive marker of response to treatment in TNBC patients

Begoña Pineda Merlo[1] , Angel Diaz-Lagares[2] , Jose Alejandro Perez-Fidalgo[3] , Elisa Alonso[4] , Ines Gonzalez[3] , Eduardo Tormo Martin[5] , Anna Adam Artigues[1] , Paula Cabello[1] , Iris Garrido[1] , Birlipta Pattanayak[1] , Octavio Burgues[4] , Manel Esteller[6] , Ana Lluch[3] , Pilar Eroles[1]

1) Institute of Health Research (INCLIVA), Valencia, Spain 2) Cancer Epigenomics-Translational Medical Oncology Group (Oncomet), Health Research Institute of Santiago (IDIS), Santiago de Compostela, Galicia, Spain 3) Hospital Clinico Universitario de Valencia, Valencia, Spain 4) Phatology Deparment, Hospital Clinico Valencia, Valencia, Spain 5) CIBERONC : Centro de Investigación Biomédica en Red Cáncer 6) Institut d'Investigación Biomedica de Bellvitge (IDIBELL), Barcelona, Spain

INTRODUCTION:Triple negative breast cancer (TNBC) presents an aggressive phenotype. Currently TNBC patients are treated with chemotherapy (CT) because there is no specific treatment for TNBC. Because of that, it is important to find treatment response markers and therapeutic targets that help in the diagnosis and treatment of the disease. Some studies suggest that the predictive ability of complete pathological response (RCB = 0) in TNBC patients treated with neoadjuvant CT is approximately 30%. DNA methylation may play an important role in the response to treatment in TNBC.
OBJECTIVE: to study methyloma in TN patients and to find potential epigenetic markers of response to treatment.
METHODS: 24 patients with TNBC treated with neoadjuvant chemotherapy were grouped according to their RCB (residual cancer burden) in responders (RCB = 0) and non-responders (RCB> 0). A methyloma study (Infinium HumanMethylation450 array, Illumina) was performed from the DNA of tumor biopsies prior to treatment. Differentially methylated genes obtained from this study were validated by pyrosequencing (PyroMark Q96 System version 2.0.6, Qiagen) in an independent cohort of TN patients (N = 30) and in TN cell lines (basal and treated with demethylating agents). In the same way, expression studies (qPCR) of the validated genes were performed.
RESULTS: Array analysis showed a different methylation pattern between responder and non-responder patients. Selecting those differentially methylated CpGs located only in promoter regions, 9 genes (genes 1 to 9) were identified: 6 presented higher methylation in non-responder patients (genes 1 to 6) and 3 greater methylation in responders (genes 7 to 9). These genes were related to cellular functions such as the epithelial-mesenchymal transition, cell migration and the Wnt and Hedgehog pathways. After validation, the predictive ability of methylation of two genes (genes 7 and 8) to treatment response(RCB = 0) or absence of response (RCB ? 0) was evaluated using a statistical model by constructing an ROC curve (0.91, CI95%= 0.805- 1) obtaining a predictive capacity of complete pathological response of 60%. Gene expression studies correlated with methylation levels in both patients and cell lines.
CONCLUSIONS: DNA methylation may be a predictive marker of response to treatment in TNBC and could be important to the clinic from the point of view that it would allow the selection of patients who do not benefit from the current treatment and therefore would be candidates for other alternative treatments.