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In This Issue

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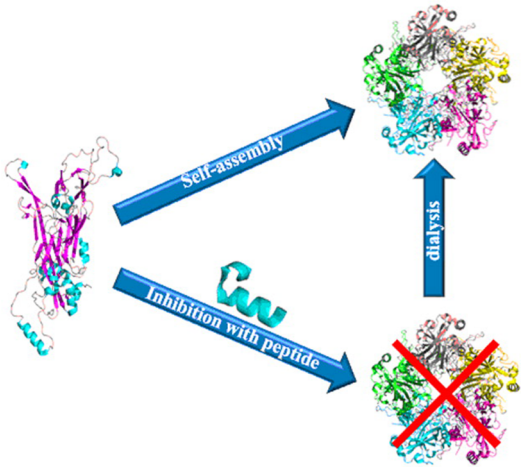
PEPTIDE INHIBITORS FOR HPV

Human papillomaviruses (HPVs) are known to cause cervical cancer. In spite of the availability of vaccine, HPV infection remains a major global health burden due to limitations with the current HPV vaccine. As such, there remains a need for a cost-effective and broad-spectrum protective agent for different HPV subtypes.

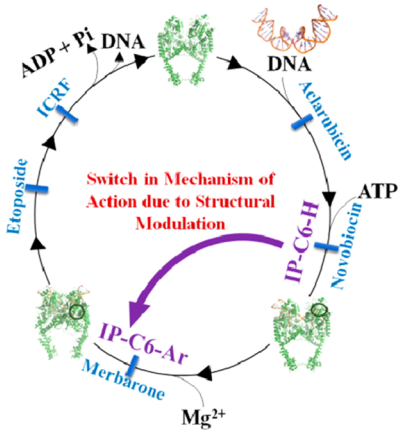
Previous study has identified a specific binding segment, helix 5 of HPV 16L1, which is a potential new target. Here, Fu et al. (DOI: 10.1021/ml500392y) reports a peptide targeting this helix, which shows nanomolar inhibitory activity. Further, this peptide exhibited activity against different HPV subtypes. The study paves the way for prospective high-efficiency, broad-spectrum inhibitors of HPV, which might be developed as a new class of agents for anti-HPV, and can be extended to other viruses.



"CHOICE-BASED CHANGE" STRATEGY FOR DRUG DISCOVERY

DNA topoisomerase plays an important role in various DNA processes. Currently, about 50% of chemotherapeutic regimens use at least one drug that targets DNA topoisomerases.

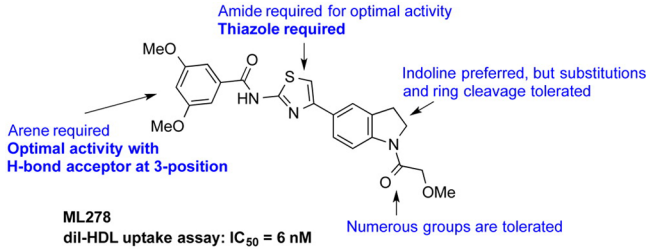
Featured on the cover is the study by Baviskar et al. (DOI: 10.1021/acsmedchemlett.5b00040), illustrating an unprecedented target-specific ligand-structural modulation approach that offers "choice-based change" in mode of inhibition of an enzyme. The authors describe the synthesis and characterization of selective inhibitors of hTopoIIα, while not showing TopoI inhibition and DNA binding. The reported ligands were found to be more potent than an hTopoIIα-inhibiting anticancer drug etoposide against cancer cells, while relatively less toxic to normal cells. A set of important residues has also been explored for the first time. Such unprecedented strategy will encourage research on "choice-based change" in target-specific mode of action for rapid drug discovery.



NEW INHIBITORS OF SCAVENGER RECEPTOR-BI

High-density lipoprotein (HDL) particles are well-known as the "good cholesterol". HDL delivers excess cholesterol to the liver, where it can be processed. The transfer of the cholesterol occurs when HDL particles dock to Scavenger Receptor B, Type I (SR-BI); however, this transfer mechanism is poorly understood.

Here, Dockendorff et al. (DOI: 10.1021/ml500154q) report on the new class of small molecule inhibitors of SR-BI, called "indoline-thiazoles". While there have been many previously reported inhibitors, these compounds are shown to have improved potency and are not cytotoxic. These compounds can not only serve as tool compounds for studying lipid trafficking but also as entry inhibitors against parasites and viruses that hijack SR-BI to invade vulnerable cells.



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