Structural Role of Extracellular Domain 1 of \(\alpha\)-Platelet-derived Growth Factor (PDGF) Receptor for PDGF-AA and PDGF-BB Binding*

(Received for publication, February 10, 1995, and in revised form, August 31, 1995)

Daruka Mahadevan‡§, J in-Chen Yu‡, Jose W. Saldanha†, Narmada Thangkì, Peter McPhie**, Akyt Urent‡, William J. LaRochelle‡, and Mohammad A. Heidarant ‡‡

From the†Laboratory of Cellular and Molecular Biology, National Cancer Institute, Bethesda, Maryland 20892, the‡‡Laboratory of Biochemical Pharmacology, NIDDK, Bethesda, Maryland 20892, and the§§Medical Research Council Collaborative Centre, 1-3 Burtonhole Lane, Mill Hill, London, United Kingdom.

The purpose of this study was to bacterially express, purify, and refold combinations of the extracellular immunoglobulin (Ig) domains of the human \(\alpha\)-platelet-derived growth factor receptor (\(\alpha\)-PDGFR) to characterize molecular interactions with its ligand, platelet-derived growth factor (PDGF). The far UV circular dichroism spectroscopy of the \(\alpha\)-PDGFR extracellular domains (ECDs) revealed a predominantly \(\beta\)-sheet protein, with a structure consistent with folded Ig-like domains. The addition of PDGF-BB to these ECD types changed the conformation of all three types with a decrease in mean residue ellipticity in the following rank order: 1–5 = 1–3 > 2–3. In striking contrast, addition of PDGF-AA to these ECD types markedly changed the conformation of ECD 2–3, by an increased mean residue ellipticity and no changes were observed for ECDs 1–3 and 1–5. PDGF-AA bound to the immobilized ECD types 2–3, 1–3, and 1–5 at concentrations of 30, 11, and 7.5 nM, respectively. In contrast, PDGF-BB bound the ECD types 2–3, 1–3, and 1–5 at concentrations of 3, 3, and 2.2 nM, respectively. Scatchard analysis of binding studies using labeled ECDs indicated that PDGF-BB and PDGF-AA bound ECD 1–3 and ECD 2–3 with \(K_D\) values of 74 and 72 nM, respectively. While, PDGF-AA bound ECD 1–3 and ECD 2–3 with \(K_D\) values of 33 and 87 nM, respectively. Therefore, our results indicated that the loss of ECD 1 impaired the binding affinity of \(\alpha\)-PDGFR ECD 1–3 toward PDGF-AA without having a similar effect on PDGF-BB binding. Together all of our data suggest that ECD 1 is differentially required for proper orientation of PDGF-AA but not PDGF-BB binding determinant within ECDs 2 and 3.

Platelet-derived growth factor (PDGF)\(^1\) is a potent serum mitogen, promoting the growth of mesenchymal cells (for a review, see Ref. 1). PDGF exists as a disulfide-linked dimer (M, 28,000), composed of two homologous polypeptide chains designated A and B (2–4). Both homodimers (AA and BB) and a heterodimer (AB) have been isolated from serum (5) and bind with high affinities to either or both cell surface-glycosylated receptors designated as \(\alpha\) (6) and \(\beta\) (7) of 180 and 185 kDa, respectively. Although both receptors are highly homologous, the three PDGF isoforms bind the \(\alpha\)-PDGFR (8) while the \(\beta\)-PDGFR primarily binds the PDGF-BB form (4).

The PDGFRs are members of the receptor tyrosine kinases, which possess five immunoglobulin-like extracellular domains, a single transmembrane spanning motif, and a split intracellular tyrosine kinase domain (7). Ligand binding leads to receptor dimerization, which activates the tyrosine kinase leading to trans-autophosphorylation of the receptor (9, 10). The tyrosine-phosphorylated receptor now becomes a target for binding Src homology region 2 (SH2) domains of a number of signaling molecules, which include phosphatidylinositol-3-kinase, GTPase-activating protein, phospholipase C\(_Y\) (PLC\(_Y\)), Src, Grb2, Nck, and the tyrosine phosphatase Syt (for a review, see Ref. 11), which activate a number of inter-linked downstream signaling pathways.

A number of other growth factor receptors have been shown to dimerize in the presence of ligand. These include the soluble extracellular domain of the epidermal growth factor receptor (12), the human growth hormone receptor (13), and the \(\alpha\) (14) and \(\beta\)-PDGFR (15). For the PDGFR, both groups expressed all five immunoglobulin-like domains in Chinese hamster ovary cells (15) and in baculovirus-infected insect cells (14). These glycosylated receptor extracellular domains were shown to exist as dimers but when deglycosylated appeared as monomers (15). These soluble receptors dimerized in the presence of added PDGF (14, 15), confirming the conclusion that receptor dimerization is essential for tyrosine kinase activation.

The expression of reciprocal chimeric \(\alpha/\beta\)-PDGFRs in an interleukin-3-dependent cell line (32D), showed that Ig-like domains 2–3 of the \(\alpha\)-PDGFR must contain the major high affinity determinants for PDGF-AA binding (16–18). Furthermore, deletion within the second Ig-like loop of the \(\alpha\)-PDGFR resulted in a marked decrease in binding PDGF-AA but not PDGF-BB (17). To further evaluate the structural roles of Ig-like domains 2 and 3 in PDGF binding, we expressed and purified combinations of the \(\alpha\)-PDGFR ECDs (2, 3, 1, 3, and 1–5) in quantities suitable for structure-function studies.

EXPERIMENTAL PROCEDURES

Construction of Expression Vectors—The DNA representing the human \(\alpha\)-PDGFR extracellular domains 2–3 (ECD 2–3\(^{301–341}\)), 1–3 (ECD 1–3\(^{341–384}\)), and 1–5 (ECD 1–5\(^{354–529}\)) (6) were synthesized by the polymerase chain reaction method with a BamHI and HindIII site at the 5’ and 3’ ends, respectively. The polymerase chain reaction products were cloned into the pQE9 plasmid (type 4) possessing an NH\(_2\)-terminal

---

**The abbreviations used are:** PDGF, Platelet-derived growth factor; \(\alpha\)-PDGFR, \(\alpha\)-platelet derived growth factor receptor; ECD, extracellular domain; PAGE, polyacrylamide gel electrophoresis; PBS, phosphate-buffered saline; mAb, monoclonal antibody.
six-histidine tag (Qiagen). DNA sequencing confirmed the authenticity of the cloned inserts. The recombinant vectors were transfected into competent M15 Escherichia coli cells carrying the plasmid pREP4.

Protein Expression, Refolding, and Purification—Protein expression and nickel-affinity purification was performed as described previously (19). The three domain types (2–3, 1–3, and 1–5) were refolded by dialysis into 0.1 M urea buffer (100 mM phosphate, pH 7.4, containing 1 mM EDTA, 150 mM NaCl, and 0.1% β-mercaptoethanol. Subsequently, the proteins were dialyzed into refolding buffer consisting of 100 mM phosphate, 150 mM NaCl, 2 mM reduced glutathione, 1 mM oxidized glutathione, 1 mM EDTA at pH 7.4. The refolded proteins were then dialyzed into 100 mM phosphate buffer, pH 7.4, to remove the reduced and oxidized glutathione. The refolded domains were further purified by FPLC (Mono Q) (Pharmacia) and analyzed by 4–20% SDS-PAGE (Bio-Rad) under reducing and nonreducing conditions.

Solid-phase Binding Assays—Direct immobilization of the α-PDGFR extracellular domains (ECDs) 2–3, 1–3, and 1–5 were performed by overnight incubation in immunosorbent 96-well plates (Falcon 3912) at room temperature using 80 ng of purified protein in 50 μl of PBS in 0.02% sodium azide. Binding studies were performed with the monoclonal antibody to ECD 2 of the α-PDGFR (mAb αR1), PDGF-AA, and -BB. The bound PDGF-AA or -BB were detected by anti-PDGF antibodies to the COOH-terminal region (20). The NH2-terminal SH2 domain of GTPase-activating protein was also directly immobilized and used as controls. For competition experiments, suramin was added at increasing concentrations in the presence of PDGF-AA (10 nM) or -BB (10 nM). Immunodetection was followed as described previously (21).

Ligand Binding Assay—ECD 1–3 or ECD 2–3 was labeled by the chloramine-T method (specific activity 8 × 104 cpm/μg). PDGF-AA or PDGF-BB (40 μg) were immobilized by overnight incubation in immunosorbent 96-well plates (Falcon 3912) at room temperature in 50 μl of PBS in 0.02% sodium azide. Immobilized PDGF ligands were washed by ice-cold HEPES binding buffer (25 mM HEPES, 150 mM NaCl, 5 mM KCl, 1.2 mM MgSO4, and 0.1% bovine serum albumin, pH 7.5) once and incubated in the presence of 5 ng/ml labeled ECD preincubated in the presence of increasing concentrations of unlabeled ECD, PDGF-AA, or PDGF-BB for 2 h at 16°C. Free125I-ECD was removed by washing wells three times with ice-cold HEPES binding buffer and bound125I-ECD was quantitated and analyzed by the method of Scatchard.

Far UV Circular Dichroism Spectroscopy—The α-PDGFR ECD 2–3, 1–3, and 1–5, for circular dichroism spectroscopy were prepared in PBS at a protein concentration of 0.15 mg/ml. The protein concentrations of the stock solutions, used in CD measurements, were determined spectrophotometrically (23) and the spectra scaled according to standard CD spectra for immunoglobulins. The spectra were recorded using a 1-mm demountable “strain free” quartz cuvette on a JASCO J-500C spectropolarimeter in the wavelength range of 260–195 nm at room temperature. The following settings were used: bandwidth, 1 nm; time constant, 2.0 s; step resolution, 0.1 nm; scan speed, 10 millidegree/min; sensitivity, 1 millidegree/cm. Each spectrum represents an average of 4 scans with 5 measurements subtracted.

The three domain types, recombinant human PDGF-AA, PDGF-BB, and EGF (UBI) at a concentration of 0.15 mg/ml was added and the spectra were recorded as described above. The spectra for the growth factors alone were also measured as described above. In order to measure conformational changes assuming 1:1 stoichiometry, the combined changes and to study ligand-induced conformational changes. The CD spectra of the purified ECD 2–3, 1–3, and 1–5 possesses the determinants that may mediate the receptor oligomerization of ECD 1–3 and ECD 1–5 by interdisulfide bonds.

α-PDGFR ECDs 2–3, 1–3, and 1–5 Are Recognized by Receptor-specific Monoclonal Antibody—A neutralizing mAb αR1 directed against the α-PDGFR, bound the native receptor with high affinity (25). The epitope recognized by the mAb αR1 was shown to be denatured under reducing conditions (18). Furthermore, the major αPDGFR epitope binding to mAb αR1 was localized to Ig-like domain 2 (18). These findings indicated that high affinity binding of mAb αR1 to α-PDGFR requires proper folding of determinants within Ig-like domain 2. Therefore, bacterially expressed domains 2–3, 1–3, and 1–5 were analyzed for proper folding by solid phase binding assays with the monoclonal antibody of the α-PDGFR (mAb αR1). Results shown in Fig. 2 indicated binding to the ECD 1–5, ECD 1–3 with a half-maximal value of about 0.4 nM while ECD 2–3 showed half-maximal binding at concentration of about 0.6 nM. This confirmed that all three receptor ECD types were correctly refolded, however, the maximal binding of ECDs 1–3 and 1–5 was estimated to be approximately 2-fold higher than that of ECD 2–3. Therefore, our results suggest that ECD 1 may be indirectly involved in binding of mAb αR1.

CD Spectroscopic Studies of PDGF-AA and -BB-induced Conformational Changes in the Three ECD Types—Far-UV CD spectroscopy was performed to investigate the folding of the three ECD types, to determine whether they possessed Ig-like structures and to study ligand-induced conformational changes. The CD spectra of the purified ECD 2–3, 1–3, and 1–5...
indicated domains composed essentially of $\beta$-sheet (trough at 215 nm) similar to that observed for Ig-like domains and also confirmed that they were correctly folded. The calculated secondary structure for the 3 ECD types are 45–56% $\beta$-sheet and 44–56% turns (Table I) (28). Fig. 3, A–C, show the far-UV CD spectra of the the ECDs and their recorded spectra of a 1:1 mixture with the indicated PDGF ligands. Moreover, a calculated spectra for a 1:1 mixture of ECD and PDGF ligand is indicated. Fig. 3D, shows the spectrum of PDGF-AA or -BB which has calculated $\beta$-sheet content of 60%. The addition of PDGF-AA at an equimolar ratio to the three ECD types showed a significant conformational change for domains 2–3 (increased mean residue ellipticity) in which the $\beta$-sheet content increased from 56 to 100% but not for domains 1–3 and 1–5 (Table I). However, the addition of EGF to these ECD types did not show conformational changes, eliminating the possibility of nonspecific binding and conformational changes (data not shown).

Interestingly, the addition of PDGF-BB to ECD 2–3, 1–3, and 1–5 markedly changed their conformation in the following order: 1–5 = 1–3 > 2–3 (decreased mean residue ellipticity) (Fig. 4, A–C). These conformational changes are in the opposite direction to that observed when PDGF-AA was added to ECD 2–3 (Fig. 3, A–C).

Binding of PDGF-AA and -BB to ECDs 2–3, 1–3, and 1–5—The wild type receptor as well as the eukaryotic expression of all five Ig-like domains have shown high affinity binding to PDGF-AA or PDGF-BB with $K_D$ values of 33 nm. A similar analysis of $^{125}$I-ECD 2–3 binding to PDGF-BB measured a similar number of binding sites with a $K_D$ value of 72 nm (Fig. 6B). Furthermore, as shown in Fig. 6C, Scatchard analyses of $^{125}$I-ECD 1–3 binding to PDGF-AA estimated high affinity binding sites with a $K_D$ value of 33 nm. In striking contrast, $^{125}$I-ECD 2–3 reproducibly showed a similar number of binding sites with a $K_D$ value of 87 nm (Fig. 6D). Thus deletion of ECD 1 impaired the affinity of ECD 2–3 for PDGF-AA binding by more than 2-fold, without having a comparable effect on PDGF-BB binding. Under these conditions, the binding of $^{125}$I-ECD 1–3 or 2–3 was also competed by increasing concentrations of unlabeled PDGF-AA or PDGF-BB with similar kinetics as shown with unlabeled ECDs (data not shown). These results are consistent with the finding that the soluble $\beta$-PDGF receptors have $K_D$ values of 30–100 nm, but when immobilized provided a value of 0.4 nm (27). Furthermore, $\beta$-PDGF ECD 1–3 was expressed in NIH 3T3 cells as a Fc fusion protein bound to PDGF-BB with an affinity of 1.5 nM. The $\alpha$-PDGF ECD 1–3 competed with the $\beta$-PDGF ECD 1–3 for PDGF-BB binding with a half-maximal value of 10 nM (21), thus confirming that the recombinant $\alpha$-PDGF ECD types

![Image](http://www.jbc.org/)

**Table I**

| ECD 2–3 | ECD2–3+AA | ECD2–3+BB |
|---------|------------|-----------|
| 56% $\beta$ + 44% t | 100% $\beta$ | 51% $\beta$ + 49% t |
| ECD 1–3 | ECD1–3+AA | ECD1–3+BB |
| 49% $\beta$ + 51% t | 49% $\beta$ + 51% t | 39% $\beta$ + 61% t |
| ECD 1–5 | ECD1–5+AA | ECD1–5+BB |
| 45% $\beta$ + 54% t | 45% $\beta$ + 54% t | 38% $\beta$ + 62% t |

![Fig. 3](http://www.jbc.org/)

**Fig. 3.** The far-UV CD of the uncomplexed (A) ECD 2–3 (thin line) (B) ECD 1–3 (thin line) (C) ECD 1–5 (thin line), and (D) PDGF (AA or BB) (thin line) recorded at a protein concentration of 0.15 mg/ml in PBS. A–C also shows the spectrum of PDGF-AA complexed ECD types (dash lines) and the combined spectrum of the PDGF-ECD complexes calculated (dotted lines).
shown here compare well with those expressed in eukaryotic systems. Furthermore, our findings suggest that the extent of complex formation between PDGF and ECDs is at least 78% in an equimolar mixture since the $K_D$ value of ECD for PDGF-AA or PDGF-BB is not greater than 80 nM. Thus, our data indicates that most ECDs exist in complexes with PDGF under the experimental conditions used for CD spectroscopy.

To further demonstrate the specificity of the binding interaction, we utilized suramin as a potent PDGF antagonist. Competition studies demonstrated that suramin inhibited PDGF-AA or -BB binding to the ECD types with half-maximal values in the range 1.25–2.5 nM (Fig. 7, A and B). This assay provides means to test potential agonists or antagonists as described previously (21, 22).

**DISCUSSION**

In this report we describe bacterial expression, purification, and refolding of the α-PDGFR ECDs 2–3, 1–3, and 1–5 to evaluate structural features that contribute to PDGF binding. The nativeness of ECDs was confirmed by 1) CD spectroscopy and 2) a monoclonal antibody (mAb αR1) which recognizes a nonlinear epitope within ECD 2. In vitro binding studies using an immunosorbent assay indicated that immobilized ECD types 2–3, 1–3, and 1–5 each bound to PDGF-BB at very similar concentrations (2–3 nM). However, ECD 2–3, 1–3, and 1–5 bound PDGF-AA at concentrations of 20, 11, and 7.5 nM, respectively. Scatchard analyses of binding studies using labeled ECD 1–3 and ECD 2–3 cross-competed with unlabeled ECD types or PDGF ligands, indicated that deletion of ECD 1 from ECD 1–3 impaired PDGF-AA binding by more than 2-fold without affecting PDGF-BB binding. Therefore, our results suggest that αPDGFR extracellular domain 1 is differentially required for high affinity interaction with PDGF-AA but not PDGF-BB.

Previously, it was shown that an α/β chimeric PDGFR, in which domain 1 of the α-PDGFR was substituted for domain 1 of the β-PDGFR, bound to PDGF-AA with high affinity. Another α/β chimeric PDGFR in which ECD 1–3 of the β-PDGFR was substituted for the ECD 1–3 of the α-PDGFR also bound to PDGF-AA with high affinity (16). In addition, a carboxyl-terminal deletion mutants encoding the first two Ig-like domains (αR1–216) and an internal deletion mutants lacking Ig-like loop 3 (αR150–235–290) did not bind to PDGF-AA (18). Moreover, an internal deletion mutant lacking Ig-like loop 2 (αR150–189) did not affect PDGF-BB binding but affected PDGF-AA binding (17). Taken together these results suggest that α-PDGFR extracellular domain 1 is differentially required for high affinity interaction with PDGF-AA but not PDGF-BB.
affinity binding to PDGF-BB.

We have also examined the physical characteristics of the α-PDGFR ECD types in the absence and presence of PDGF. Our data indicate that PDGF induces distinct conformational changes in the three ECD types. PDGF-AA significantly changed the conformation of ECD 2–3 by increasing the mean residue ellipticity but did not change the conformation of ECDs 1–3 or 1–5. It is postulated that the orientation of ECD 2–3, with respect to each other by domain 1, may be essential for correct exposure of the binding determinants. This observation is reflected in the direct binding assay where the efficiency of ECD 2–3 for PDGF-AA binding is enhanced in the presence of ECD 1. In contrast, PDGF-BB binding changed the conformation of all three domain types with the following rank order: 1–5 > 1–3 > 2–3 by decreasing the mean residue ellipticity. Since direct binding of the three ECD types to PDGF-BB are very similar, the conformational change observed here is likely to be due to an induced fit mechanism.

The crystal structure and mutagenesis studies performed on PDGF-BB has allowed the identification of three surface loops, two at one end of the molecule (loops 1 and 3) and the third (loop 2) at the opposite end of the elongated twisted β-sheet monomer. The dyad axis relating the two monomers brings loops 1 and 3 of one monomer close to loop 2 of the symmetry related monomer (29–31). Since, PDGF-BB and -AA have a high degree of sequence similarity they are predicted to possess similar three-dimensional structures. The sequences within the same three loops in PDGF-AA, when compared with those identified for PDGF-BB, have changed from basic to hydroxy amino acids. These major sequence differences between PDGF-AA and -BB loop regions may contribute to the different affinities and mode of interaction with the α-PDGFR observed in this study.

Taken together, all of our findings are consistent with the proposed model depicted in Fig. 8, A and B, demonstrating the molecular interaction of PDGF-AA and PDGF-BB with the ECD 1–3 and ECD 2–3. According to this model, during the refolding process, the determinants within ECD 1 induce conformational changes within ECD 2 required for a tight interaction with PDGF-AA but not with PDGF-BB. As shown in Fig. 8A the requirement of ECD 1-induced changes in ECD 2 and 3 for PDGF-AA binding is further necessitated by the distinct physiochemical properties of binding determinants within PDGF-AA in comparison to PDGF-BB (see discussion above). Fig. 8B also illustrates how the loss of determinants within ECD 1 leads to lack of conformational change within ECD 2 and 3 necessary for tight PDGF-AA bindings. The physical consequence of this effect is PDGF-AA-induced conformational changes in ECD 2 and 3 (measured by CD and reflected by the reduced affinity) to allow such binding. In contrast the binding of PDGF-BB to ECD 2–3 is not affected since the binding site for this ligand is in the correct orientation.

In conclusion, we show that for PDGF-AA binding, ECD 2...
and 3 are necessary and that ECD 1 orients these domains with respect to each other so that binding determinants are correctly positioned in three-dimensional space. However, for PDGF-BB, ECD 2-3 are correctly oriented for high affinity binding. The availability of large amounts of purified α-PDGFR ECDs will allow us to define the molecular interactions with PDGF in detail using x-ray crystallography. Furthermore, since PDGF and its receptor are implicated in a number of disease states including cancer, the immunosorbent assay system developed will help screen and identify potential agonists and antagonists of the α-PDGFR that could be of therapeutic value.

Acknowledgments—We thank Alex DeSeabra for excellent technical support, Amal Salama for reading this manuscript, and Drs. Jacalyn Pierce and Steve Tronick for support and encouragement.

REFERENCES
1. Heldin, C.-H. (1992) EMBO J. 11, 4251–4259
2. Waterfield, M. D., Scarce, G. T., Whittle, N., Stroobant, P., Johnson, A., Westmark, B., Heldin, C.-H., Huang, T. S., and Seul, T. F. (1983) Nature 304, 35–39
3. Hammacher, A., Melstrom, K., Heldin, C.-H., and Westmark, B. (1989) EMBO J. 8, 2489–2495
4. Heldin, C.-H., Backstrom, G., Ostman, A., Hammacher, A., Ronnstrand, L., Rubin, K., Nister, M., and Westmark, B. (1988a) EMBO J. 7, 1387–1393
5. Hart, C. E., Bailey, M., Curtis, D. A., Osborn, S., Raines, E., Ross, R., and Forstrom, J. W. (1990) Biochemistry 29, 166–172
6. Matsui, T., Heidaran, M. A., Miki, T., Popescu, N., Lacrochelle, W., Kraus, M., Pierie, J., and Aaronson, S. A. (1989) Science 243, 800–804
7. Yarden, Y., Escobedo, J. A., Kuang, W.-J., Yang-Feng, T. L., Daniel, T. O., Tremble, P., Shen, E. Y., Ando, M. E., Harkins, R. N., Frankie, Y., Vu, V., Ulirich, A., and Willians, L. T. (1986) Nature 323, 226–232
8. Heidaran, M. A., Pierie, J., Yu, J.-C., Lombardi, D., Artrip, J. E., Fleming, T. P., Thomson, A., and Aaronson, S. A. (1991) J. Biol. Chem. 266, 29232–29237
9. Bishayee, S., Majumdar, S., Khere, J., and Das, M. (1989) J. Biol. Chem. 264, 11699–11705
10. Eriksson, A., Ronson, S., Ernlund, A., Cleasson-Welsh, L., and Heldin, C.-H. (1992) Growth Factors 6, 1–14
11. Pawson, A., and Schlessinger, J. (1993) Curr. Biol. 3, 434–441
12. Kurwitz, D. R., Emanuel, S. L., Nathan, M. H., Sarver, N., Ulirich, A., Felder, S., Lax, I., and Schlessinger, J. (1991) J. Biol. Chem. 266, 22035–22043
13. de Vos, A. M., Ulltisch, M., and Kossiakoff, A. A. (1992) Science 255, 306–312
14. Herren, B., Rooney, B., Weyer, K. A., Iberg, N., Schmid, G., and Pech, M. (1993) J. Biol. Chem. 268, 15088–15095
15. Duan, D. R., Pazin, M. J., Fretto, L. J., and Williams, L. T. (1991) J. Biol. Chem. 266, 413–418
16. Heidaran, M. A., Pierie, J. H., Jensen, R. A., Matsui, T., and Aaronson, S. A. (1990) J. Biol. Chem. 265, 18741–18744
17. Heidaran, M. A., Yu, J.-C., Jensen, R. A., Pierie, J. H., and Aaronson, S. A. (1992) J. Biol. Chem. 267, 2884–2887
18. Yu, J.-C., Mahadevan, D., LaRochelle, W. J., Pierie, J. H., and Heidaran, M. (1994) J. Biol. Chem. 269, 10668–10674
19. Mahadevan, D., Thanki, N., McPhie, P., Beeler, J., Yu, J.-C., Wlodawer, A., and Heidaran, M. A. (1994) Biochemistry 33, 746–754
20. LaRochelle, W. J., May-Siroff, M., Robbins, K., and Aaronson, S. A. (1991) Genes & Dev. 5, 1191–1199
21. Heidaran, M. A., Mahadevan, D., and LaRochelle, W. J. (1995) FASEB J. 9, 140–145
22. Middaugh, C. R., Mach, H., Burke, C. J., Volkin, D. B., Dabora, J. M., Tsai, P. K., Bruner, M. W., Ryan, J. A., and Marfa, K. E. (1992) Biochemistry 31, 9016–9024
23. Prasad, K., Lippoldt, R. E., Edelbach, H., and Lewis, M. S. (1988) Biochemistry 25, 5214–5219
24. Timm, D. E., and Neet, K. E. (1992) Protein Sci. 1, 236–244
25. LaRochelle, W. J., Jensen, R. A., Heidaran, M. A., May-Siroff, M., Wang, L.-M., Aaronson, S. A., and Pierie, J. H. (1993) Cell Growth & Differ. 4, 547–553
26. Jensen, R. A., Beeler, J. F., Heidaran, M. A., and Aaronson, S. A. (1992) Biochemistry 31, 10887–10892
27. Heldin, C.-H., Ernlund, A., Ronson, S., and Ronnstrand, L. (1989) J. Biol. Chem. 264, 8905–8912
28. Provender, S. W., and Gluckner, J. J. (1981) Biology 20, 33–37
29. Oefner, C., D’Arcy, A., Winkler, F., Eggimann, B., and Hosang, M. (1992) EMBO J. 11, 3921–3926
30. LaRochelle, W. J., Pierie, J. H., May-Siroff, M., Giese, N., and Aaronson, S. A. (1992) J. Biol. Chem. 267, 10704–10707
31. Ostman, A., Anderson, M., Hellman, U., and Heldin, C.-H. (1991) J. Biol. Chem. 266, 10073–10077
32. Scatchard, G. (1949) Ann. N. Y. Acad. Sci. 51, 660–672
Structural Role of Extracellular Domain 1 of α-Platelet-derived Growth Factor (PDGF) Receptor for PDGF-AA and PDGF-BB Binding
Daruka Mahadevan, Jin-Chen Yu, Jose W. Saldanha, Narmada Thanki, Peter McPhie, Aykut Uren, William J. LaRochelle and Mohammad A. Heidaran

J. Biol. Chem. 1995, 270:27595-27600.
doi: 10.1074/jbc.270.46.27595

Access the most updated version of this article at http://www.jbc.org/content/270/46/27595

Alerts:
- When this article is cited
- When a correction for this article is posted

Click here to choose from all of JBC's e-mail alerts

This article cites 32 references, 14 of which can be accessed free at http://www.jbc.org/content/270/46/27595.full.html#ref-list-1