Small Angle X-ray Studies of the EGF Receptor Ectodomain

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The ectodomain of Epidermal Growth Factor Receptor - EGFR - is a 100 KDa membrane glycoprotein and mediates the biological effects of polypeptide mitogens such as EGF and TGF-\(\alpha\), playing an important role in the normal and pathological growth control. Overexpression has been observed in many types of human tumours [1] and therefore structure-based drug design for therapeutic modulation of receptor functions is of high medical interest. EGFR has been crystallised in the presence of ligand giving crystals of the space group \(P2_1 2_1 2_1\) with resolution of 4.5 Å [2].

Different preparations of the complex in a molar ratio 1:1 in the concentration range 5-20 mg/ml were investigated at the EMBL beam lines X-13 and X-33. The calculated radius of gyration \(R_g\) falls in the range from 3.8 to 4.2 nm. Additional measurements with the receptor alone indicate partial dimerization of the receptor. Initial calculations indicate that about 25\% of the receptor is dimerized.

The initial results showed the possibility of studying the EGFR structure in complex with its ligand. This structure shall give evidence of regions with high flexibility that may not be essential for ligand binding. Further analysis and preparations are being carried out to enable a more detailed analysis of this system.