



**Susan G. Komen
Research Grants – Fiscal Year 2014**

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Combinatorial adaptive resistance therapy in breast cancer

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Lead Organization: UT M.D. Anderson Cancer Center

Grant Mechanism: KS

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Public Abstract:

The ability to target HER2 with Herceptin or lapatinib has greatly improved outcomes for patients with amplified HER2. Unfortunately only a subset of breast cancer patients with amplification of HER2 benefit from therapies targeting HER2. We have new data that indicates that when cells are cultured in systems that mimic the growth of tumors in patients, resistance to targeted drugs is due to signals induced by the drug itself. The striking observation is that targeting the events induced by the drugs results in a massive death of the tumor cells. We call this ability to identify rational combinations of drugs combinatorial adaptive response therapy or CART. We have explored CART with three drugs targeting the HER2 family (Iressa, Lapatinib and Neratinib). This has led to discovery of a number of possible combinations that could increase the activity of each of these drugs. We will explore this further to identify rational drug combinations that would increase the response of patients to HER2 targeted drugs