Determining Most Effective Method of Inhibiting Breast Cancer Inducing Protein RAD52, Year 2

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The BRCA1/2 proteins and the RAD52 protein are part of the DNA damage response pathway. Breast cancer can be caused by mutations to the BRCA1/2 pathway. RAD52 and BRCA1/2 are synthetically lethal: the loss of RAD52 in BRCA1/2 mutated cells leads to apoptosis. RAD52 inhibition allows for the selective killing of tumor cells; healthy cells are unaffected. A list of potential molecular ligand inhibitors for RAD52 was identified during the previous year of research. The ligand molecules were tested on mutated versions of the protein structure to determine the scope of the inhibition capability. Each mutated protein structure was first tested, using a control set of molecules, to ensure that ligand interaction was altered. A delta-G-bind value was calculated for each interaction, converting it to quantifiable data. A Chi-Square (x2) Goodness of Fit statistical analysis test was conducted to determine significant differences between wild-type and mutated structure affinity. Mutations such as B:156 Glutamic Acid (x2=319.53) and A:144 Histidine (x2=289.98) showed a statistically significant difference in control molecule affinity. Molecules such as 384 ChemDiv 6661 (delta-G-bind-wild= -27.93, x2=6.068) and Asinex 3943 (delta-G-bind-wild= -24.55, x2=1.029) displayed strong interaction capabilities with the mutated structures. These results suggest that select ligand inhibitors can interact with both the wild-type and mutated versions of the RAD52 protein structure. These interactions could alter the protein structure and inhibit function: leading to tumor cell death and the eradication of the tumor. Further in vitro and in vivo research will be conducted to validate these in silico findings.