s1.m5.p19 **Structural Studies of WD Repeat Proteins.** David K. Wilson, David Cerna, A. Yarrow Madrona and Walter Voegtli, *Section of Molecular & Cellular Biology, University of California, Davis, USA. E-mail: dave@alanine.ucdavis.edu*

Keywords: Protein interaction; Beta Propeller; WD40 repeat

WD repeats (also known as beta-transducin or WD40 repeats) are ~40 amino acid sequence motifs that are weakly conserved and have been found in hundreds of mostly eukaryotic proteins. In general, they appear to function by mediating the protein-protein interaction involved in a large and diverse number of physiologically relevant processes. WD repeat proteins are coded for by a significant portion of well-characterized genomes, more than 1% in the case of budding yeast and nearly 2% in other eukaryotes. The structure of the beta subunit of the G protein has previously defined the structure for this family of proteins as a beta-propeller. Each WD repeat effectively generates one blade of the propeller which is composed of a four-stranded beta-sheet. Structures of G-beta and several other proteins have demonstrated that seven of these repeats yield seven blades in the propeller. Examination of genomic data indicates that perhaps the majority of these proteins have fewer or more than seven repeats. Is the beta propeller motif able to accommodate a variable number of blades or are the sequences of some WD repeats unrecognizable within a stable, 7-bladed fold?

In order to understand the structural diversity of this family, we have determined the crystal structures of four WD-repeat proteins with greater and less than seven repeats as identified by sequence. Functionally, these proteins are completely unrelated, playing roles in the mitotic checkpoint (Bub3p), mRNA degradation (Ski8p), actin depolymerization (Aip1p) and histone deacetylation (Sif2p). Surprisingly, almost all of these contain domains that fold into the canonical seven-bladed motif implying that many of these repeats may not be identified by sequence using current criteria. Since similar structure often indicates similar function, the regions of the WD repeat proteins responsible for partner protein binding are being mapped using a variety of techniques. A common surface area seems to be emerging on the "top" of the propeller, a region that is composed of many loops. These loops are not as well conserved as the core of the propeller suggesting that modulation of the protein interaction surface specificity can be easily altered without affecting the overall structure, reminiscent of what is seen in antibodies.

s1.m6.p1 **Structure and function of the fatty acid binding protein (Sm14) from *Schistosoma mansoni*, a vaccine canditate.** Angelucci, F., Bellelli, A., Johnson, K.A., Baiocco, P., Miele, A.E., Gourlay, L., *Valle, C., *Liberti , P.,* Cioli, D., Tsernoglou, D. and Brunori, M., *Dept. of Biochemical Sciences "A. Rossi Fanelli", Univ. Of Rome "La Sapienza", Italy, *Institute of Cell Biology, National Research Council, Rome, Italy. E-mail: francesco.angelucci@uniroma1.it*

Keywords: Schistosomiasis; Vaccine; Fatty acids

Schistosoma mansoni fatty acid binding protein (Sm14) is one of the six candidates to prepare a vaccine against schistosomiasis, the second most prevalent parasitic disease in humans [1]. Schistosome is unable to synthetize fatty acids, and thus the supply depends on its host [2]. Available data support the role for Sm14 in the uptake of lipids from human serum. This work reports the crystal structure of Sm14 in complex with oleic (C18:1) and arachidonic (C20:4) acid at 1.85Å and 2.4Å, respectively. In the three-dimensional structure of the complex between Sm14 and oleic acid the hydrocarbon tail of the fatty acid is present in a double conformation, demonstrating limited fitness in the protein cavity; on the other hand the complex with arachidonic acid shows that the aliphatic chain adopts a stable hairpin-looped conformation. Kinetic and equilibrium constants determined for different fatty acids, showing enhanced specificity for arachidonic acid. The binding properties can very well be rationalized by the structures. We conclude that the binding specificity of Sm14 towards arachidonic acid is possibly the result of additional and stronger interactions in respect to other FABPs that belong to the same family. Moreover functional studies at different pH shows the presence of a pH-dependent conformational change, possible of physiological relevance for the parasite pathogenicity.

[1] World Health Organization (1996) F*act sheet on schistosomiasis*, World Health Organition, Geneva.

[2] Meyer, F., Meyer, H. and Bueding, E (1970) Lipid metabolism in the parasitic and free-living flatworms, *Schistosoma mansoni and Dugesia dorotocephala. Biocem. Biophys. Acta*, **210**, 256-266