s1.m6.p18 **Structural studies on collagen-binding integrin I domains.** Lenita Viitanen, Anna-Maria Brandt, Heidi Kidron, Yvonne Nymalm-Rejström, Tomi Airenne and Tiina Salminen*, *Abo Akademi University, Department of Biochemistry and Pharmacy, Turku, Finland. E-mail: tsalmine@abo.fi*

**Keywords: Integrin; I-domain; Collagen-binding**

Integrins are cell surface receptors that play a central role in cell-cell interactions and signaling and, thus, are involved in numerous disease states, such as cancer, inflammation, arthritis, and wound scarring [1,2]. Inhibitors of integrin function are interesting as pharmaceuticals against these diseases, but should bind specifically to an integrin subtype to have the required effect.

The integrin molecule is a heterodimer composed of a particular combination of α and β chains that determines its binding specificity. Of the 26 integrin heterodimers identified so far, α1β1, α2β1, α10β1 and α11β1 are the only ones that bind collagen. The α chains of these integrins have an inserted 200 residue sequence (the I domain) that is responsible for recognition of native collagen [3]. α1β1 and α2β1 are the most studied collagen-binding integrins, while α10β1 and α11β1 were discovered more recently. The crystal structures of ?1 and α2 I domains have been solved [4,5,6] as well as a complex structure of α2 I domain bound to a collagen-like peptide [7].

Emsley et al. (2000) observed large conformational changes in the α2 I domain upon binding of the collagen-like peptide. Our aim is to study how peptide and small molecular inhibitors bind to I domains of collagen-binding integrins and whether any conformational changes occur upon binding.

[1] Hynes R.O. *Cell* , 1992, **69**, 11-26.
[2] Pigott R. and Power C., The Adhesion Molecule Facts Book, 1993, Academic Press, London.
[3] Kamata T., Puzon W., Takada Y. *J. Biol. Chem*., 1993, **269**, 9659-9663.
[4] Nolte M., Pepinsky B., Venyaminov S.Yu., Koteliansky V., Gotwals P.J., Karpusas M. *FEBS Lett.*, 1999, **452**, 279-385
[5] Rich R.L., Deivavayagam C.C., Owens R.T., Carson M., Hook A., Moore D., Symersky J., Yang V.W., Narayana S.V., Hook M., *J. Biol. Chem*., 1999, **27**4, 24906-24913
[6] Emsley J., King S.L., Bergelson J.M., Liddington R.C. *J. Biol.Chem*. **272**, 1997, 28512-28517
[7] Emsley J., Knight G., Farndale R.W., Barnes M.J., Liddington R.C. *Cell* , 2000, **101**, 47-56

s1.m6.p19 **X-ray Crystallographic Analysis of nicotinic acid mononucleotide adenylyltransferase from *Pseudomonas aeruginosa*.** Hye-Jin Yoon, Hye-Lee Kim, and Se Won Suh, *School of Chemistry, Seoul National University, Seoul 151-742, Korea*. *E-mail: yoonhj@snu.ac.kr*

**Keywords: Nicotinic acid mononucleotide adenylyltransferase; Nicotinamide adenine dinucleotide; *Pseudomonas aeruginosa***

The enzyme nicotinic acid mononucleotide adenylyltransferase (NaMN AT; EC 2.7.7.18) is essential for the synthesis of nicotinamide adenine dinucleotide and is a potential target for antibiotics. It catalyzes the transfer of an adenyl group from ATP to nicotinic acid mononucleotide to form nicotinic acid adenine dinucleotide. We determined the three-dimensional structure of NaMN AT at 1.70 Å resolution by the multiwavelength anomalous diffraction method. In order to determine the structure of NaMN AT from *Pseudomonas aeruginosa*, we have crystallized it by hanging drop vapour-diffusion method at 291 K. The crystal of NaMN AT is tetragonal, belonging to the space group $P4_322$ with unit cell parameters of $a = b = 65.02$, $c = 109.80$ Å. The presence of one monomer in the asymmetric unit gives a reasonable $V_M$ of 2.15 $Å^3$ $Da^{-1}$, with a solvent content of 42.7%. The overall protein structure is similar to that of NaMN AT from *E. coli.* The present structural study is expected not only to reveal the mode of binding of the natural substrate NaMN or ATP, but also to provide further information about the role of active-site residues.

[1] Olland et al., *J. Biol. Chem*. **277**, 3698-3707 (2002)
[2] Zhang et al., *Structure,* **10**, 69-79 (2002)