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The identification of highly potent peptide scaffolds for the treatment of hormone resistant prostate cancer

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The risk of prostate cancer in men has grown significantly over the last 5 years while the chemotherapeutic market for prostate cancer treatment is a $5 billion dollar global industry. The growth of hormone sensitive cases of cancer treatment failure has motivated the rise of alternative approaches to its chemotherapeutic treatment. One such approach involves targeting the microtubule-associated protein/microtubule affinity-regulating kinase 4 (MARK4) protein. MARK4 is a kinase involved in signal transduction and is a possible chemotherapeutic target for prostate cancer treatment. Peptides possess a large chemical space that can rapidly identify potent scaffolds for drug design strategies. We populated a virtual library of over 50,000 unique, lead-like synthesisable peptides suited to drugging the MARK4 catalytic ATP recognition site using DerivatizeME an in-house development virtual library builder. High-throughput virtual screening of the virtual library identified 100 hits based on binding probabilities expressed as molecular docking binding energies. Rapid simulation based screening of these hits identified 10 highly potent peptide scaffolds for chemical synthesis in order to identify peptide inspired drug precursors. Further interrogation of these hits for the treatment of hormone resistant prostate cancer through perturbing signal transduction via targeting the MARK4 protein will enable us to be better positioned to win the war against prostate cancer.

HPC content

We employed rapid simulation and evaluation of hit candidates using HPC architecture.

We employed the massively paralleled high-throughput virtual screening of a large virtual library using the CHPC architecture.

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