BEYOND GENOMES: STRUCTURE AND FUNCTION OF HUMAN CANCER-RELATED PROTEINS

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Representing an initiative in human cancer structural proteomics, the aim of this work is the characterization of putative cancer-related proteins through their 3D structure determination using solution Nuclear Magnetic Resonance (NMR). Using the tool SAGE anatomical viewer, approximately 100 out of 729 poorly characterized genes were identified with high variance of expression level between normal and neoplasic human tissues, based on the differential expression analysis of their corresponding ESTs. From this initial group we selected fifteen potential NMR targets that had no significant similarity of amino acid sequence with proteins that had their 3D structure determined, had less than 25 kDa, and did not have predicted transmembrane regions. The cDNA sub-cloning of these targets was performed for heterologous expression in *Escherichia coli*. A second round of screening included: 1- selection of the best clone and best expression conditions that give the highest level of soluble recombinant protein production; 2- gel filtration chromatography to access the aggregation state of the targets, and 3- 1D ^{1}H NMR to identify well folded proteins. Our screening procedure identified seven unfolded proteins with high tendency of oligomerization, and one well-folded target that had its 3D structure determined recently by solution NMR. The second round of screening of the other targets had begun.

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