Experiment title	**Crystal structure of the human mineralocorticoid receptor ligand-binding domain**
Experiment number	**30-01-663**
Date of experiment	**8 - 9 April 2004**

The mineralocorticoid hormone aldosterone plays an important role in sodium homeostasis and in the regulation of blood pressure. Alterations of this regulation are associated with several pathologies (hypertension, cardiovascular diseases, heart failure). Aldosterone produces its effects through the mineralocorticoid receptor (MR) which is a ligand-activated transcription factor. Aldosterone antagonists such as progesterone bind to MR with the same affinity as aldosterone but maintain the receptor in an inactive conformation (1). Aldosterone and its antagonists binding site is located at the C-terminal domain of the MR, the ligand-binding domain (LBD). In the precedent proposal (30-01-636) we analyzed the crystal structure of a mutant MR characterized by an altered activating mechanism. During the present experiment (proposal 30-01-663), we investigated the structural study of the complex between the LBD of the wild type MR and deoxycorticosterone, a compound as potent as aldosterone to activate the receptor.

Crystallization assays resulted in reproducible crystals of about 200 µ. The protein crystallizes in the P31 space group with cell parameters a = 119.77 Å, b = 119.77 Å, c = 41.50 Å and $\alpha = \beta = 90.0$, $\gamma = 120.0$. A complete native data set has been collected to 2.47 Å resolution (oscillation range 1°, 60 sec exposition). The statistics of the data collection are summarized in Table I.

Resolution (Å)	2.47
wavelength (Å)	0.979757
No. of observations	64434
No. of unique reflections	19020
R_{sym} (%)	6.8 (34.0)
Multiplicity	3.4 (3.1)
Completeness (%)	78.7 (78.6)
$I / \sigma (I)$	12.4 (2.9)

Table I. Statistics of data collection. The values in parenthesis are for the highest resolution shell (1.8 - 1.7 Å).

Molecular replacement with BEAST from the ccp4 package using a homology model previously generated (Fagart et al. 1998) gave a unique rotation solution. With this solution three translated positions were found. Refinement of the solution is in process.