SUPPLEMENTAL MATERIAL

Figure S1. Expression of the extracellular domain (residues 25-361) of the receptor 2 isoform IIIc (exdFGFR2IIIc). The expression cassette was constructed by the polymerase chain reaction (PCR) using pTK14 as the template (1) and ProteoExpert (Biomax Informatics AG) proposed modifications for optimal expression of the protein in *E. coli*. The cassette includes, the T7 promoter of phage RNA-polymerase (cyan), exdFGFR2IIIc with a His-tag fused to its C-terminus and optimized for Ni^{2+}-chelating solid phase chromatography, and a 3' UTR optimized for protein expression in which a T7 phage RNA-polymerase terminator is included (cyan). Initiating and terminating codons are in red characters.

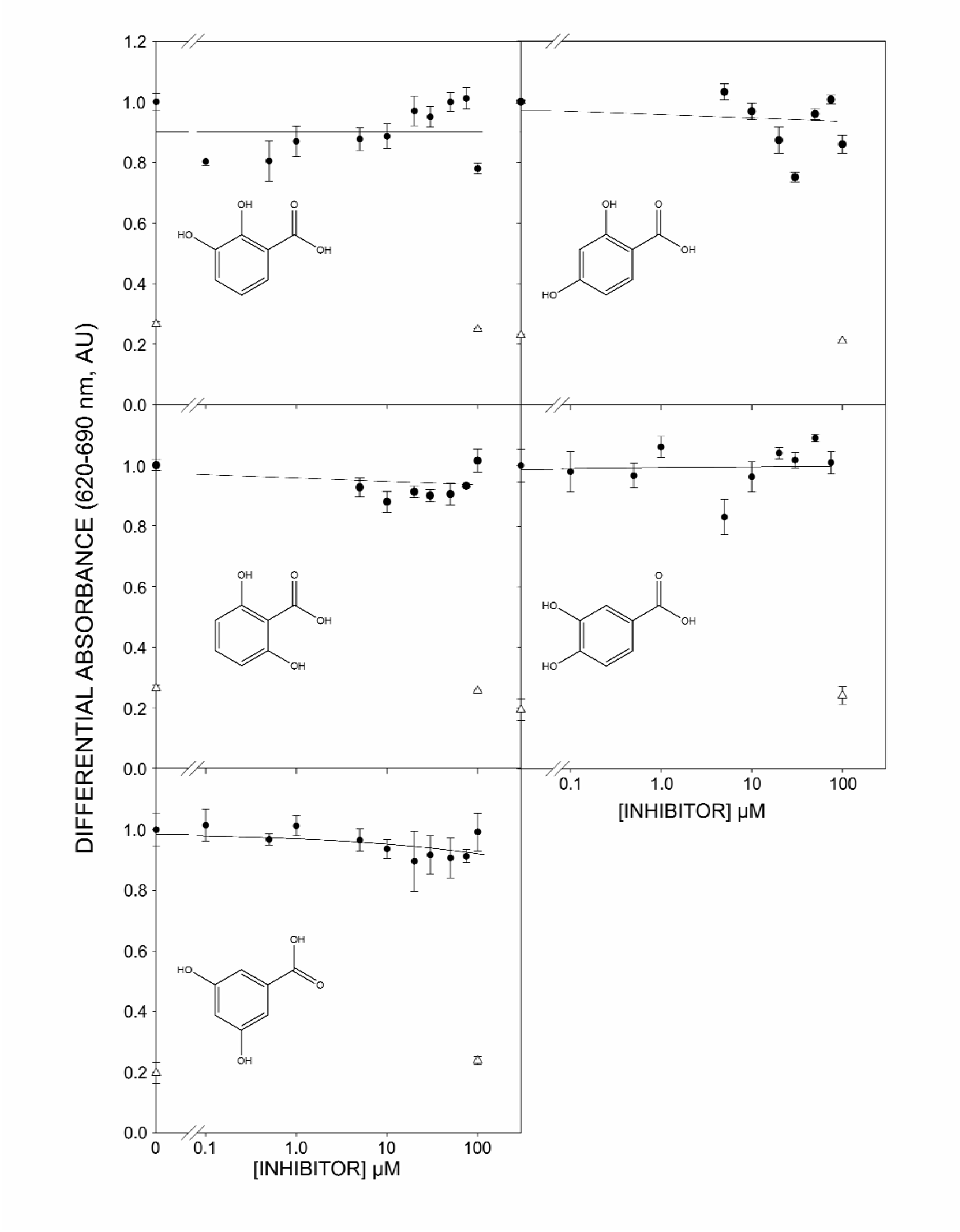

Figure S2. Effect of the whole set of GA isomers on the FGF-1 induced mitogenesis of Balb/C 3T3 fibroblasts cultured *in vitro*. The isomers tested in each assay appear as an inset of the corresponding plot. Empty symbols represent the cell proliferation in unstimulated cultures, in the presence and absence of the corresponding isomer at the concentration indicated. The compounds do not seem to have any appreciable effect on the cell viability in quiescent cultures.

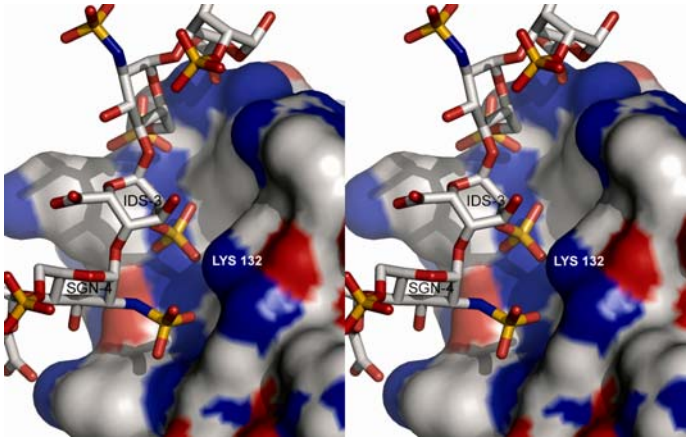

Figure S3. Stereoviews of the three-dimensional structure of the FGF-1:heparin complex at the 2,5DHPS and GA binding site (heparin shown as stick-and-ball model, with carbon, nitrogen, oxygen, and sulfur atoms colored white, blue, red, and yellow, respectively). The Van der Waals volume of the protein was generated with PyMOL (DeLano Scientific LLC) with the atoms colored as above. IDS-3, O2-sulfo-glucuronic acid at position 3 (from the reducing end). SGN-4, N,O6-disulfo-glucosamine at position 4.

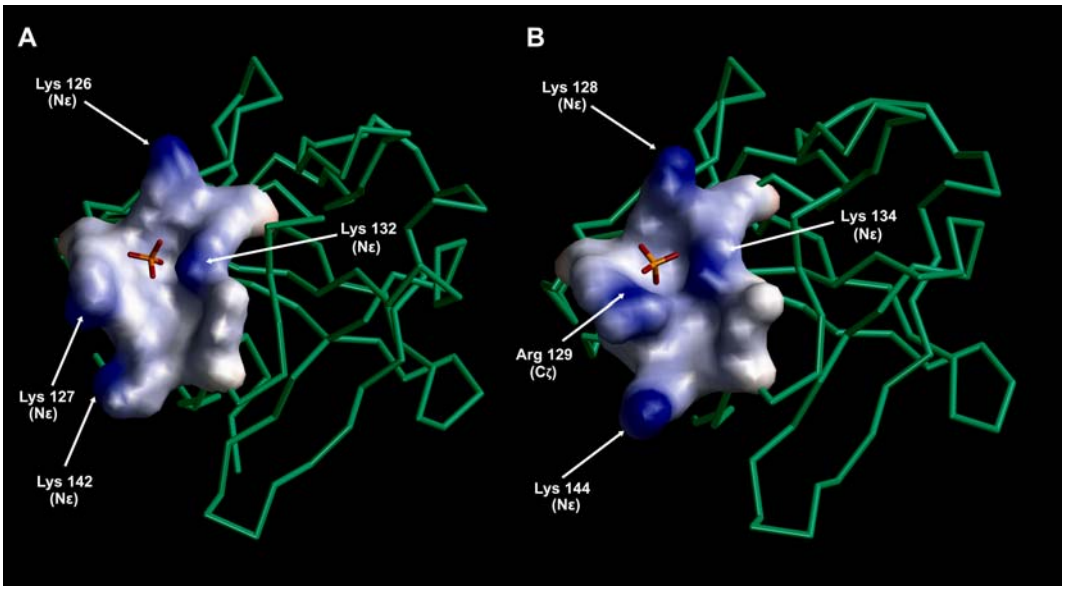

Figure S4. Three-dimensional representation of the region of the heparin binding-site to which 2,5DHPS and GA dock in crystals obtained in the absence of ligands. The graphical representation corresponds to FGF-1 (A) showing a phosphate anion at the docking site (2,3). The walls of the groove at which the phosphate anion, 2,5DHPS and GA bind is made up of the Asn 32, Leu 125, Lys 126, Lys 127, Lys 132, Lys 142, Gln 141, and Ala 143 residues. When the amide backbones of the FGF-1 and FGF-2 three-dimensional structures are superimposed, these amino acids align with residues: Asn 36, Leu 127, Lys 128, Arg 129, Lys 134, Lys 144, Gln 143 and Ala 145 of FGF-2 (B), which also create a groove at which a selenate anion docks at an equivalent relative position to that of the phosphate in the case of FGF1 (4). The electrostatic potential of the protein surface, is mapped in blue (positive) and red (negative) and it was generated with the Discovery Studio Visualizer program (2.0.1.7347; Accelrys Software Inc.) using its internal calculation parameters.

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