A novel subgroup of estrogen receptor positive breast cancer may benefit from Super-Enhancer guided patient selection for retinoic acid receptor agonist treatment

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Aims: A recent reanalysis of a large public breast cancer dataset revealed a subset of patients whose estrogen receptor (ER) and HER2 status were discordant [1]. These patients showed increased efficacy or prolonged benefit from retinoic acid receptor (RAR) agonists in the treatment of ER+/HER2- breast cancer. We assessed whether the ER+/HER2- subgroup of patients could be defined by molecular profiling. Methods: A cohort of 42 primary breast cancer patients with discordant ER and HER2 status were profiled using a trascriptome-wide high-resolution screen. Gene expression changes were stratified into two categories: super-enhancers (SEs) with high RARA expression and those with low RARA expression. Results: A subset of patients defined by high super-enhancer expression responds to RARA agonists. Conclusion: Super-enhancer profiling may be linked to improved survival in patients with discordant ER and HER2 status.


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