Peptidomimetic Inhibitors of the Estrogen Receptor – Steroid Recruitment Coactivator Interaction

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The estrogen receptor (ER) belongs to the nuclear receptor family of proteins, which serve as ligand-dependent transcription factors. Several diseases, including breast and uterine cancer, can result from increased expression of genes controlled by the ER. The traditional approach to inhibition of estrogen receptor activity uses antagonists (e.g. tamoxifen) to prevent ER from recruiting transcription machinery. However, cancer cells develop a functional resistance to tamoxifen treatment, resulting in recurrence. Inhibition of the ER – steroid recruitment coactivator (SRC) protein provides a novel therapeutic target. Peptidomimetic molecules have functional groups that have the same relative spatial orientation as the side groups of the target protein. Choosing the appropriate location for substitution on a teraryl scaffold allows for mimicry for the *i*, *i* + 3, and *i* + 4 residues of an α-helix. A library of diaryloxazoles is being developed using aryl iodides, amino acids and benzoic acids.