s1.m6.p4 **Towards the crystal structure of the Isoquinoline Oxidoreductase from *Brevundimonas diminuta*.** D. Roeland Boer[a], Axel Müller[a], David J. Lowe[b], Susanne Fetzner[c], Maria J. Romao[a], [a] *REQUIMTE/CQFB, Departamento de Química, Faculdade de Ciencias e Tecnologia, Universidade Nova de Lisboa, 2829-516 Caparica, Portugal.* [b] *John Innes Centre, Norwich Research Park, Colney, Norwich, NR4 7UH, UK* [c] *Westfälische Wilhelms-Universität Münster, Institut für Molekulare Mikrobiologie und Biotechnologie, Corrensstr. 3 D-48149 Münster, Germany. E-mail: boer@dq.fct.unl.pt*

Keywords: Isoquinoline Oxidoreductase; Xanthine Oxidase family; *Brevundimonas diminuta*

Isoquinoline oxidoreductase from *Brevundimonas diminuta* (IOR) is a mononuclear molybdenum-containing enzyme that catalyzes the conversion of isoquinoline to 1-oxo-1,2-dihydroquinoline. The reaction is a two-step oxo-transfer process generating two electrons. The enzyme is member of the xanthine oxidase (XO) family of proteins, which all consist of a large subunit or domain containing the Mo atom coordinated to a pyranopterin cofactor and a small subunit/domain containing two Fe_2S_2 clusters that transport electrons from the molybdenum active center. Several structures have been solved of proteins of the XO family, including the XO from bovine milk and *Rhodobacter capsulatus*. The IOR differs in mechanistic as well as primary structure from the other members of the family. Purification of the IOR has been described [1] but reproducibility of the published method is not optimal. We have improved the purification method as well as its reproducibility. We have been able to obtain crystals and the progress towards obtaining the crystal structure of the enzyme will be discussed.

[1] Lehmann, M.; Tshisuaka, B.; Fetzner, S.; Roger, P.; Lingens, F. (1995), *J. Biol. Chem.* **269**, 11254-60.

s1.m6.p5 **DNA-targeted drugs - untwisting the tangled web of interactions.** Teixeira, S.C.M., Thorps, J.H., Gale, B.C., Gan, Y, Brogden, A.M. and Cardin, C.J., *School of Chemistry, The University of Reading, Whiteknights, Reading, RG6 6AD. www.helix.rdg.ac.uk, E-mail: c.j.cardin@reading.ac.uk*

Keywords: DNA; drug binding

Our structural studies of the binding of antitumour agents of the acridine and phenazine-4-carboxamide families have highlighted the difficulty inherent in going from a comparatively straightforward study of the binary DNA-drug complex to understanding by what mechanism the subsequent antitumour action actually occurs.

A key finding from most of our studies has been the multiple binding modes of monointercalators of this class when contracted with the more ordered binding found for bisintercalators, which also have much longer residence times on the DNA.

While 9aminoDACA (an acridine-4-carboxamide) is a topoisomerase II poison, for example, a bisintercalator derived from this may primarily interact with RNA polymerase II. Atomic resolution studies of the binding of 9aminoDACA to $d(CGTACG)_2$ have shown a possible bond-weakening mechanism at the TA/TA step.