BMC Bioinformatics

BioMed Central

Poster presentation

Open Access

Computational methods to identify novel methyltransferases

Tanya C Petrossian and Steven G Clarke

Address: Department of Chemistry and Biochemistry and the Molecular Biology Institute, University of California, Los Angeles, California, 90095-169, USA

from Fifth International Society for Computational Biology (ISCB) Student Council Symposium
Stockholm, Sweden 27 June 2009

Published: 19 October 2009

BMC Bioinformatics 2009, **10**(Suppl 13):P7 doi: 10.1186/1471-2105-10-S13-P7

This article is available from: http://www.biomedcentral.com/1471-2105/10/S13/P7

Background

1.2% of the yeast genes are estimated to encode enzymes that catalyze the transfer of a methyl group from *S*-adenosylmethionine (AdoMet) to protein, nucleic acid, lipid, and small molecule substrates [1]. These enzymes function in biosynthesis, regulating metabolic pathways, and controlling gene expression, including writing the histone code. BLAST and MEME/MAST analysis using the amino acid sequence of motifs have previously generated a list of putative Class I methyltransferases [2]. Recently we have used a combination of a new search algorithm and structural information to refine this analysis [3]. This study utilizes these updated methods of identifying motifs and scanning the proteome to predict new members of the different families of methyltransferases in different organisms. These new members may function in novel pathways or new modes of regulation.

Materials and methods

Advanced hidden Markov models (HMM) profiles, predicted secondary structures, and solved crystal structures are used to identify the AdoMet-binding motifs of the different families of methyltransferases [1,3]. To generate a list of putative methyltransferases, we used both our newly developed program "Multiple Motif Scanning" [3,4] and HHpred [5]. Sequence similarity networks are then used to predict the probable substrates for the putative methyltransferases [3]. Additionally, several of the candidate methyltransferases were incubated with radioactive AdoMet to reveal binding by detection of the radioactive protein-ligand via SDS-PAGE separation [1].

Conclusion

The putative list of methyltransferases for *S. cerevisiae* among four of the methyltransferases families are italicized (see Table 1). Known methyltransferases are shown for only the SET and SPOUT families. Several putative methyltransferases are found to bind AdoMet through UV-crosslinking experiments (designated * in Table 1). This approach validated previously suggested putative enzymes and additionally identified several new candidates [3]. Extending this analysis to the human proteome surprisingly reveals little expansion of family members (Figure 1). Our goal is to enhance the functional identification of novel methyltransferases by providing lists of the best candidates for biochemical analyses.

Table 1: Proteins classified into four families of methyltransferases

Seven-Beta Strand (Class I) (Not shown here are 33 known species)		SET	SPOUT	N6-Adenosine
YBR141C	*YLR137W*	Set1	Trm10	*Ime4*
YBR225W	*YMR209C**	Set2	Mrm1	*Kar4*
*YBR261C**	*YMR228W*	*Set3*	Trm3	*YGR001C*
YBR271W	*YNL022C*	*Set4*	*Emg1*	
YDR316W	*YNL024C*	*Set5*	*YGR283C*	
*YHR209W**	*YNL092W*	*Set6*	*YMR310C*	
YIL064W	*YOR239W*	Rkm1	*YOR021C*	
YIL110W		Rkm2		
*YJR129C**		Rkm3		
*YKL155C**		Rkm4		
YKL162C		Ctm1		
YLR063W				*YHL039W*

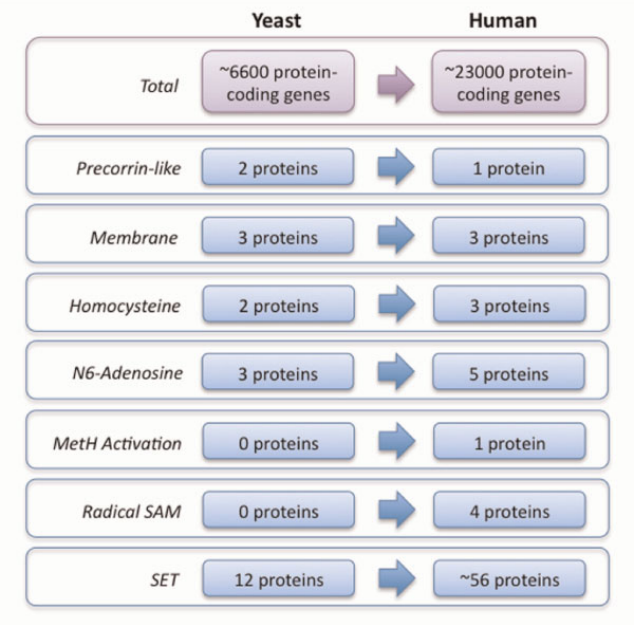

Figure 1
Comparison of the number of known and putative yeast and human methyltransferases in several families.

Acknowledgements

This research was supported by the National Institutes of Health Grant GM026020 and the Office of Science (BER), U.S. Department of Energy, Grant No. DE-FG02-06ED64270. T.C.P. was supported by the UCLA Chemistry-Biology Interface Training Grant GM008496.

References

1. Petrossian TC and Clarke SG: **Bioinformatic identification of novel methyltransferases.** *Epigenomics* 2009 in press.
2. Katz JE, Dlakić M and Clarke S: **Automated identification of putative methyltransferaess from genomic open reading frames.** *Mol Cell Proteomics* 2003, **2:**525–540.
3. Petrossian TC and Clarke SG: **Multiple Motif Scanning to identify methyltransferases from the yeast proteome.** *Mol. Cell. Proteomics* 2009, **8:**1516–1526.
4. **Multiple Motif Scanning.** http://www.chem.ucla.edu/files/Motif-Setup.Zip.
5. Söding J, Biegert A and Lupas AN: **The HHpred interactive server for protein homology detection and structure prediction.** *Nucleic Acids Res* 2005, **33:**W244–W248.