Crystallization and X-ray Analysis of the Catalytic Domain of Human PDE 3B

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The catalytic domain of human phosphodiesterase 3B has been cloned, expressed in *Escherichia coli*, and purified in the presence of the PDE3 inhibitors IBMX (3-isobutylmethylxanthine) or MERCK1 by affinity chromatography. Initial screening of crystallization conditions for these complexes in the hanging-drop vapor-diffusion mode resulted in three different crystal forms, all characterized by quite large unit cell parameters, elevated solvent content and poor diffraction quality. Subsequent optimization of these conditions led to crystals that diffract to 2.4 Å and belong to space group C2, with unit cell parameters a=146.7, b=121.5, c=126.3 Å, β=100.6^{o}. Rotation function analysis indicates that the asymmetric unit contains four copies of the monomeric enzyme, corresponding to a solvent content of 64% [1]. The structures of the catalytic domain of human PDE3B in complex with IBMX and MERCK1 have been solved to 2.4 Å using these optimized crystals. These structures explain the dual cAMP/cGMP binding capabilities of PDE3, provide the molecular basis for inhibitor specificity, and can supply a valid platform for the design of improved compounds [2].

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