

表6 其它相关计算工具

数据库名称	网址	特征描述
Motif-X	http://motif-x.med.harvard.edu/	该工具是一种用于提取任何序列数据组中过度反应模式的软件工具。
PhosphoBlast ^[67]	http://phospho.elm.eu.org/pELMBlastSearch.html	有了该工具，用户可以查询目的蛋白相关的磷酸化短肽。
RLIMS-P	http://pir.georgetown.edu/pirwww/iprolink/rlimsp.shtml	该工具用于提取蛋白磷酸化相关的蛋白激酶、底物和磷酸化位点相关的信息。
KEA	http://www.nzdl.org/Kea/	该工具可用于激酶富集分析。
DOG 1.0	http://dog.biocuckoo.org/software.php	该工具是一种绘制蛋白结构域图片的工具，图片质量可以达到公开发表的水平。

表7 通过质谱数据检测潜在磷酸化位点的工具

数据库名称	网址	特征描述
PhosphoScore	http://dir.nhlbi.nih.gov/papers/lkem/phosphoscore/	该工具是一种磷酸化分配程序，能够与所有级别的串联质谱兼容。这个程序采用费用函数将匹配度和正常化的丰度与理论值相比较。
Ascore ^[68]	http://ascore.med.harvard.edu/	该工具能够测量正确的磷酸化位点定位的概率。
DeBunker ^[69]	http://fields.scripps.edu/download.php	该工具一种SVM软件，能够自动验证串联质谱得到的磷酸化多肽的数据。
APIVASE 2.2	http://bioanalysis.dicp.ac.cn/proteomics/software/APIVASE.html	该工具通过整合多级质谱数据从而验证多肽磷酸化情况。
InsPecT ^[70]	http://proteomics.ucsd.edu/LiveSearch/	该工具可用于验证磷酸化短肽串联质谱的数据，而无须手动验证。

七、展望

蛋白质的磷酸化修饰是生物体内重要的共价修饰方式之一。磷酸化修饰本身所具有的简单、灵活、可逆的特性以及磷酸基团的供体ATP的易得性，使得磷酸化修饰被真核细胞所选择接受成为一种最普遍的调控手段。蛋白质的磷酸化和去磷酸化这一可逆过程，几乎调节着包括细胞的增殖、发育、分化、细胞骨架调控、细胞凋亡、神经活动、肌肉收缩、新陈代谢及肿瘤发生等生命活动的所有过程，并且可逆的蛋白质磷酸化是目前所知道的最主要的信号转导方式。用蛋白质组学方法研究蛋白质磷酸化，对研究高等真核生物的调控机制非常重要，对于生命科学领域的影响也将是非常远大的。同时，用蛋白质组学方法研究蛋白质磷酸化也处于蛋白质组学和信号转导领域的前沿。

目前已知有许多人类疾病是由于异常的磷酸化修饰所引起，而有些磷酸化修饰却是某种疾病所导致的结果。在心血管系统中，部分蛋白激酶通过与AT II、ET-1、PDGF等多种血管活性物质的相互调控，影响血管平滑肌细胞和内皮细胞的功能和结构，直接参与心血管疾病的发展。用蛋白磷酸化酶抑制剂防治动脉粥样硬化、高血压、冠脉痉挛和心肌缺血等疾病的研究得到了显著效果。蛋白磷酸化酶抑制剂防治心血管病研究的初步成果令人鼓舞，但是还需要更多的临床试验证实这些发现。作为一类全新的药物，蛋白磷酸化酶抑制剂很有希望为心血管疾病的防治开辟一条新的途径。

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