	Human p53 DNA-binding domain in complex to DNA	MX-1316
ID23-2	from 24th of June 2011 to 25th of June 2011	
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Experiment report

Aim of the experiment and specific background :

We aim to solve the co-crystal structure of the human transcription factor p53 DNA-binding domain dimer bound to DNA. We have already determined the structure of the co-crystal structure of that complex (Figure 1) (1-2). Our structure shows two p53 dimers, having in total four DNA binding domains, bound to double stranded DNA. We observed that the loop L1 that interacts with DNA has two different conformations, recessed and extended. We demonstrated that the p53-DNA binding occurs via an induced fit mechanism with a switch in the conformation that involves the loop L1 (2). We now want to test p53-DNA crystals that contains point mutations in the loop L1. Furthermore, we aim to solve the structure of p53 bound to the natural CDKN1A(p21) p53-response element.

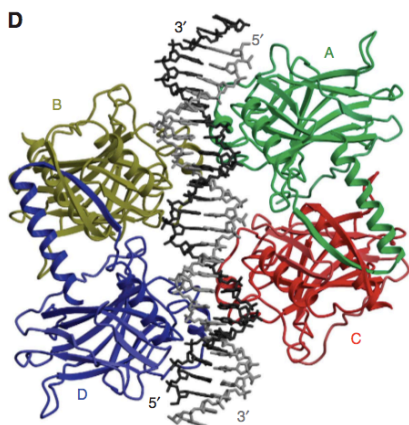


Figure 1. Overall three-dimensional structure of two p53CR2 dimers bound to DNA (2).

We obtained p53(loop mutant)-DNA crystals with different sizes in a range of 100 to 300 microns (Figure 2), as well as crystals of p53 bound to the natural CDKN1(p21) p53-response element (Figure 3).



Figure 2. Crystals of new p53 mutant bound to DNA

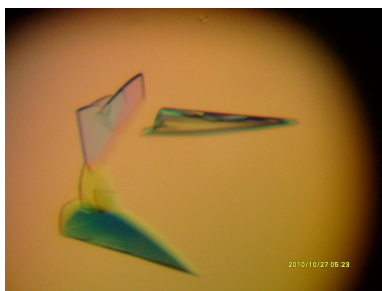


Figure 3. Crystals of p53 bound to the natural CDKN1A(p21) p53-response element.

Results :

We obtained a resolution of 2.9 Ångströms for p53(loop mutant)-DNA crystals and 2.8 Ångströms for crystals of p53 bound to the natural CDKN1A(p21) p53-response element. For both complexes we were able to solve the structure and already published the second one (4).

References :

1. MX-832 report
2. Petty TJ, Emamzadah S, Costantino L, Petkova I, Stavridi ES, Saven JG, Vauthey E, Halazonetis TD. *An induced fit mechanism regulates p53 DNA binding kinetics to confer sequence specificity.* EMBO J. 2011 Jun 1;30(11):2167-76. Epub 2011 Apr 26
3. Emamzadah S, Tropia L, Halazonetis TD. *Crystal structure of a multidomain human p53 tetramer bound to the natural CDKN1(p21) p53-response element.* Mol Cancer Res. 2011 Sep 20. [Epub ahead of print]

