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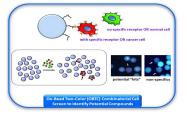
Biochemistry, Glycomics & Amino Acids

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Peptoid-combinatorial strategies to target non-protein biomarkers in the tumor microenvironment

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Chemotherapies are nonspecific and have side effects. Targeted therapies are expensive and fail on larger patient populations due to the heterogeneity of their target protein biomarkers. This suggests that effective cancer treatments need to be either personalized or find universal biomarkers - probably beyond proteins. We have been exploring peptoids as an emerging class of highly bio-compatible synthetic molecules as future drug leads. Peptoids are serum stable, non-immunogenic, cell permeable, easy to synthesize and optimize. Also, the cost of peptoid development is significantly lower than for small organic molecules, peptides and antibodies. We design and synthesize large on-bead peptoid combinatorial libraries and developed a



unique on-bead two-color (OBTC) cell screen to directly identify most specific compounds targeting biomarkers on the cell surface. As an approach to overcome the protein biomarker heterogeneity problem, we applied our OBTC assay at an unbiased fashion and identified a lipid- phosphatidylserine (PS) binding peptoid. PS is universally found on the outer layer of tumor endothelium and on many cancer cells as compared to normal cells. Our peptoid is found to be cytotoxic on various tumor types such as lung, breast and prostate and not on normal cells, indicating a wider but tumor specific treatment method.

Biography

Gomika Udugamasooriya has been working in the fields of Medicinal Chemistry and Chemical Biology and is trained in both Rational Drug Design and High Throughput Combinatorial Approaches. He has been exploring peptoids, an emerging class of biologically amenable and easy to synthesize peptidomimetics with great drug-like properties focusing on cancer treatment and imaging. The development of a unique on-bead two-color (OBTC) combinatorial cell screen to directly identify the highest specificity ligands for cell surface biomarkers was one of the major milestones in his career.

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