The novel co-activator CRABPII binds to RARα and RXRα via two nuclear receptor interacting domains and does not require the AF-2 'core'

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Abstract We identify the RARα, RXRα and CRABPII domains required for the physical interaction of these proteins. On RARα and RXRα, the sequences correspond to the DEF and DE domains, respectively, but the interaction with CRABPII does not require the AF-2AD 'core'. On CRABPII, two interacting domains are identified (NRID1 and NRID2), one of which contains the only enhancement transactivation domain of CRABPII. The interaction is ligand-independent and does not require the ligand-binding domain of CRABPII. These results further stress that interaction of CRABPII with the nuclear receptors defines a novel level of transcriptional control.

Key words: Retinoic acid; RAR; RXR; CRABPII; Co-activator

1. Introduction

Retinoic acid (RA) is a vital signal for vertebrate development, cell growth and differentiation. Mammalian cells contain two small proteins (15 kDa), CRABPI and CRABPII, which belong to the family of intracellular lipid-binding proteins that bind small hydrophobic molecules such as retinoids and fatty acids [1]. These two proteins, products of separate genes, exhibit a high degree of amino acid sequence conservation, but are immunologically distinct. Moreover, they possess different binding affinities for RA and show distinct patterns of expression during the various stages of development [2]. Indeed, while CRABPI is ubiquitously expressed, the expression of CRABPII is restricted to certain tissues such as adult testicules, skin [1,3] and hematopoietic cells [4,5]. The role of the CRABP proteins was so far restricted to the regulation of intracellular concentrations of free RA [6].

We and others have recently shown that CRABPII, and not CRABPI, enhances transactivation of RA target genes in the presence of transfected RA receptors in Cos-1 cells [4,7] or endogenous receptors in human cells [4,8,9], thus placing CRABPII as a novel co-activator of nuclear receptors. Enhancement of transactivation is abolished when three amino acids of CRABPII (Gln 75, Pro 81 and Lys 102) are simultaneously mutated [10]. The biological relevance and mechanism(s) involved in this novel co-activator function are just beginning to unravel. By a fluorescence titration assay, Dong et al. have elegantly shown a channeling of all-*trans* RA from CRABPII to RAR which suggested protein–protein interactions [7]. This was indeed confirmed when we evidenced that CRABPII and not CRABPI physically interacted with both nuclear RA receptors in vitro and in vivo in mammalian cells [4]. By demonstrating the presence of CRABPII in the transcriptional RA nuclear complex bound to its RARE (RA response element), the RANC (RA-dependent nuclear complex), we brought further arguments for this co-activator function [4]. Taken together, all the accumulated data demonstrate protein–protein interactions between the RA nuclear receptors and CRABPII, identification of the interacting domains whether on the nuclear receptors or on CRABPII was still pending.

Most members of the nuclear receptor superfamily share a common domain structure [11]. The N-terminus contains the variable A/B region, which also includes the ligand-independent AF-1 activation domain. This domain is followed by a highly conserved DNA-binding domain (C region). The C-terminal domain (DEF region) contains not only the LBD (ligand-binding domain) but also the ligand-dependent AF-2 activation function and a dimerization domain [11]. This domain plays a critical role in transactivation through the ligand-dependent recruitment of co-activators [12].

In this study, we evidence that, in contrast to most co-activator interactions identified so far, CRABPII does not interact with the AF-2AD 'core' domain of RAR and RXR. This feature is correlated with the absence of an LXXLL motif in CRABPII and therefore stresses that CRABPII defines indeed a novel level of regulation of nuclear receptor activity. We also characterize two domains of CRABPII (NRID1 and NRID2) that directly interact with RAR and RXR. These domains contain key structures of the ligand pocket entrance of CRABPII but not the LBD itself.

2. Materials and methods

2.1. Materials

Plasmids encoding GST-hRARα, GST-hRARαDEF, GST-hRARα DEFΔ(408–416) (DEF domains deleted of the AF-2AD 'core' domain), GST-mRARαAB, GST-mRXRα, GST-mRXRαDE, and

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GST-mRXRαDEΔ(455–467) (DE domains of RXRα deleted of the AF-2AD 'core' domain) were kindly provided by Prof. P. Chambon [13]. For Western blotting, mouse monoclonal antibody directed against CRABPII (5CRA3B3), and rabbit polyclonal antibodies against the F region of RARα (RPα (F)) or the A region of RXRα (RPRXα (A)) were used as described [4]. All-*trans* RA was supplied by Hoffmann-La Roche (Basel, Switzerland).

The SwissProt accession numbers: human (h) RARα (P10276), mRXRα (P28700) and hCRABPII (P29373).

2.2. DNA constructs

All plasmid constructs were generated using standard cloning procedures and verified by restriction enzyme analysis and DNA sequencing. Details of each construction are available upon request. hCRABPII (1–138) and mutated variants of hCRABPII ((1–111), (1–60), (61–111), (61–138), (85–138)) were constructed by PCR using the following flanking primers: forward (1–111 and 1–60) 5′-CCCGAATTCATGCCCAACTTCTCTGGC-3′; reverse (1–111) 5′-AGTGGATCCTCAGGTCCACGAGGTCTT-3′; forward (61–138 and 61–111) 5′-CCCGAATTCATGACCACAGAGATTAAC-3′; reverse (1–60) 5′-AGTGGATCCTCAGCGCACGGTGGTGGA-3′; forward (85–138) 5′-CCCGAATTCATGCTGGTGAAATGGGAG-3′; reverse (61–138 and 85–138) 5′-AGTGGATCCTCACTCTCGGACGTAGACCCT-3′. Each PCR product was digested by *Eco*RI/*Bam*HI and cloned into the corresponding sites of the pSG5 vectors. The GST-mutated CRABPII constructs were made by subcloning an *Eco*RI/*Sal*I fragment from corresponding pSG5-mutated CRABPII into pGEX4T. For in vitro binding assays, the cDNAs for full length RARα and RXRα were fused to GST in the pGEX2T plasmid. All constructs created by PCR amplification were verified by sequencing.

2.3. Mammalian cell culture and transfection experiments

Cos-1 cells were routinely maintained in DMEM (Gibco-BRL) supplemented with 10% fetal bovine serum. Cos-1 cells were transfected with pSG5-RARα, pSG5-RXRα and pSG5-hCRABPII by the calcium phosphate precipitation technique.

2.4. GST pull-down assay

To identify which nuclear receptor domains interact with hCRABPII, GST pull-down assays were performed with purified, bacterially produced GST-RARα, GST-RXRα proteins and Cos-1 cell extracts overexpressing hCRABPII. Reciprocally, to identify the CRABPII domains involved in the interaction with nuclear receptors, GST pull-down assays were performed with purified, bacterially produced GST-hCRABPII proteins (wild-type or deleted) and Cos-1 cell extracts overexpressing RARα or RXRα. GST and GST fusion proteins were expressed in *Escherichia coli* and purified on glutathione-Sepharose beads (Pharmacia). Purified proteins were quantified by a Bradford protein assay and by Coomassie staining after separation by SDS–PAGE. Total extracts from transfected Cos-1 cells (50 μg) were incubated at 4°C for 1 h with 20 μg of each of the different GST fusion proteins bound to glutathione-Sepharose beads in a 100 μl total volume of binding buffer (50 mM Tris–HCl (pH 7.5), 300 mM KCl, 10 mM $MgCl_2$, 0.3 mM dithiothreitol, 5% glycerol, 0.1% Nonidet P-40). Reactions were performed in the presence or absence of 1 μM all-*trans* RA. Beads were then washed four times with the same buffer, and bound proteins were eluted with 30 μl of SDS loading buffer, resolved by SDS–PAGE and analyzed by Western blotting.

3. Results

In order to define which regions of CRABPII are involved in CRABPII nuclear receptor interactions, a series of hCRABPII fragments were fused to GST proteins (Fig. 1A). Due to the small size of the protein and reported proteolytic sensitivity of some sequences [14], we were obliged to limit the size of the mutants to minimal sequences of 50 amino acids or more to generate specific and stable GST fusion proteins.

The interaction of these different hCRABPII mutants with RAR and RXR was explored using a GST pull-down assay (Figs. 2 and 3). We first studied whether the amino acids participating to RA-binding are involved in this interaction. We tested three different constructs (Fig. 1A). The first construct (1–111) (Fig. 1A) comprises Arg 30 and Arg 60, two amino acid residues known to facilitate the entrance of RA into the ligand-binding pocket. Another GST fusion protein is constituted of the C-terminal part of CRABPII (amino acids 61–138) (Fig. 1A) comprising two arginine residues (Arg 112 and Arg 133) and one tyrosine (Tyr 135) involved in the RA-binding pocket (Fig. 1B). The third construct (61–111) (Fig. 1A) does not depict amino acids implicated in RA-binding. To note, the three fusion proteins harbor this (61–111) amino acid sequence which includes the three amino acids essential for the transactivation function of CRABPII (Gln 75, Pro 81 and Lys 102) (Fig. 1B) [10].

As shown in Fig. 2, RARα failed to interact with immobilized GST alone (Fig. 2A,B, lane 2), but interacted with GST-hCRABPII as efficiently as with GST-mCRABPII [4] in the presence or absence of RA (Fig. 2A,B, lane 3). RARα also interacted with GST-(1–111), GST-(61–138), and GST-(61–111) (Fig. 2A, lanes 4–6) but less efficiently than with full length CRABPII. Note that a partial instability was evidenced for GST-(1–111) mutant (data not shown). The data obtained with these mutants confirm that the interaction of CRABPII with RARα is ligand-independent [4] and indicate that it does not require the LBD of hCRABPII (Fig. 2A, lanes 4 and 6; Fig. 2B, lanes 4 and 5).

Other constructs of similar size were generated which did not contain the (61–111) amino acid sequence. The tridimensional (3-D) structure of these hCRABPII mutants is shown in Fig. 1B. The N-terminal deletion mutant corresponds to the amino acid region 1–60 (Fig. 1A). As the construct corresponding to the 112–138 amino acid sequence was too small, we generated the GST-(85–138) mutant (Fig. 1A). Interestingly, RARα still interacts with the GST-(1–60) (Fig. 2B, lane 5) revealing that direct interaction between RARα and hCRABPII is not restricted to a domain comprising the three amino acid residues (Gln 75, Pro 81 and Lys 102) (Fig. 1B) necessary for hCRABPII-mediated transcriptional co-activation [10]. The GST pull-down assay, unlike the fluorescence titration assay, allows the identification of a interacting domain independent of the RA transfer hCRABPII function.

In addition, RARα does not interact with the GST-(85–138) (Fig. 2B, lane 6). These data show that the (85–138) domain comprising the LBD of hCRABPII is not involved in the direct RARα–hCRABPII interaction. We can further note that the presence of Lys 102 (one of the three amino acid residues involved in the transactivation function of hCRABPII) does not confer alone the ability to interact with RARα. Thus, these two interacting regions, the N-terminal region and the mid-region of hCRABPII were named NRID1 and NRID2 for nuclear receptor interacting domains 1 and 2, respectively.

Similar results were obtained when extracts from Cos-1 cells transfected with pSG5-hRXRα were incubated with the different GST fusion proteins. GST-hCRABPII interacted with RXRα in the absence (Fig. 3A,B, lane 3) or presence of its natural ligand, 9-*cis* RA (data not shown). As RARα, RXRα interacted with GST-(1–111), GST-(61–138), GST-(61–111) and GST-(1–60) (Fig. 3A, lanes 4–6 and Fig. 3B, lane 5, respectively). As for RARα, RXRα failed to interact with GST-(85–138) (Fig. 3B, lane 6). An apparent weaker binding of RXRα to the GST fusion proteins compared to RARα is observed for the full length protein as well as for the mutants.

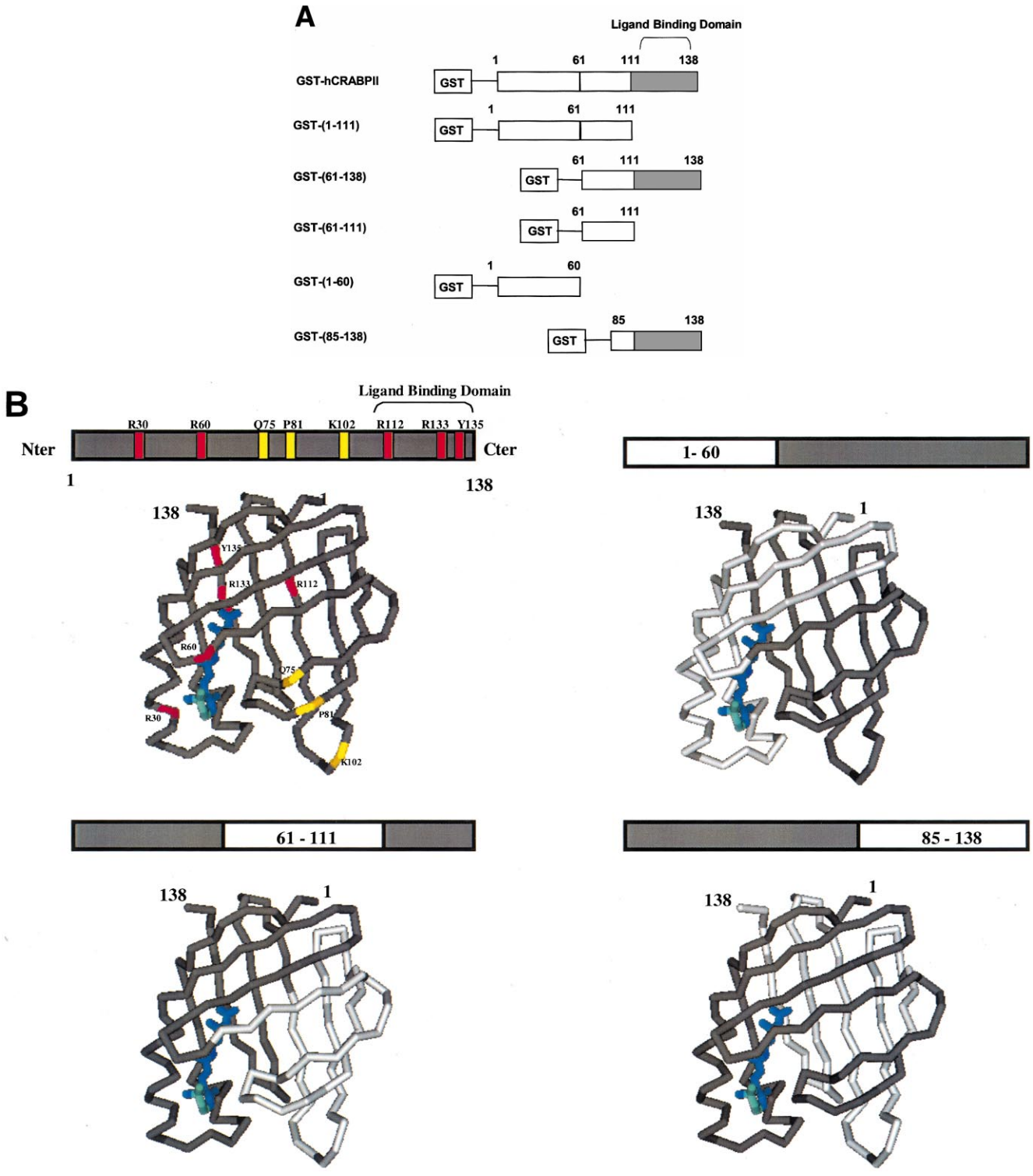

Fig. 1. Representation of full length and truncated versions of the hCRABPII. A: The full length hCRABPII is indicated with its LBD (top line) and various hCRABPII deletion mutants (bottom lines) fused to GST. Deletion constructs were generated as described in Section 2. B: The figure illustrates modeled CRABPII according to the crystallographic determined structure (Kleywegt et al., 1994). The positions of the different mutants are highlighted in white. RA is in blue. Q75, P81, and K102 (yellow) correspond to the three amino acid residues involved in CRABPII's transactivation activity. R30, R60, R112, R133 and Y135 (red) participate to the RA-binding [14].

Thus, physical interactions between hCRABPII and retinoid nuclear receptors are not restricted to RARα and are equally ligand-independent in vitro.

In order to identify the regions of RAR that are essential for interaction with hCRABPII, extracts from Cos-1 cells transfected with pSG5-hCRABPII were incubated with different GST fusion proteins corresponding to wild-type and deleted RARα (Fig. 4A). After immunoblotting of the bound proteins with an anti-CRABPII, hCRABPII was found to bind to RARα (Fig. 4B, lane 3) as previously shown with

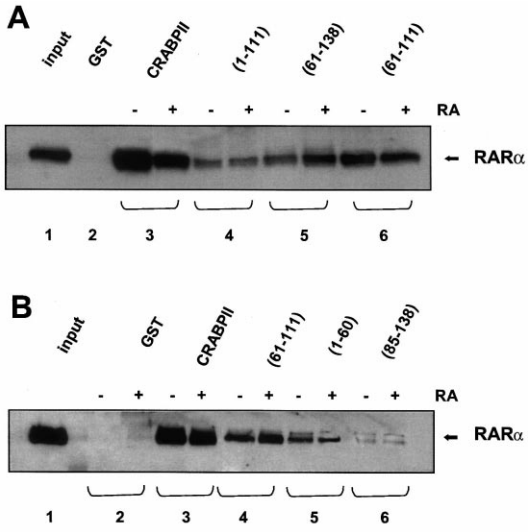

Fig. 2. Determination of CRABPII domains required in CRABPII–RARα interactions. GST pull-down assays in the presence or absence of RA using GST-hCRABPII deletion mutants and cellular extracts from Cos-1 cells transfected with pSG5-RARα. Input 4% (lane 1); controls were run concurrently with immobilized GST alone (lane 2). Western blot were performed with an anti-RARα antibody. A: CRABPII (lane 3); 1–111 (lane 4); 61–138 (lane 5); 61–111 (lane 6). B: CRABPII (lane 3); 61–111 (lane 4); 1–60 (lane 5); 85–138 (lane 6).

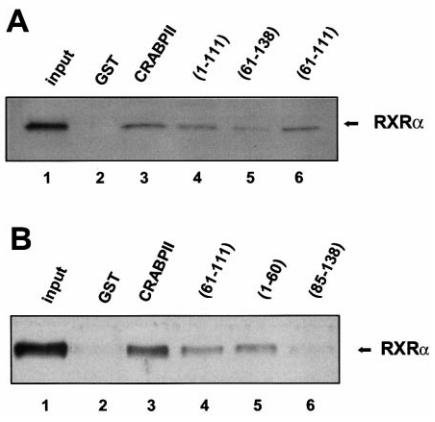

Fig. 3. Determination of CRABPII domains required in CRABPII–RXRα interactions. GST pull-down assays using GST-hCRABPII deletion mutants and cellular extracts from Cos-1 cells transfected with pSG5-RXRα. Input 4% (lane 1); controls were run concurrently with immobilized GST alone (lane 2). Western blots were performed with an anti-RXRα antibody. A: CRABPII (lane 3); 1–111 (lane 4); 61–138 (lane 5); 61–111 (lane 6). B: CRABPII (lane 3); 61–111 (lane 4); 1–60 (lane 5); 85–138 (lane 6).

murine CRABPII [4]. No binding was observed with GST-RARαAB (Fig. 4B, lane 6) suggesting that the interaction CRABPII–RARα is AF-1-independent. Therefore, the hCRABPII–RARα interaction involves the DEF domain of RARα (Fig. 4B, lane 4). Surprisingly, this binding persisted with the GST-RARαDEFΔ(408–416) fusion protein (Fig. 4B, lane 5), demonstrating that the interaction does not require the AF-2AD 'core' of RARα. Similar results were obtained in the presence of 1 μM RA (data not shown).

hCRABPII was also found to bind RXRα (Fig. 5B, lane 3), as previously described with the murine CRABPII [4]. hCRABPII bound GST-RXRαDEΔ(455–467) and RXRαDE (Fig. 5B, lanes 4 and 5) indicating that the interaction with the DE domain did not involve the AF-2AD 'core' of RXR. These interactions were also ligand-independent (data not shown).

Hence, hCRABPII interacts, independently of the presence

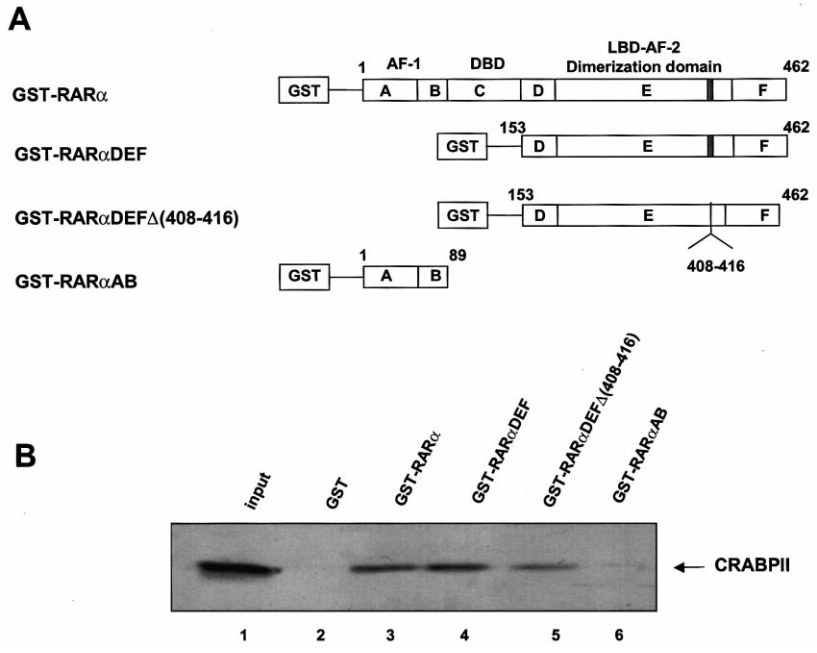

Fig. 4. Mapping of regions in RARα required for CRABPII interactions. A: Schematic representation of the various RARα fragments fused to GST and used as baits in in vitro pull-down assays. The gray box corresponds to the AF-2 'core' domain (408–416) of RARα. B: GST pull-down assays using GST-RARα deletion mutants and cellular extracts from Cos-1 cells transfected with pSG5-hCRABPII. Input 4% (lane 1); controls were run concurrently with immobilized GST alone (lane 2). RARα (lane 3); GST-RARαDEF (lane 4); GST-RARαDEFΔ (408–416) (lane 5); RARαAB (lane 6).

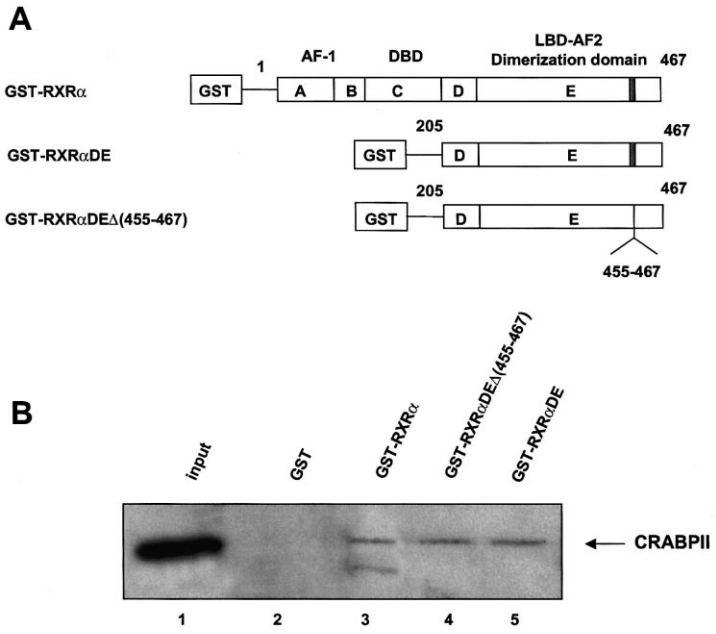

Fig. 5. Mapping of regions in RXRα required for CRABPII interactions. A: Schematic representation of the various RXRα fragments fused to GST and used as baits in in vitro pull-down assays. All domains are indicated. The gray box corresponds to the AF-2 'core' domain (455–467) of RXRα. B: GST pull-down assays using GST-RXRα deletion mutants and cellular extracts from Cos-1 cells transfected with pSG5-hCRABPII. Input 4% (lane 1); controls were run concurrently with immobilized GST alone (lane 2). RXRα (lane 3); GST-RXRαDEΔ (455–467) (lane 4); GST-RXRαDE (lane 5).

of RA, with the C-terminal domains of RARα and RXRα, within the two critical domains, DEF and DE of RAR and RXR, respectively. Interestingly, these interactions do not involve the AF-2AD 'core' previously described as a key motif for ligand-dependent protein–protein interactions with transcriptional co-activators.

4. Discussion

CRABPII is the first co-activator which brings the ligand itself to the nuclear receptor. Indeed, enhancement of CRABPII-mediated transactivation is exclusively observed in the presence of the ligand, and only with the natural ligands, all-*trans* RA or 9-*cis* RA, suggesting that each partner, the nuclear receptor and CRABPII, bound to RA, plays a role in transactivation activity [4]. At the molecular level, the enhancement of transactivation can result from an increased affinity of the nuclear receptor complex for the RARE [4]. The ligand-binding property of CRABPII is in accordance with the fact that it is a specific co-activator of RA nuclear receptors as it does not bind to other nuclear receptors [4]. We have shown that CRABPII does not enhance transactivation by itself, and thus enhancement of RA-mediated transactivation requires its physical association to the receptors (RAR and RXR) [4]. Potential interactions between CRABPII and at least RARα were strongly supported by a fluorescence titration assay [7] and physical interactions were evidenced for RARα and RXRα by GST pull-down and co-immunoprecipitation assays [4].

CRABPII was characterized as containing one non-autonomous enhancement transactivation domain (ETD) for enhancement of RAR-mediated transactivation which includes three crucial amino acid residues (Gln 75, Pro 81 and Lys 102) [7]. Simultaneous mutations of these residues completely abolish the enhancement of transactivation underlining the fact that no other CRABPII amino acid sequence harbors an enhancement transactivation function (Fig. 6) [10]. In addition, these CRABPII residues conferred to CRABPI the ability to enhance activity of RAR-mediated transactivation [10]. Therefore, the ETD stretching from amino acid residues 75 to 102 is necessary and sufficient to enhance RAR-mediated transactivation in the presence of RA [10].

Using GST pull-down assays, we identified two NRIDs (NRID1 and NRID2) of CRABPII which directly interact with RARα and RXRα in a ligand-independent manner. NRID2 contains the ETD previously identified [10]. The fact that CRABPII deleted of its LBD can still interact with RARα and RXRα corroborates this ligand-independent interaction. Since we identified ligand-independent interactions for the NRIDs, these data could not have been obtained with a fluorescence titration assay, and as thus complementary.

The RA pocket entrance of CRABPII comprises the second helix α and the βC–βD and βE–βF loops involved in the conformation and dynamics of CRABPII in the presence of RA (Fig. 6). RA is localized in the RA-binding pocket through its carboxyl group interacting with the side chains of two arginine residues (Arg 112 and Arg 133) and one tyrosine (Tyr 135) at the bottom of the pocket (Fig. 6). In the light of our present results, the sequence of the hCRABPII protein can be described as containing three important regions: (1) a C-terminal region (LBD: 112–138) which does not interact with RAR and RXR since the 85–138 domain does not physically interact with retinoid nuclear receptors. (2) An N-terminal domain (NRID1: 1–60) involved in CRABPII–RAR and CRABPII–RXR ligand-independent interactions which comprises Arg 30 and Arg 60, two amino acid residues known to facilitate the entrance of RA into the ligand-binding pocket (NRID1 protrudes in front of the ligand-binding pocket [14]) (Fig. 6). (3) A mid-region (NRID2: 61–111), containing the sole ETD of CRABPII

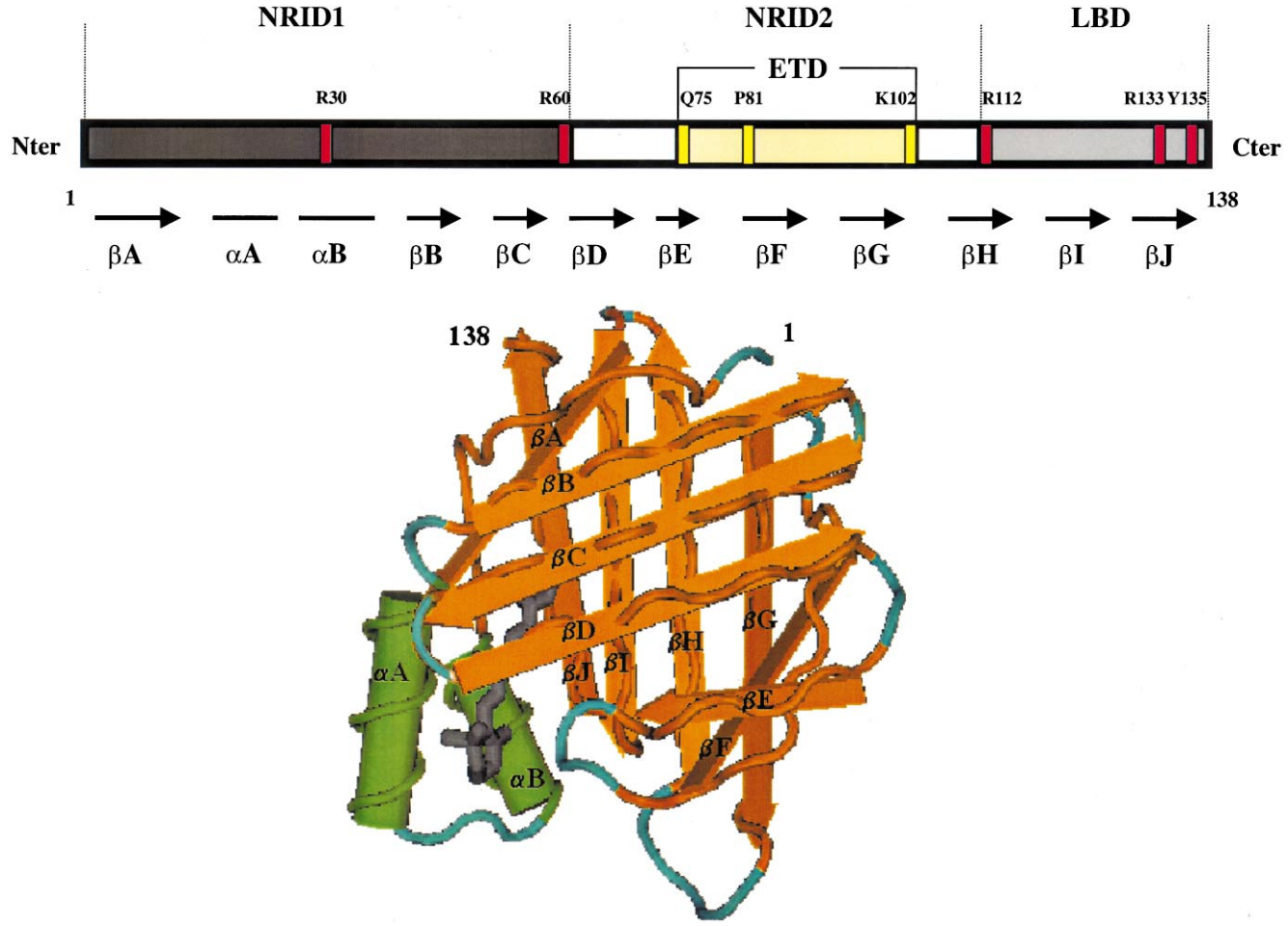

Fig. 6. Schematic representation and stereo molecular model of human holo-CRABPII. (Top line) The schematic representation of holo-CRABPII indicates NRID1 and NRID2. The ETD characterized by the three spatially aligned residues (Q75, P81, and K102 (yellow)) is located into NRID2 (pale yellow). R30, R60, R112, R133 and Y135 (red) participate to the RA-binding. Helix A and B and β-sheets A–J are indicated. In the bottom line, the 3-D structure of human holo-CRABPII consists of a helix-turn-helix motif (green), two nearly orthogonal five-stranded β-sheets (orange), and loops of β-sheets (blue). RA is in gray.

[10], which also physically interacts in a ligand-independent manner with the nuclear receptors. It is interesting to note that both interacting regions (NRID1 and NRID2) define at the structural and conformational levels the entrance of the ligand-binding pocket of CRABPII (Fig. 6).

Though in a number of respects CRABPII appears to share most of the functional features of the co-activators described so far, the interaction domains identified in this study suggest a distinct mechanism of co-activator function, some of which have already been described in newly discovered co-activators. Indeed, a ligand-independent physical interaction of a co-activator with a nuclear receptor has been observed in the case of RAP250/ASC-2 [15,16] and ASC-1 [17]. The fact that CRABPII binding to the receptor does not require the AF-2AD 'core' is in accordance with the absence of LXXLL motifs in its sequence.

In the light of the results presented here and the recently published data on the subject, the following schematic scenario of CRABPII's function in the RANC may be proposed. In the nucleus, holo-CRABPII docks to the apo-receptors bound to the promoter region of the target gene. The docking occurs around the key structures of both CRABPII and RAR or RXR ligand entrance pockets. This conformation brings the two ligand entrance pockets in communication and may thus facilitate the release and channeling of RA from holo-CRABPII to apo-RARα or apo-RXRα. Devoid of its ligand, apo-CRABPII remains bound to the holo-receptors, impeding the release of the ligand from the nuclear receptor. The channeling of the retinoid from CRABPII to the receptors has been observed in vitro with all-*trans* RA and RARα [7]. This channeling may explain the enhancement of transactivation only observed in the presence of retinoids which bind both CRABPII and RAR or RXR [4]. CRABPII by facilitating the formation of an active transcriptional RAR [7] or RXR complex, increasing the stability of the RA transcriptional complex bound to the response element [4], and/or preventing the dissociation of RA from RAR and RXR, may thus contribute to the enhancement of the RA-mediated transactivation.

Identifying the other partners of CRABPII in this complex may help to understand the true impact of CRABPII in RA signaling pathways.

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References

[1] Napoli, J.L. (1996) FASEB J. 10, 993–1001.
[2] Ong, D.E., Newcomer, M.E. and Chytil, F. (1994) in: The Retinoids: Biology, Chemistry and Medicine (Sporn, M.B., Roberts, A.B. and Goodman, D.S., Eds.), 2nd edn., pp. 288–317, Raven Press, New York.
[3] Åström, A., Tavakkol, A., Pettersson, U., Cromie, M., Elder, J.T. and Vorrhees, J.J. (1991) J. Biol. Chem. 266, 17662–17666.
[4] Delva, L., Bastie, J.-N., Rochette-Egly, C., Kraïba, R., Balitrand, N., Despouy, G., Chambon, P. and Chomienne, C. (1999) Mol. Cell. Biol. 19, 7158–7167.
[5] Kreutz, M., Fritsche, J., Andreesen, R. and Krause, S.W. (1998) Biochem. Biophys. Res. Commun. 248, 830–834.
[6] Napoli, J.L. (1997) Semin. Cell Dev. Biol. 8, 403–415.
[7] Dong, D., Ruuska, S.E., Levinthal, D.J. and Noy, N. (1999) J. Biol. Chem. 274, 23695–23698.
[8] Jing, Y., Waxman, S. and Mira-y-Lopez, R. (1997) Cancer Res. 57, 1668–1672.
[9] Wolf, G. (2000) Nutr. Rev. 58, 151–153.
[10] Budhu, A., Gillilan, R. and Noy, N. (2001) J. Mol. Biol. 305, 939–949.
[11] Chambon, P. (1996) FASEB J. 10, 940–954.
[12] Glass, C.K. and Rosenfeld, M.G. (2000) Genes Dev. 14, 121–141.
[13] vom Baur, E., Zechel, C., Heery, D., Heine, M.J., Garnier, J.M., Vivat, V., Le Douarin, B., Gronemeyer, H., Chambon, P. and Losson, R. (1996) EMBO J. 15, 110–124.
[14] Wang, L., Li, Y., Abildgaard, F., Markley, J.L. and Yan, H. (1998) Biochemistry 37, 12727–12736.
[15] Caira, F., Antonson, P., Pelto-Huikko, M., Treuter, E. and Gustaffson, J.A. (2000) J. Biol. Chem. 275, 5308–5317.
[16] Lee, S.K., Anzick, S.L., Choi, J.E., Bubendorf, L., Guan, X.Y., Jung, Y.K., Kallioniemi, O.P., Konomen, J., Trent, J.M., Azorsa, D., Jhun, B.H., Cheong, J.H., Lee, Y.C., Meltzer, P.S. and Lee, J.W. (1999) J. Biol. Chem. 274, 34283–34293.
[17] Kim, H.J., Yi, J.Y., Sung, H.S., Moore, D.D., Jhun, B.H., Lee, Y.C. and Lee, J.W. (1999) Mol. Cell. Biol. 19, 6323–6332.