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Glucocorticoid signaling is a molecular mechanism to define the heterogeneity of different subtypes of breast cancer

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Glucocorticoid (GC) signaling has emerged as a major mechanism to regulate breast cancer (BC) development and responsiveness to therapy. Since GC is commonly administrated as a co-treatment during BC chemotherapy with controversial chemoresistant or pro-survival activities, it is imperative to elucidate specific functions of glucocorticoid receptor (GR) in different subtypes of BC. By using BC pathway specific gene expression array in this study, we identified that luminal A (MCF-7) and triple negative (MDA-MB-231) subtype BC cells showed different gene expression patterns to dexamethasone (Dex, synthetic GC) treatment. MDA-MB-231 cells showed more Dex-regulated genes than MCF-7 cells. Shared by both cells, the highly regulated genes are those involved in cell adhesion, epithelial-mesenchymal transition (EMT), signal transduction, cell division and apoptosis, including SERPIN-E1, CDKN2A, c-Myc, Snai2, THBS1 and E-cadherin. Real-time cell assay revealed that Dex promoted MDA-MB-231 cell adhesion and migration but not for MCF7 cells, suggesting the cell-specific effects of GC/GR in different subtypes of BC. As the interaction of GR with NFkB plays an important role in the anti-inflammatory activity of GC, the expression of NFkB target genes upon Dex treatment was also examined. Distinct patterns of Dex regulation were identified again in MCF7 and MDA-MB-231 cells, wherein NFkB was trans-repressed by GC/GR in MCF7 cells but not in MDA-MB-231 cells. Different GR phosphorylation, localization, and activation patterns were identified to be a mechanism underlying the differential effects of GC. The results from this study will help improve the selective use of GC and the personalized therapy of BC.

Biography

Jun Ling obtained his PhD degree in Biochemistry and Molecular Biology from Shanghai Institute of Biochemistry and Cell Biology, Chinese Academy of Sciences. He finished his Post-doctoral research at University of California, Riverside. Currently he is an Assistant Professor at the Commonwealth Medical College. He has published over fifty peer-reviewed papers and currently serves as an Executive Editor for an OMICS group journal *(Biochemistry and Analytical Biochemistry)*.

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