Supporting information for Lortat-Jacob *et al*. (2002) *Proc. Natl. Acad. Sci. USA* **99** (3), 1229–1234. (10.1073/pnas.032497699)

Detailed Computational Procedure

Calculation of the Chemokines Connoly Surfaces. The coordinates of all chemokines studied were taken from the Protein Data Bank (1). All hydrogen atoms were added by using the Sybyl molecular modeling package (2) and partial atomic charges were derived by using the Pullman procedure. The positions of all hydrogen atoms were optimized with the Tripos force field (3). The Connolly surfaces of the proteins were calculated by using the MOLCAD program (4) from the Sybyl package.

Modeling the heparin chains. The coordinates of the extended conformation of heparin were taken from the NMR-derived structures (5) deposited in the Protein Data Bank (ID code 1HPN). A variety of chain conformation were also generated using the following procedure. Polysaccharides consisting of 18 monomers were built with alternating 2-*N*-sulfated, 6-*O*-sulfated α-D-Glc, and 2-*O*-sulfated β-L-IdoA monosaccharides. The coordinates of the monosaccharides were taken from a databank of three-dimensional structures (http://infopc2.cermav.cnrs.fr/databank/monosaccharides/).

All of the glycosidic linkages were considered to be able to adopt two different conformations selected in a 4 kcal/mol energy window in the Ramachandran type (Φ, Ψ) energy map previously published for these disaccharides or for closely related ones (6, 7). Defining the torsional angles of the glycosidic linkage as Φ = Θ(O-5*i* C-l*i* O-l*i* C-4*j*) and Ψ = Θ(C-l*i* O-l*i* C-4*j* C-5*j*), the following conformations were considered:

α-D-Glc(1-4)β-L-IdoA(^2S_O) repeating unit: (Φ = 80°, Ψ = –160°) and (Φ = 130°, Ψ = –100°)

α-D-Glc(1-4)β-L-IdoA($^1C_4$) repeating unit: (Φ = 90°, Ψ = –150°) and (Φ = 90°, Ψ = –70°)

β-L-IdoA(^2S_O)(1-4)α-D-Glc repeating unit: (Φ = –90°, Ψ = 170°) and (Φ = –90°, Ψ = –110°)

β-L-IdoA($^1C_4$)(1-4)α-D-Glc repeating unit: (Φ = –80°, Ψ = –170°) and (Φ = –80°, Ψ = –110°).

Several dozen chain conformations were generated by randomly selecting both the occurrence of ^2S_O and $^1C_4$ ring shapes for the iduronic acid and the conformational state of each glycosidic linkage. Few conformations were rejected because of steric conflicts. Atom types and partial charges were defined according to the PIM energy parameters for carbohydrates (8, 9) to be used within the Tripos force field (3).

Docking procedure. The GRID program (10) was used to predict the most favorable anchoring position for a charged sulfate group at the surface of the chemokines with known crystal structure. The probe used in the calculation is the charged oxygen of a

sulfate or phosphate group. The grid spacing was set to 1 Å. From our library of heparin chain conformations those that display an appropriate shape for fitting of sulfate groups with the GRID lowest iso-energy contour were selected. The polysaccharide chains were merged with the protein structure in the docking mode that brings the sulfate in close contact with the protein surface without generating steric conflicts.

Optimization of the complexes. The geometry of each of the complexes was optimized by several cycles of energy minimization. The hydrogen atoms and pendant groups were first optimized. Finally, the whole heparin moiety, together with the side chain of the amino acids in the positively charged area, were fully optimized. All energy calculations were performed with the Tripos force field (3) together with energy parameters especially derived for carbohydrates (8) and sulfated derivatives (9). The permitivity was set as a distance-dependant function and a Powell-type minimizer was used through the calculations. To evaluate the energy of interaction, the complex was also optimized with the heparin chain at a distance of 50 Å away from the protein, out of the range of intermolecular interaction.

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