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An Unprecedented Revolution in Medicinal Science

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Abstract: With the explosive growth of biological sequences in this century, medicinal science has been undergoing an unprecedented revolution. Driven by the avalanche of biological sequences generated in the postgenomic age, medicinal science is currently undergoing an unprecedented revolution [1,2], as indicated by, but not limited to, the following four aspects.

I. Post Biological Sequence Modification

Cancer and many other major diseases are often caused by a variety of subtle protein modifications, typically by various different post-translational modifications (PTMs or PTLM) in proteins [3,4]. In order to reveal their pathological mechanisms and find new and revolutionary strategies to treat them, many efforts have been made with the aim to predict the possible modified sites in various proteins concerned (see, e.g., [5-12] and a recent review paper [13]). Meanwhile, to provide efficient tools for the aforementioned researches, the pseudo amino acid composition (PseAAC) [14] and general PseAAC [15] were proposed. And the corresponding web-servers have been established [16-19] that can be used by researchers to generate various different modes of PseAAC to catch the key features of protein/peptide sequences according to their needs. The concept of PseAAC and its approaches to deal with protein/peptide sequences have been widely used in medical science and related areas (see, e.g., [11,20-46] as well as the Editorial [47] for a special Molecular Science issue focused on "Drug Development and Biomedicine"). Similar subtle modifications, the post-replication modification (PTRM) and post-transcription modification (PTCM), also occur respectively in DNA [48] and RNA sequences [49], causing many major diseases as well. Actually, considerable endeavors to develop high-throughput tools for predicting the possible modified sites of DNA/RNA sequences have also been underway (see, e.g., [1,13,50,51].

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II. Genome Analysis

Genetic disorders are illnesses caused by one or more abnormalities in the genome, or by changes or variants in genes. To help understand these kinds of genetic or genomic diseases and find revolutionary therapeutic strategies to treat them, many in-depth genome analyses have been carried out recently (see, e.g., [52-69] and a review paper [70]). During the process of the aforementioned studies, inspired by the successes of using PseAAC in dealing with protein/peptide sequences, the pseudo K-tuple nucleotide composition or PseKNC was proposed to formulate various feature vectors for DNA/RNA sequences [71]. And the corresponding web-servers have been established as well [72-75], which can be used by researchers to do the same in computational genomics and genome analysis as done in computational proteomics and proteome analysis.

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III. Personalized Medicine

Different patients may have different responses to the same drug in clinical treatments even they have the same plasma concentration. The reports from World Health Organization (WHO) indicates that, the percentages of patients having bad responses by using the marketed drugs are 10% ~20%, of which 5% are dead [76]. These kinds of bad responses are mainly due to individual differences, a formidable barrier against clinical treatments and pharmaceutical industry. Therefore, it is an inevitable direction to develop personalized medicines [77-80]. To realize this, it is important to establish personalized medical profile including personal genome, genetic, or genomic data. Personal genomics is the branch of genomics concerned with the sequencing and analysis of the genome of an individual. Again, the aforementioned tools are very useful in this regard..

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IV. Drug-Target Interactions within Cellular Networking

Identifying drug-target interaction is one of the key steps for developing new medicines [81]. A typical tool used for this is molecular docking simulation (see, e.g., [52,82-95]). To conduct molecular docking, however, an indispensable entity is a reliable 3D (three dimensional) structure of the target protein. Although X-ray crystallography is a powerful tool in determining protein 3D structures, not all proteins can be successfully and timely crystallized, particularly for membrane proteins. Although NMR is a very powerful tool for determining the 3D structures of membrane proteins as reported by a series of recent publications (see, e.g., [96-102]), it is time-consuming as well. To timely acquire the 3D structural information, one has to resort to various structural bioinformatics tools [90], including the homologous modelling approach as utilized for a series of protein receptors urgently needed during the drug-developing process [103-110] and other computational modelling methods [111-113]. Unfortunately the number of dependable templates for developing high quality 3D protein structures via homology modelling is very limited [90], while the 3D structure developed purely by the approach of energy minimization or molecular dynamics without a good initial template might be far from the

true structure owing to the local minimization problems. To pre-exclude those compounds, which are not likely to interact with the target proteins concerned, some sequence-based methods (see, e.g., [28,33,35,114,115] and a review paper [116]) have been developed that can serve to predict the interaction of the drug compounds with various kinds of target proteins in cellular networking. These newly developed methods can help us enormously in reducing the search scope and speeding up the pace of developing new drugs [117].

References and Notes

Chou, K. C. Impacts of bioinformatics to medicinal chemistry, *Medicinal Chemistry*, **2015**, *11*, 218-234.

[2] Zhou, G. P. *et al.* Perspectives in Medicinal Chemistry, *Current Topics in Medicinal Chemistry*, **2016**, *16*, 381-382.

[3] Foster, M. W. *et al.* Protein S-nitrosylation in health and disease: a current perspective, *Trends Mol Med*, **2009**, *15*, 391-404.

[4] Uehara, T. *et al.* S-nitrosylated protein-disulphide isomerase links protein misfolding to neurodegeneration, *Nature*, **2006**, *441*, 513-517.

[5] Xu, Y. *et al.* iSNO-PseAAC: Predict cysteine S-nitrosylation sites in proteins by incorporating position specific amino acid propensity into pseudo amino acid composition *PLoS ONE*, **2013**, *8*, e55844.

[6] Xu, Y. *et al.* iSNO-AAPair: incorporating amino acid pairwise coupling into PseAAC for predicting cysteine S-nitrosylation sites in proteins, *PeerJ*, **2013**, *1*, e171.

[7] Qiu, W. R. *et al.* iMethyl-PseAAC: Identification of Protein Methylation Sites via a Pseudo Amino Acid Composition Approach, *Biomed Res Int (BMRI)*, **2014**, *2014*, 947416.

[8] Xu, Y. *et al.* iHyd-PseAAC: Predicting hydroxyproline and hydroxylysine in proteins by incorporating dipeptide position-specific propensity into pseudo amino acid composition, *Int. J. Mol. Sci.*, **2014**, *15*, 7594-7610.

[9] Xu, Y. *et al.* iNitro-Tyr: Prediction of nitrotyrosine sites in proteins with general pseudo amino acid composition, *PLoS ONE*, **2014**, *9*, e105018.

[10] Qiu, W. R. *et al.* iUbiq-Lys: Prediction of lysine ubiquitination sites in proteins by extracting sequence evolution information via a grey system model *Journal of Biomolecular Structure and Dynamics (JBSD)* **2015**, *33*, 1731-1742.

[11] Jia, C. *et al.* Prediction of Protein S-Nitrosylation Sites Based on Adapted Normal Distribution Bi-Profile Bayes and Chou's Pseudo Amino Acid Composition, *Int J Mol Sci*, **2014**, *15*, 10410-10423.

[12] Zhang, J. *et al.* PSNO: Predicting Cysteine S-Nitrosylation Sites by Incorporating Various Sequence-Derived Features into the General Form of Chou's PseAAC, *Int J Mol Sci*, **2014**, *15*, 11204-11219.

[13] Xu, Y. *et al.* Recent progress in predicting posttranslational modification sites in proteins, *Curr Top Med Chem*, **2016**, *16*, 591-603.

[14] Chou, K. C. Prediction of protein cellular attributes using pseudo amino acid composition, *PROTEINS: Structure, Function, and Genetics (Erratum: ibid., 2001, Vol.44, 60)*, **2001**, *43*, 246-255.

[15] Chou, K. C. Some remarks on protein attribute prediction and pseudo amino acid composition (50th Anniversary Year Review), *J. Theor. Biol.*, **2011**, *273*, 236-247.

[16] Shen, H. B. *et al.* PseAAC: a flexible web-server for generating various kinds of protein pseudo amino acid composition, *Anal. Biochem.*, **2008**, *373*, 386-388.

[17] Du, P. *et al.* PseAAC-Builder: A cross-platform stand-alone program for generating various special Chou's pseudo-amino acid compositions, *Anal. Biochem.*, **2012**, *425*, 117-119.

[18] Cao, D. S. *et al.* propy: a tool to generate various modes of Chou's PseAAC, *Bioinformatics*, **2013**, *29*, 960-962.

[19] Du, P. *et al.* PseAAC-General: Fast building various modes of general form of Chou's pseudo-amino acid composition for large-scale protein datasets, *International Journal of Molecular Sciences*, **2014**, *15*, 3495-3506.

[20] Zhou, X. B. *et al.* Using Chou's amphiphilic pseudo-amino acid composition and support vector machine for prediction of enzyme subfamily classes, *J. Theor. Biol.*, **2007**, *248*, 546–551.

[21] Esmaeili, M. *et al.* Using the concept of Chou's pseudo amino acid composition for risk type prediction of human papillomaviruses, *J. Theor. Biol.*, **2010**, *263*, 203-209.

[22] Yu, L. *et al.* SecretP: Identifying bacterial secreted proteins by fusing new features into Chou's pseudo-amino acid composition, *J. Theor. Biol.*, **2010**, *267*, 1-6.

[23] Mohammad Beigi, M. *et al.* Prediction of metalloproteinase family based on the concept of Chou's pseudo amino acid composition using a machine learning approach, *Journal of Structural and Functional Genomics*, **2011**, *12*, 191-197.

[24] Nanni, L. *et al.* Identifying bacterial virulent proteins by fusing a set of classifiers based on variants of Chou's pseudo amino acid composition and on evolutionary information, *IEEE-ACM Transaction on Computational Biolology and Bioinformatics*, **2012**, *9*, 467-475.

[25] Zia-ur-Rehman *et al.* Identifying GPCRs and their Types with Chou's Pseudo Amino Acid Composition: An Approach from Multi-scale Energy Representation and Position Specific Scoring Matrix, *Protein & Peptide Letters*, **2012**, *19*, 890-903.

[26] Gupta, M. K. *et al.* An alignment-free method to find similarity among protein sequences via the general form of Chou's pseudo amino acid composition, *SAR QSAR Environ Res (SAR AND QSAR IN ENVIRONMENTAL RESEARCH)*, **2013**, *24*, 597-609.

[27] Khosravian, M. *et al.* Predicting Antibacterial Peptides by the Concept of Chou's Pseudo-amino Acid Composition and Machine Learning Methods, *Protein & Peptide Letters*, **2013**, *20*, 180-186.

[28] Min, J. L. *et al.* iEzy-Drug: A web server for identifying the interaction between enzymes and drugs in cellular networking, *BioMed Research International (BMRI)*, **2013**, *2013*, 701317.

[29] Mohabatkar, H. *et al.* Prediction of Allergenic Proteins by Means of the Concept of Chou's Pseudo Amino Acid Composition and a Machine Learning Approach, *Medicinal Chemistry*, **2013**, *9*, 133-137.

[30] Chou, K. C. Using amphiphilic pseudo amino acid composition to predict enzyme subfamily classes, *Bioinformatics*, **2005**, *21*, 10-19.

[31] **Pacharawongsakda, E.** *et al.* Predict Subcellular Locations of Singleplex and Multiplex Proteins by Semi-Supervised Learning and Dimension-Reducing General Mode of Chou's PseAAC, *IEEE Transactions on Nanobioscience*, **2013**, *12*, 311-320.

[32] Xiao, X. *et al.* iAMP-2L: A two-level multi-label classifier for identifying antimicrobial peptides and their functional types, *Anal. Biochem.*, **2013**, *436*, 168-177.

[33] Xiao, X. *et al.* iGPCR-Drug: A web server for predicting interaction between GPCRs and drugs in cellular networking, *PLoS ONE*, **2013**, *8*, e72234.

[34] Ding, H. *et al.* iCTX-Type: A sequence-based predictor for identifying the types of conotoxins in targeting ion channels, *BioMed Research International (BMRI)*, **2014**, *2014*, 286419.

[35] Fan, Y. N. *et al.* iNR-Drug: Predicting the interaction of drugs with nuclear receptors in cellular networking, *Intenational Journal of Molecular Sciences (IJMS)*, **2014**, *15*, 4915-4937.

[36] Hajisharifi, Z. *et al.* Predicting anticancer peptides with Chou's pseudo amino acid composition and investigating their mutagenicity via Ames test, *J. Theor. Biol.*, **2014**, *341*, 34-40.

[37] Li, L. *et al.* Prediction of bacterial protein subcellular localization by incorporating various features into Chou's PseAAC and a backward feature selection approach, *Biochimie*, **2014**, *104*, 100-107.

[38] Ahmad, S. *et al.* Identification of heat shock protein families and J-protein types by incorporating dipeptide composition into Chou's general PseAAC, *Computer methods and programs in biomedicine*, **2015**, *122*, 165-174.

[39] Ali, F. *et al.* Classification of membrane protein types using voting feature interval in combination with Chou's pseudo amino acid composition, *J. Theor. Biol.*, **2015**, *384*, 78-83.

[40] Dehzangi, A. *et al.* Gram-positive and Gram-negative protein subcellular localization by incorporating evolutionary-based descriptors into Chou's general PseAAC, *J. Theor. Biol.*, **2015**, *364*, 284-294.

[41] Fan, G. L. *et al.* DSPMP: Discriminating secretory proteins of malaria parasite by hybridizing different descriptors of Chou's pseudo amino acid patterns, *J. Comput. Chem.*, **2015**, *36*, 2317-2327.

[42] Khan, Z. U. *et al.* Discrimination of acidic and alkaline enzyme using Chou's pseudo amino acid composition in conjunction with probabilistic neural network model, *J. Theor. Biol.*, **2015**, *365*, 197-203.

[43] Kumar, R. *et al.* Prediction of beta-lactamase and its class by Chou's pseudo-amino acid composition and support vector machine, *J. Theor. Biol.*, **2015**, *365*, 96-103.

[44] Liu, B. *et al.* PseDNA-Pro: DNA-binding protein identification by combining Chou's PseAAC and physicochemical distance transformation, *Molecular Informatics*, **2015**, *34*, 8-17

[45] Sanchez, V. *et al.* A new signal characterization and signal-based Chou's PseAAC representation of protein sequences, *Journal of bioinformatics and computational biology*, **2015**, 1550024.

[46] Chou, K. C. Pseudo amino acid composition and its applications in bioinformatics, proteomics and system biology, *Current Proteomics*, **2009**, *6*, 262-274.

[47] Zhong, W. Z. *et al.* Molecular science for drug development and biomedicine, *Intenational Journal of Molecular Sciences*, **2014**, *15*, 20072-20078.

[48] Kobayashi, Y. *et al.* DNA methylation profiling reveals novel biomarkers and important roles for DNA methyltransferases in prostate cancer, *Genome Research*, **2011**, *21*, 1017-1027.

[49] Cantara, W. A. *et al.* The RNA Modification Database, RNAMDB: 2011 update, *Nucleic Acids Res.*, **2011**, *39*, D195-201.

[50] Liu, Z. *et al.* iDNA-Methyl: Identifying DNA methylation sites via pseudo trinucleotide composition, *Analytical Biochemistry (also, Data in Brief, 2015, 4: 87-89)*, **2015**, *474*, 69-77.

[51] Chen, W. *et al.* iRNA-Methyl: Identifying N6-methyladenosine sites using pseudo nucleotide composition *Analytical Biochemistry (also, Data in Brief, 2015, 5: 376-378)*, **2015**, *490*, 26-33.

[52] Cai, L. *et al.* Identification of Proteins Interacting with Human SP110 During the Process of Viral Infections, *Medicinal Chemistry*, **2011**, *7*, 121-126.

[53] Chen, W. *et al.* iNuc-PhysChem: A Sequence-Based Predictor for Identifying Nucleosomes via Physicochemical Properties, *PLoS ONE*, **2012**, *7*, e47843.

[54] Cai, L. *et al.* Prostate Cancer with Variants in CYP17 and UGT2B17 Genes: A Meta-Analysis, *Protein & Peptide Letters*, **2012**, *19*, 62-69.

[55] Chen, W. *et al.* iRSpot-PseDNC: identify recombination spots with pseudo dinucleotide composition *Nucleic Acids Res.*, **2013**, *41*, e68.

[56] Chen, W. *et al.* iTIS-PseTNC: a sequence-based predictor for identifying translation initiation site in human genes using pseudo trinucleotide composition, *Anal. Biochem.*, **2014**, *462*, 76-83.

[57] Chu, W. Z. *et al.* Apolipoprotein E gene variants of Alzheimer's disease and vascular dementia patients in a community population of nanking, *Med Chem* **2014**, *10*, 783-788.

[58] Chen, W. *et al.* iSS-PseDNC: identifying splicing sites using pseudo dinucleotide composition, *Biomed Research International (BMRI)*, **2014**, *2014*, 623149.

[59] Guo, S. H. *et al.* iNuc-PseKNC: a sequence-based predictor for predicting nucleosome positioning in genomes with pseudo k-tuple nucleotide composition, *Bioinformatics*, **2014**, *30*, 1522-1529.

[60] Lin, H. *et al.* iPro54-PseKNC: a sequence-based predictor for identifying sigma-54 promoters in prokaryote with pseudo k-tuple nucleotide composition, *Nucleic Acids Res.*, **2014**, *42*, 12961-12972.

[61] Qiu, W. R. *et al.* iRSpot-TNCPseAAC: Identify recombination spots with trinucleotide composition and pseudo amino acid components, *Int J Mol Sci (IJMS)*, **2014**, *15*, 1746-1766.

[62] Cai, L. *et al.* Gestational influenza increases the risk of psychosis in adults, *Medicinal Chememistry*, **2015**, *11*, 676-682.

[63] Liu, B. *et al.* Identification of real microRNA precursors with a pseudo structure status composition approach, *PLoS ONE*, **2015**, *10*, e0121501.

[64] Liu, B. *et al.* iMiRNA-PseDPC: microRNA precursor identification with a pseudo distance-pair composition approach, *Journal of Biomolecular Structure & Dynamics (JBSD), doi:10.1080/07391102.2015.1014422*, **2015**.

[65] Liu, B. *et al.* iEnhancer-2L: a two-layer predictor for identifying enhancers and their strength by pseudo k-tuple nucleotide composition, *Bioinformatics*, **2015**, doi:10.1093/bioinformatics/btv1604.

[66] Liu, B. *et al.* Identification of microRNA precursor with the degenerate K-tuple or Kmer strategy *Journal of Theoretical Biology*, **2015**, *385*, 153-159.

[67] Liu, J. *et al.* Association of EGF rs4444903 and XPD rs13181 polymorphisms with cutaneous melanoma in Caucasians, *Medicinal Chemistry*, **2015**, *11*, 551-559.

[68] Cai, L. *et al.* Modulation of cytokine network in the comorbidity of schizophrenia and tuberculosis, *Curr Top Med Chem*, **2016**, *16*, 655-665.

[69] Zhu, Y. *et al.* Antithrombin is an importantly inhibitory role against blood clots, *Curr Top Med Chem*, **2016**, *16*, 666-674.

[70] Chen, W. *et al.* Pseudo nucleotide composition or PseKNC: an effective formulation for analyzing genomic sequences, *Mol BioSyst*, **2015**, *11*, 2620-2634.

[71] Chen, W. *et al.* PseKNC: a flexible web-server for generating pseudo K-tuple nucleotide composition, *Anal. Biochem.*, **2014**, *456*, 53-60.

[72] Chen, W. *et al.* PseKNC-General: a cross-platform package for generating various modes of pseudo nucleotide compositions, *Bioinformatics*, **2015**, *31*, 119-120.

[73] Liu, B. *et al.* repDNA: a Python package to generate various modes of feature vectors for DNA sequences by incorporating user-defined physicochemical properties and sequence-order effects, *Bioinformatics*, **2015**, *31*, 1307-1309.

[74] Liu, B. *et al.* repRNA: a web server for generating various feature vectors of RNA sequences *Molecular Genetics and Genomics, DOI:10.1007/s00438-015-1078-7*, **2015**.

[75] Liu, B. *et al.* Pse-in-One: a web server for generating various modes of pseudo components of DNA, RNA, and protein sequences *Nucleic Acids Res.*, **2015**, *43*, W65-W71.

[76] Wang, J. F. *et al.* Review: Pharmacogenomics and personalized use of drugs, *Current Topics of Medicinal Chemistry*, **2008**, *8*, 1573-1579.

[77] Wang, J. F. *et al.* 3D structure modeling of cytochrome P450 2C19 and its implication for personalized drug design, *Biochem Biophys Res Commun (BBRC) (Corrigendum: ibid, 2007, Vol.357, 330)*, **2007**, *355*, 513-519.

[78] Wang, J. F. *et al.* Molecular modeling of two CYP2C19 SNPs and its implications for personalized drug design, *Protein & Peptide Letters*, **2008**, *15*, 27-32.

[79] Wang, J. F. *et al.* Review: Structure of cytochrome P450s and personalized drug, *Current Medicinal Chemistry*, **2009**, *16*, 232-244.

[80] Wang, J. F. *et al.* Structure of cytochrome p450s and personalized drug, *Curr Med Chem*, **2009**, *16*, 232-244.

[81] Knowles, J. *et al.* A guide to drug discovery: Target selection in drug discovery, *Nat Rev Drug Discov*, **2003**, *2*, 63-69.

[82] Chou, K. C. *et al.* Binding mechanism of coronavirus main proteinase with ligands and its implication to drug design against SARS. (Erratum: ibid., 2003, Vol.310, 675), *Biochem Biophys Res Comm (BBRC)*, **2003**, *308*, 148-151.

[83] Zhou, G. P. *et al.* NMR studies on how the binding complex of polyisoprenol recognition sequence peptides and polyisoprenols can modulate membrane structure, *Current Protein and Peptide Science*, **2005**, *6*, 399-411.

[84] Du, Q. S. *et al.* Molecular modelling and chemical modification for finding peptide inhibitor against SARS CoV Mpro, *Anal. Biochem.*, **2005**, *337*, 262-270.

[85] Huang, R. B. *et al.* An in-depth analysis of the biological functional studies based on the NMR M2 channel structure of influenza A virus, *Biochem. Biophys Res Comm. (BBRC)*, **2008**, *377*, 1243-1247.

[86] Du, Q. S. *et al.* Energetic analysis of the two controversial drug binding sites of the M2 proton channel in influenza A virus, *J. Theor. Biol.*, **2009**, *259*, 159-164.

[87] Wei, H. *et al.* Investigation into adamantane-based M2 inhibitors with FB-QSAR, *Medicinal Chemistry*, **2009**, *5*, 305-317.

[88] Du, Q. S. *et al.* Designing inhibitors of M2 proton channel against H1N1 swine influenza virus, *PLoS ONE*, **2010**, *5*, e9388.

[89] Wang, S. Q. *et al.* Insights from investigating the interaction of oseltamivir (Tamiflu) with neuraminidase of the 2009 H1N1 swine flu virus, *Biochemical and Biophysical Research Communications (BBRC)*, **2009**, *386*, 432-436.

[90] Chou, K. C. Review: Structural bioinformatics and its impact to biomedical science, *Current Medicinal Chemistry*, **2004**, *11*, 2105-2134.

[91] Liao, Q. H. *et al.* Docking and Molecular Dynamics Study on the Inhibitory Activity of Novel Inhibitors on Epidermal Growth Factor Receptor (EGFR), *Medicinal Chemistry*, **2011**, *7*, 24-31.

[92] Li, X. B. *et al.* Novel Inhibitor Design for Hemagglutinin against H1N1 Influenza Virus by Core Hopping Method, *PLoS One*, **2011**, *6*, e28111.

[93] Ma, Y. *et al.* Design novel dual agonists for treating type-2 diabetes by targeting peroxisome proliferator-activated receptors with core hopping approach, *PLoS One*, **2012**, *7*, e38546.

[94] Wang, J. F. *et al.* Insights from modeling the 3D structure of New Delhi metallo-beta-lactamase and its binding interactions with antibiotic drugs, *PLoS ONE* **2011**, *6*, e18414.

[95] Wang, J. F. *et al.* Insights into the Mutation-Induced HHH Syndrome from Modeling Human Mitochondrial Ornithine Transporter-1, *PLoS One*, **2012**, *7*, e31048.

[96] Berardi, M. J. *et al.* Mitochondrial uncoupling protein 2 structure determined by NMR molecular fragment searching, *Nature*, **2011**, *476*, 109-113.

[97] Schnell, J. R. *et al.* Structure and mechanism of the M2 proton channel of influenza A virus, *Nature*, **2008**, *451*, 591-595.

[98] OuYang, B. *et al.* Unusual architecture of the p7 channel from hepatitis C virus *Nature* **2013** *498*, 521-525.

[99] Call, M. E. *et al.* The structural basis for intramembrane assembly of an activating immunoreceptor complex, *Nature Immunology*, **2010**, *11*, 1023-1029.

[100] Wang, J. *et al.* Solution structure and functional analysis of the influenza B proton channel, *Nature Structural and Molecular Biology*, **2009**, *16*, 1267-1271.
[101] Bruschweiler, S. *et al.* Substrate-modulated ADP/ATP-transporter dynamics revealed by NMR relaxation dispersion, *Nat Struct Mol Biol* **2015**, *22*, 636-641.
[102] Berardi, M. J. *et al.* Fatty acid flippase activity of UCP2 is essential for its proton transport in mitochondria, *Cell metabolism*, **2014**, *20*, 541-552.
[103] Chou, K. C. Modelling extracellular domains of GABA-A receptors: subtypes 1, 2, 3, and 5, *Biochemical and Biophysical Research Communications (BBRC)*, **2004**, *316*, 636-642.
[104] Chou, K. C. Insights from modelling the 3D structure of the extracellular domain of alpha7 nicotinic acetylcholine receptor, *Biochemical and Biophysical Research Communication (BBRC)*, **2004**, *319*, 433-438.
[105] Chou, K. C. Molecular therapeutic target for type-2 diabetes, *Journal of Proteome Research*, **2004**, *3*, 1284-1288.
[106] Chou, K. C. Coupling interaction between thromboxane A2 receptor and alpha-13 subunit of guanine nucleotide-binding protein, *Journal of Proteome Research*, **2005**, *4*, 1681-1686.
[107] Chou, K. C. Insights from modelling three-dimensional structures of the human potassium and sodium channels, *Journal of Proteome Research*, **2004**, *3*, 856-861.
[108] Chou, K. C. Insights from modelling the tertiary structure of BACE2, *Journal of Proteome Research*, **2004**, *3*, 1069-1072.
[109] Chou, K. C. Insights from modeling the 3D structure of DNA-CBF3b complex, *Journal of Proteome Research*, **2005**, *4*, 1657-1660.
[110] Chou, K. C. Modeling the tertiary structure of human cathepsin-E, *Biochem. Biophys. Res. Commun. (BBRC)*, **2005**, *331*, 56-60.
[111] Carlacci, L. *et al.* A heuristic approach to predicting the tertiary structure of bovine somatotropin, *Biochemistry*, **1991**, *30*, 4389-4398.
[112] Chou, K. C. Energy-optimized structure of antifreeze protein and its binding mechanism, *J. Mol. Biol.*, **1992**, *223*, 509-517.
[113] Chou, K. C. The convergence-divergence duality in lectin domains of the selectin family and its implications, *FEBS Lett.*, **1995**, *363*, 123-126.
[114] Xiao, X. *et al.* iCDI-PseFpt: Identify the channel-drug interaction in cellular networking with PseAAC and molecular fingerprints, *J. Theor. Biol.*, **2013**, *337C*, 71-79.
[115] Xiao, X. *et al.* iDrug-Target: predicting the interactions between drug compounds and target proteins in cellular networking via the benchmark dataset optimization approach, *Journal of Biomolecular Structure & Dynamics (JBSD)*, **2015**, *33*, 2221-2233.
[116] Xiao, X. *et al.* Predict drug-protein interaction in cellular networking, *Current Topics in Medicinal Chemistry*, **2013**, *13*, 1707-1712.
[117] Sirois, S. *et al.* Assessment of chemical libraries for their druggability, *Computational Biology & Chemistry*, **2005**, *29*, 55-67.

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