Susan G. Komen
Research Grants – Fiscal Year 2014

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Investigation of ILF2 as a novel breast cancer therapeutic target

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Lead Organization: Stanford University
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Public Abstract:
Many breast cancer cells rely on the overproduction of oncoproteins to help them survive, grow, resist therapeutic drugs, and invade nearby tissues. Some of these overexpressed oncoproteins are on the surface of cancer cells and have been used as targets for therapy (e.g. HER2 receptor), but many of these proteins are located inside of cells and are not easily targeted by current drugs (e.g. c-MYC). Many oncoproteins including those that are not easily targeted by current drugs are produced using a "backdoor" method of protein synthesis; this process is called alternative (cap-independent) translation. An alternative approach to inhibiting these oncoproteins and thereby kill cancer cells or cause them to be more sensitive to current drug therapies is to prevent or interrupt their production by targeting the proteins involved in alternative translation. The overall goal of this proposal is to examine whether proteins called IRES-transactivating factors (ITAFs), which play a necessary role in alternative translation, can be effective drug targets. This proposal specifically examines one of these ITAFs, interleukin enhancer factor 2 (ILF2), that we have recently determined to be correlated with basal breast cancer and has a negative correlation with lung relapse free survival. Basal breast cancer currently has no effective targeted drug treatments and is enriched in underserved populations including African American and younger women. This particular ITAF is also important in that it controls proteins known to be involved in breast cancer drug resistance. This project is focused on "closing the backdoor" that breast cancer cells use to produce oncoproteins. The investigator will use advanced techniques to inhibit ILF2, and then analyze the effects on breast cancer cells using laboratory tests and preclinical modeling in mice. In addition, clinical specimens from breast cancer patients will be analyzed to determine the usefulness of this therapeutic idea. If successful, this study will reveal whether ILF2 is relevant to breast cancer patients as either a biomarker and/or therapeutic target and its potential as an intervention point to treat breast cancer. It will also provide critical information for future drug targeting strategies.