Selection of Proteins for Structure Determination with NMR Spectroscopy

Wojciech Augustyniak[1], Lukasz Slabinski[2], Lukasz Jaroszewski[3]

[1] The Scripps Research Institute, 10550 North Torrey Pines Road, La Jolla, CA 92037, USA

[2] Silesian University of Technology, Gliwice, Poland

[3] Burnham Institute for Medical Research, 10901 North Torrey Pines Road, La Jolla, CA 92037, USA

An appropriate target selection is used for increasing the success rate of structure determination in structural genomics. The initial selection must be based on bioinformatics criteria and these criteria are studied here in detail to establish reliable filter for selection of proteins suitable for structure determination using NMR spectroscopy.

It was assumed that the targets suitable for structure determination shall be similar to the proteins solved by NMR spectroscopy. To avoid the competition with X-ray crystallography, the convenient targets shall also differ from proteins solved by crystallographers. The appropriate protein characteristics were identified in order to select targets fulfilling these two major requirements. The procedure consisted of the following steps:

1) Variety of protein parameters were calculated starting from amino acid sequences. The compared parameters includes for example: occurrence of amino acids residues and predicted physicochemical parameters.

2) Distribution of proteins versus each calculated parameter was computed.

3) The obtained distributions were compared between proteins solved by NMR spectroscopy and i) annotated proteins - to identify the properties favored by NMR spectroscopists; and ii) proteins solved by X-ray crystallography - to find the parameters disfavored by crystallographers.

4) The selected protein parameters were used to construct a filtering function for target selection. The function i) calculates the parameters; and ii) computes the score for each parameter; the score reflects the extent to which the protein shall be favored by NMR.

The obtained results yielded in-depth insights into preferences of NMR spectroscopists and X-ray crystallographers. These findings resulted in creation of a filtering function, which will facilitate target selection for NMR spectroscopy in the future.

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