

## Poster Presentation

**BM.P27**

### *Structure and dynamics of the DBHS protein family members SFPQ, NONO and PSPC1*

G. Knott<sup>1</sup>, M. Lee<sup>2</sup>, D. Passon<sup>3</sup>, A. Sadowska<sup>4</sup>, A. Fox<sup>4</sup>, M. Conte<sup>5</sup>, C. Bond<sup>1</sup>

<sup>1</sup>University of Western Australia, School of Chemistry and Biochemistry, Perth, Western Australia, <sup>2</sup>La Trobe University, Melbourne, Victoria, <sup>3</sup>EMBL-Hamburg, Germany, <sup>4</sup>West Australian Institute of Medical Research, Perth, Western Australia, <sup>5</sup>Randall Division of Cell and Molecular Biophysics, King's College London

The Drosophila behaviour/human splicing (DBHS) proteins are a family of obligatory dimeric proteins found in higher order mammals down to the simplest invertebrates. 'Multifunctional protein family' essentially captures what is understood regarding DBHS protein function where they are cited to regulate transcriptional initiation, the processing and export of RNA, maintenance of genomic DNA, nuclear pH homeostasis and carcinogenesis [1]. Furthermore, with roles in binding a diverse range of RNAs and both single and double stranded DNA, it is difficult to establish a coherent picture for their nuclear activities. In humans, the family consists of three highly conserved members, namely Non-POU domain-containing octamer-binding protein (NONO/p54nrb), splicing factor proline/glutamine rich (SFPQ/PSF) and paraspeckle protein component 1 (PSPC1). The conserved DBHS region of these proteins comprises tandem RNA recognition motifs (RRMs), a NOPS domain and a C-terminal coiled-coil domain. The unique structural arrangement of these domains facilitates an intimate dimerisation interface that gives rise to a novel arrangement of RRM [2]. Given this interface, it is not surprising that DBHS proteins likely exist as either homo- or heterodimers in vivo. Here we report the first structure of the ancestral *C. elegans* DBHS protein, NONO-1, refined to 2.8 Å. The structure clearly illustrates the consistent obligatory nature of DBHS dimerisation and through isothermal titration calorimetry we have demonstrated that human DBHS proteins prefer a heterodimeric state in vitro. There is a growing appreciation for the fundamental significance of DBHS proteins in human health and disease and this work highlights the critical need for a more robust assessment of in vivo DBHS function.

[1] Y. Shav-Tal, D. Zipori, *FEBS Lett* 2002, 531, 109 -114, [2] D. Passon, M. Lee, O. Rackham, et al, *Proc Natl Acad Sci USA*, 2012, 109, 4846-50

**Keywords:** DBHS dimerisation, NONO-1, Multifunctional proteins