SH3-spot: a new method to predict the specificity of interaction of protein domains.

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We developed a procedure able to evaluate the binding specificity of an SH3 domain (Pawson and Gish, 1992; Pawson and Schlessinger, 1993) sequence. The procedure is based on informations extracted from the position-specific contacts derived from eight SH3-peptide or SH3-protein complexes of known structure. The framework of SH3-peptide contacts defined on the structure of the complexes is enriched with the residue-residue interaction data obtained from phage displayed libraries (Rodi and Makowski, 1999) and from literature. An SH3-specific matrix is built with the frequences of position specific contacts. The matrix is then used to score any peptide or protein sequence, or database of protein sequences against the sequence of a given SH3 domain.
In silico panning experiments were performed between different SH3 sequences and a database of decapeptides, a protein sequence or a database of protein sequences.
The results of the method are very promising. More interestingly, we expect its predictive power to increase with the enrichment of the SH3-specific matrix with interaction data derived from new complex structures or phage display experiments or literature.
The procedure was developed on the SH3 domain family and its application can easily be extended to other families of protein domains (such as: SH2, MHC, PH, PDZ etc.).

Pawson, T. and Gish, G.D. (1992). SH2 and SH3 domains: from structure to function. Cell, 71, 359-362.
Pawson, T. and Schlessinger, J. (1993). SH2 and SH3 domains. Curr. Biology, 3:434-442.
Rodi, D.J. and Makowski, L. (1999). Phage-display technology--finding a needle in a vast molecular haystack. Curr .Opin. Biotechnol., Feb 10:1, 87-93.