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Design of semisynthetic analogues and 3D-QSAR study of eunicellin-based diterpenoids as prostate cancer migration and invasion inhibitors

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ABSTRACT

Prostrate cancer constitutes the second leading cause of cancer deaths in men in United States. Eunicellin-based diterpenoids are important bioactive marine natural products isolated from corals of alcyonaria species. The bioactivities of eunicellin diterpenes were correlated with their chemical structures. Recently eunicellin diterpenes from the Red Sea soft coral Cladiella pachyclados showed significant anti-migratory and anti-invasive activities against prostate cancer in wound-healing and Cultrex® invasion models. These results encouraged the semisynthetic and 3D-QSAR studies of this unique marine natural product class as possible hits for the control of metastatic prostate cancer. Ten new semisynthetic analogues of cladiellisin (1) were prepared. These include C-6 carbamoylation and Δ11−17 epoxidation. Carbamate analogues of 1 showed potent anti-migratory and anti-invasive activities against PC-3 cells. Comparative Molecular Field Analysis (CoMFA) and Comparative Molecular Similarity Indices Analysis (CoMSIA) were performed using SYBYL 8.1 program package to create a valid 3D-QSAR model to guide future design of potent eunicellin diterpenes cancer migration inhibitors. Eunicellin-based diterpenes are potential marine natural hits appropriate for optimization as inhibitors of metastatic prostate cancer.