Purification and Characterisation of Recombinant Wild Type FGFR2

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Abstract:

Apert syndrome, a serious genetic disease resulting in cranial synostosis and syndactyly during foetal development, is caused by point mutations (S252W and P253R) in the region linking Ig-like domains II and III of Fibroblast growth factor receptor 2 (FGFR2). Fibroblast growth factors (FGFs), the ligands of FGFR2, mediate their biological functions by binding to the Ig-like domains of FGFR2, resulting in the dimerisation and phosphorylation of multiple tyrosine residues on the cytoplasmic domain of the receptors. It is now known that the binding of FGF requires the presence of Heparin/Heparan sulfate proteoglycans (HSPGs), which are known to play an important role in the control of FGF receptor signalling by controlling receptor dimerisation. However, the role of differential heparin structures in controlling FGFR2 signalling remains unclear. This study is focused on the heparin/HSPG structures in controlling FGFR2 signalling. The wild type recombinant receptor proteins were expressed in mammalian cells (293T cells); functional studies carried out in 293T cells have shown that the recombinant receptor proteins (wild type) have the ability to be phosphorylated in the stimulation of FGF in vivo. Future in vitro work is being done in order to show that the recombinant wild type receptor proteins can bind to FGF in the presence of heparin, and this binding can induce the phosphorylation of receptor proteins. Future studies will be focused on the comparison of binding abilities and signalling responses between wild type and mutant FGFR2 using different structures of heparin/HSPG.