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Hedgehog and Tyrosine Kinase inhibitors for treating breast cancer

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Majority of breast cancer patients relapse and progress to metastatic disease despite initial response to chemotherapy. The reasons for chemoresistance include presence of cancer stem cell (CSC) sub-populations possessing tumorigenic potential and upregulated oncogenic pathways. Therefore, the objective of this study was to investigate the anti-proliferative effects of two tyrosine kinase inhibitors (afatinib and gefitinib) and two hedgehog inhibitors (vismodegib and cyclopamine) to identify potential synergistic combinations for treating breast cancer. The effect of afatinib, gefitinib, cyclopamine and vismodegib on the growth of breast cancer cells in vitro was first examined. Using a combination of MTT assay, isobologram analysis and response surface modeling, combination of afatinib or gefitinib with vismodegib or cyclopamine was observed to be synergistic in their ability to inhibit breast cancer cell growth. This effect was found to be dose, time, cell line and schedule dependent. Also, since the anticancer agents studied are extremely hydrophobic, polymeric micelles were fabricated using lactic acid and carbonate based copolymers to improve drug solubility. Polymeric micelle formulations were found to increase the aqueous solubility of these compounds several fold.

Biography

Michael K Danquah, MS, PhD, is an Assistant Professor of Pharmaceutical Sciences at Chicago State University College of Pharmacy (CSU-COP). He obtained his Master's degree in Chemical Engineering from the University of Kentucky, and a PhD in Pharmaceutics and Drug Delivery from the University of Tennessee Health Science Center. His research interests include: (i) Design and synthesis of novel biodegradable polymers for drug and nucleic acid delivery. He has several peer-reviewed journal articles, serves as an Editorial Board Member of 5 journals and is the author of the book "*Emerging Trends in Cell and Gene Therapy*".

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