

Structural Study of the Nucleolin~G-quartet Complex

Christophe Créze^a, Bruno Rinaldi^b, Philippe Bouvet^b, Richard Haser^a, Patrice Gouet^a, ^a*Laboratoire de BioCristallographie, IBCP IFR128, Lyon, France.* ^b*Laboratoire de Biologie Moléculaire de la Cellule, ENS, Lyon, France.* E-mail: c.creze@ibcp.fr

Nucleolin is a very abundant protein of molecular mass 70 kDa that localizes to the nucleolus. It is often used as a cell proliferation marker. Nucleolin interacts with oligonucleotides such as ribosomal RNA [1]. A 40 kDa-fragment of this protein named P40 has been purified to homogeneity. Nucleolin full-length as well as P40 interact with short DNA segments structured in G-quartet [2]. G-quartets are known as potential therapeutic agent against carcinogenesis.

Various G-rich sequences have been structured and tested in interaction with P40 by "Band-shift". Crystallisation trials have been performed for the most stable complexes. Thus, a crystallization condition has been obtained for an expected P40-4(TG4T) complex. Crystals of dimensions 200 x 100 x 20 μm^3 diffract up to 2 Å in house. They belong to space group P1 with unit-cell parameters $a=29\text{\AA}$ $b=32\text{\AA}$ $c=35\text{\AA}$ $\alpha=66^\circ$ $\beta=72^\circ$ $\gamma=83^\circ$. Such small cell volume corresponds to G-quartet only. X-ray data have been collected and the structure has been solved by molecular replacement, using as model the structure of the same G-quartet obtained in another crystal form [3]. Crystallisation trials on other complexes are under way.

[1] Allain F.H., Gilbert D.E., Bouvet P., Feigon J., *J Mol Biol.*, 2000, **303**, 227-41. [2] Hanakahi L.A., Sun H., Maizels N., *J Biol Chem.*, 1999, **274**, 15908-12. [3] Laughlan G., Murchie A.I., Norman D.G., Moore M.H., Moody P.C., Lilley D.M., Luisi B., *Science*, 1994, **265**, 520-4.

Keywords: human proteins, DNA and protein crystallography, anticancer drug structural study