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Computational Analysis Comparison Prediction of Anticancer Peptide (ACP)

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Abstract: ***Anticancer peptides (ACPs) contain short peptides composed of 10–60 amino acids that can inhibit tumors cell proliferation or migration, or suppress the formation of tumors blood vessels, and are less likely to cause drug resistance. The aforementioned merits make ACPs the most promising anti-cancer candidate. ACPs may be degraded by proteases and result in cytotoxicity in many cases. To overcome these drawbacks, a plethora of research has focused on the reconstruction or modification of ACPs to improve their anti-cancer activity, while reducing their cytotoxicity. ACPs modification mainly includes main chain reconstruction and side-chain modification. After summarizing the classification and mechanism of action of ACPs, this paper focuses on recent development and progress in their reconstruction and modification. The information collected here may provide some ideas for further research on ACPs, in particular their modification. ACPs were extracted from various search engines like PubMed, Google scholar and Patent lens. Specific searches were carried out using a combination of keywords like 'ACPs', 'antitumor peptides', 'anti-angiogenic peptides', 'anti-metastatic peptides' and 'host defence peptides. The comprehensive information related to a peptide like its source of origin, nature of the peptide, anticancer activity, N- and C-terminal modifications, conformation, etc. Additionally, CancerPPD provides information on around 249 types of cancer cell lines and 16 different assays used for testing the ACPs. In natural peptides, CancerPPD contains peptides having non-natural, chemically modified residues and D-amino acids. Besides this primary information, CancerPPD stores predicted tertiary structures as well as peptide sequences in SMILES format.***

Keywords: ACP (Anticancer Peptide),Therapeutic peptide, Sequence Alignment, Insilco method, structure Analysis.

I. INTRODUCTION

Cancer comprises a collection of diseases caused by the excessive proliferation of cells in the body that cannot be effectively regulated. Cancer is the most an emerging issue in the last decades had been reported. There are multiple methodologies had been presented to resolve this issue. The most widely used treatment is chemotherapy which involves the use of the drug at an interval of time injected into the patient body. The rapid cancer diving cells they are excepted in induce side effects on the normal cell to divide at the same rate. The most adverse effect of the drug is that it shows not only kills the cancer-causing cell but is also responsible for presenting its impact on the normal cells and tissue causing a downfall in the immunodeficiency system of the individual. (Chen et al., 2016). As a result of the discovery of peptide-based therapeutics come into existence the world has a subcategory of it anti-cancer peptide drugs. In the over decade 7000 naturally occurring peptides have been discovered which are responsible for repairing cancer and also bioactivities, and comparing it with normal cells the cancer cell membrane exhibits a larger surface because the number of microvilli increases, the negative charge of the cell membrane and higher membrane fluidity.(Tyagi et al., 2015). many therapeutic cells include DNA alkylating agents, hormone agonists and antimetabolites presenting an insufficient selectively and sequentially unspecific targeting of healthy cells and showing the deleterious. Many occurrences of myelosuppressionthrombocytopenicnic (decreased production of types of blood cells), mucositis (inflammatory events on digestive tracts) due to non–selective targeting of cells from bone marrow, gastrointestinal tracts and hair follicles. (L & F, 2005). Solid tumours without cysts or liquids areas, distinguish malignant cells and stroma where these cells maintained. The tumour masses are represented by phenotypically heterogeneous populations of cancer cells having its own ability in perforating and forming new tumours. NRC-03 and NRC-07 are two peptides from AMP pleurocidin family with activity against human breast cancer cells including healthy cell even intratumoral administration. Peptides able to binds the cancer cells and cause membrane effects through negatively charged molecules exposed on the cells membrane, heparin and chondroitin sites. The secondary alpha helix structure represent the conservation modification of peptides' backbone structure. The selectivity inhibitors proliferation of prostate and bladder cancer cell with low cyto alpha-helical activity for normal murine fibroblasts and alpha-helical conformation features for achieving an anti-cancer effect. Cell – permeable lipopeptidess CR116 that inhibits the PDZ domain of GIPC protein which is over

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expressed in breast and pancreas tumours interferences decreased proliferations , cytotoxic effects and apoptosis on breast and pancreas cancer cells . The upregulations induces an increased tumorigenicity of cancer cells in rodents models downregulations kills cancer cells renders them susceptible to apoptosis. The basic available instance in the market is buforinIIb which displays activity against 60 human tumour cell lines fused with a modified margainin sequenced, a negative charge equilibrate the overall positive change of buforin II , generating peptides turn linked by octapeptides which are expressed in tumour tissues allowing the realises of buforinIIb The cancer present formed in breast cancer are classified as leukaemia, myeloma and lymph nodes indicate non- solid tumours take advantages from electrostatic attraction NK-2 peptides derived from the cationic core regions of NK -3 has contain the positive charge and selectively kills cancer cells by necrotic mechanisms.

There are various computational analysis tools are constructed like AntiCP.ACPP, iACP, Li and Wang's method for detection of the peptides in the individuals. The most recent used methods introduced by Kabir et al developed the Target ACP for solving the problem of class imbalance presented by integrating sequential and evolutionary profile information as input and features using SVM as a classifier.

II. ANTICANCER PEPTIDES

It does not damage the normal body cell and their physiological function. They have greater selectivity and specificity.it has small peptides and usually contains 5 to 30 amino acids. These are cationic and interact with the anionic nature of the cancer cell. The main advantage is that it has a very short span half-life to decrease the probability of resistance, lowered toxicity, higher specificity and good solubility and penetrating ability. The main problem lies in its Vivo stability and high cost for production. The cationic amino acids like lysine, arginine and histidine can disrupt and help in penetrating the membrane of cancer cell. Cytotoxicity is done by the anions like glutamic and as aspartic acids. The secondary structure of the ACPs is responsible or peptide cancer cell membrane that interact leads to cancer cell disruption and cell deaths. Membrane disruption occurred either by pore formation in lipds membrane, thinning of membrane bilayer, membrane dissolution or lipids peptides domain formation.(Xu et al., 2013). Small molecules with efficient tissue penetration uptake by heterogeneouscancercells , endowed or either synergizing with existing therapeutics as excepted resulted in increased anticancer drugs higher selectively for neoplastic cells. In order to develop the machine learning approach for detection is done by the main two ways – 1.support vector machine (AntiCP, Harjisharifi, ACPP, iACP, Li) and ensemble approach (MLACP, ACPred, PTPD)(Wei et al., 2019). These belong to the category of antimicrobial peptides which have very low antigenicity proprieties. The cell targets are basically of two main types 1. First one includes peptides active against microbial and cancer cells while not being active against microbial while active against healthy cell such as cecropins and margins. The second include ACPs that are against three type's microbial, normal and cancerous cells(Papo& Shai, 2005). Various models are been proposed for a better understanding the determine the computation approaches –

SVM – developed by Tyagi, using amino acid composition and binary profile using input. the basic idea is to construct a hyperplane to maximize the margin between the positive dataset and the negative dataset.(Tyagi et al., 2015)

Hajisharifi –using Chou pseudo composition and local amino acid kernel-based methods

a) ANOVA (analysis of variance) - select the optimal features among the g-gap dipeptide composition, which measure the features variances by calculating the ratio (F-value) of features between groups and within groups. (Chen et al., 2016)

ACPred Fuse – a random forest model in conjunction with 114 features descriptors, trained to generate class information and probabilistic information used for developing a final high qualitybenchmarks datasets having largest number of peptides , thereby increasing the accuracy as well as shedding light on character tics governing anticancer activities peptides. The used of novel scoring card methods for effective and simple prediction and determination of peptides affording anticancer activity using only sequenced information. It ACPs is identify using the weighed sum score between the composition and propensity scores which is easily understood implemented by researcher.(Khatun et al., 2020)the ability of small cationic molecules disrupting and permeating dependent on the biophysical properties such as peptides secondary structures, overall net charge , amphipathic and balance between hydrophobic and polar regions.

The continuous augmentation and enrichment of ACP-related research is a strong positive signal in the research and development of new anti-tumors drugs; however, due to the special anti-tumor mechanisms of ACPs, shows the activity, toxicity and targeted efficacy for further improvement. In modern medicine, science and technology, the reconstruction and modification of ACPs have also achieved gratifying results in every single method has its own limitations. Therefore, the evaluation strategy of ACPs should be sufficiently comprehensive to attain maximum efficiency. Constant exploration and finding solutions to the many negative effects are warranted so as to create a new screening system of ACPs. Collectively, additional research is needed to better guide further modification and application development of specific ACPs. The precise mode actions dependent on the beta sheet hairpin structure and electrostatic forces as well as hydrophobic interactions which were already factors for AMP activity. SVS-1 peptide, small

designed anticancer peptides, folds only at surface of cancer cells and pore formations. SVS-1 showed cytotoxic against lung, epidermal and breast carcinoma cells and low toxicity against healthy cells (Berge et al., 2010).bacterial membrane charge coincides closely related to minimal inhibitory concentration values. (Alves et al., 2010). SVS-1 studies together with other conducted with different types of peptides show that antitumor cell activities actually not parallel AMPs mode of actions and that differences should be accepted. Theinsertion of bulky hydrophobic amino acids on cell membrane hydrophobic core with acquisition of stable structure driving events for pore formations , in which the cell deaths results of different apoptosis and necrosis which are charactertics by different cellular morphological changes. The analysis of ACPs cancer and healthy cells using microscopy and fluorescence tools common search for cell shrinkages or swelling, chromatin condensation, cytoplasmic vacuoles or even membrane blabbing. The synthesized AMP epinecidin – I selectively kills cancer cells at low concentrations and studies of necrosis inhibition test. Dermaseptin B2 necrosis inducing peptides which increased lactate dehydrogenases release, positive staining with propidium iodide (PI) as well as confocal microscopy studies points to necrotic mechanisms which in turn might be induced after binding and disruption of plasma membrane. The active healthy mammalian cells found in the tissue of epithelial tumors are associated with tumor necrosis when expressed intratumorally showed expression of mature HNP-1 in mature form may inhibits and eradicated tumors revels potential peptides that targets or mimic hormonal receptors and hormonal regulated gens for treating cancer . The ability of series of compounds formed by synthetics membranes disrupting peptides and 15 amino acids segments of beta chains chrionicgonadrotropin receptors , which have the ability to destroys metases and disseminated cells derived from human prostate cancer xenografts in nude mice and cells died by necrosis as revealed by histological examinations.

III. AS MENTIONED BELOW TWO DATABASES ARE BEEN EXPLAINED IN A BRIEF MANNER

A. iACP database

When compare with Hajisharifi methods – achieve a higher overall success rate and stability. Thebenchmark contains 138 ACPs and 206 non – ACP.The overall accuracy correlation coefficient obtained is 92.67%.it was the first computational method based on informative features. The use of support vectors machine and pseudo amino acids is used for model building and follows the concepts of evolutionary intelligent genetic algorithm-based ensemble models for improving the true classification rate.

The heat map system - the row and column represent thefirst and second amino acid residue of 1-gap dipeptides the heat map represents one of 400 1-gap dipeptides and the F score is used to analyse the. the construction of boxes represent by colour in which the blue box denotesa positive correlation with ACP and red box denotes the positively correlated by non – ACP and green box denote the irrelevant features of anti-cancer peptides and the score is 0. The 1 gap dipeptides are responsible for and associated with the anticancer peptides properties of ACPs and cancer cells.(Chen et al., 2016)

Web serve step for identifying the iACP –

1) http://lin.uestc.edu.cn/servder/iACP
2) enter the query peptides sequence in FASTA format
3) the first outcome query sequence is Anticancer peptides and the outcome for the second query is non- anticancer peptides
4) Data button to download the benchmark dataset or independent dataset used and ACP predictor and for relevant paper, documentation click on citation button.

As a Material and Method apply bioinformatics database Overview the structural analysis diversity of three classes of anticancer peptides. Each structure is labeled as common name in Protein Data Bank (PDB ID) have identification but. In cases where the PDB ID was not available, the SWISS-MODEL server (available at: https://swissmodel.expasy.org/)

Analyzing the characteristics of ACPson important amino acids and dipeptides commonly found in ACPs by using simple composition analysis approaches without the use of experimental methods. For instance, Tyagi et al. reported results of residue preference at 10 N-terminus and 10 C-terminus by using the sequence logos. When analysis Leu and Lys were typically found at the N-terminus while Cys, Leu and Lys were typically found at the C-terminus. Chen et al.that amino acids including Lys, Ile, Cys, Glu, and Gly were abundant in ACPs as compared to non-ACPs.

IV. CONCLUSION

ACP prediction model called ACP-DA is effective prediction model, we concatenated BPFs and the AAindex to represent peptide sequences. Performed data augmentation in the feature space and used the augmented data to train the prediction model. The experimental results show that the proposed method can effectively distinguish ACPs and non-ACPs. Compared with the method without data augmentation, ACP-DA achieves better performance. ACP-DA will be a useful tool for the discovery of novel potential ACPs.

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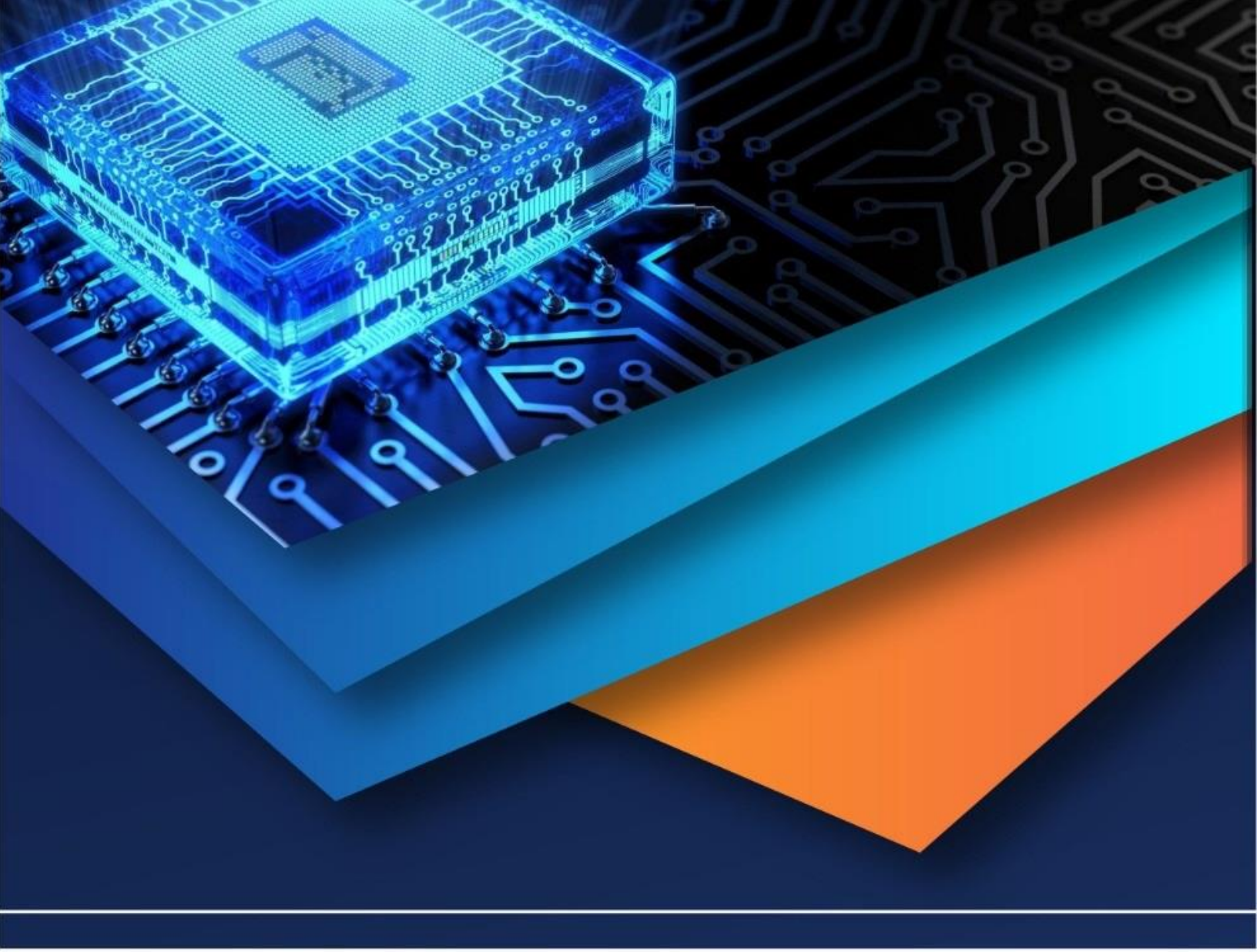
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