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Amyloid fibril formation of peptides derived from the C-terminus of CETP modulated by lipids

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ABSTRACT

Cholesteryl-ester transfer protein (CETP) is a plasmatic protein involved in neutral lipid transfer between lipoproteins. Focusing on the last 12 C-terminus residues we have previously shown that mutation $D_{470}N$ promotes a conformational change towards a β-secondary structure. In turn, this modification leads to the formation of oligomers and fibrillar structures, which cause cytotoxic effects similar to the ones provoked by amyloid peptides. In this study, we evaluated the role of specific lipid arrangements on the structure of peptide helix-*Z* ($D_{470}N$) through the use of thioflavin T fluorescence, peptide bond absorbance, circular dichroism and electron microscopy. The results indicate that the use of micelles formed with lysophosphatidylcholine and lysophosphatidic acid (LPA) under neutral pH induce a conformational transition of peptide helix-*Z* containing a β-sheet conformation to a native α-helix structure, therefore avoiding the formation of amyloid fibrils. In contrast, incubation with phosphatidic acid does not change the profile for the β-sheet conformation. When the electrostatic charge at the surface of micelles or vesicles is regulated through the use of lipids such as phospholipid and LPA, minimal changes and the presence of β-structures were recorded. Mixtures with a positive net charge diminished the percentage of β-structure and the amount of amyloid fibrils. Our results suggest that the degree of solvation determined by the presence of a free hydroxyl group on lipids such as LPA is a key condition that can modulate the secondary structure and the consequent formation of amyloid fibrils in the highly flexible C-terminus domain of CETP.

1. Introduction

CETP facilitates the transfer of neutral lipids between lipoproteins, and plays an important role in reverse cholesterol transport. The tridimensional view of the C-terminus region of CETP (aa 453–476) is composed of a β-sheet (aa 453–462) and the native amphipathic α-helix (aa 465–476) named helix-*X* (Fig. 1). Several studies have demonstrated that a critical site for the transfer process is restricted specifically to the 12 residue C-terminus domain structured as an amphipathic α-helix [1–3]. Notwithstanding, our group has reported that this domain shows conformational changes in a non-lipid microenvironment when mutation $D_{470}N$ is introduced through the use of peptide denominated helix-*Z* [4,5]. These conditions give origin to a hydrophobic cluster (^{467}LLVNFLQ^{473}) which favors the presence of a β-secondary structure, a mechanism coupled with the formation of oligomers and amyloid fibrils [5]. Employing helix-*Z* as a model peptide, we have studied the role of several lipid arrangements as potential modulators of secondary structure and potentially upon amyloid fibril formation.

It has been reported that under specific conditions, lipid molecules induce conformational changes in various amyloid precursor proteins, in addition to the key role in the formation and stabilization of amyloid fibrils [6–8]. Likewise, the interaction between oligomeric precursor species on specific domains of the cell membrane is a primary event that results in the appearance of early cytotoxic effects associated with disease [9,10]. In this case, the role of specific lipid compositions on the hydrophilic/hydrophobic interface must be critical as a recognition site that can modulate possible conformational changes in secondary structure, which in turn could modify the formation of structures controlled by order-to-disorder and disorder-to-order transitions [5–7,9,11]. In this respect, it has been described that molecules such as lysophosphatidic acid (LPA), a phospholipid derived from the enzymatic action of several extracellular phospholipases from precursor molecules such as lysophosphatidylcholine or phosphatidic acid (PA), can promote in the protein β_2-microglobulin the formation *in vitro* of amyloid fibrils [12,13]. Nevertheless, the route by which the autotaxin enzyme particularly produces a high amount of LPA from lysophosphatidylcholine, is still not well understood [14,15].

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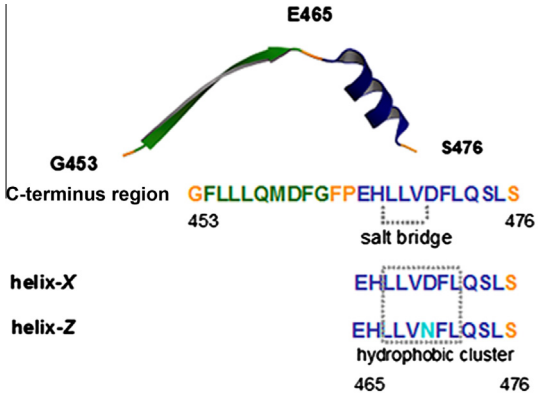

Fig. 1. Structural representation of the C-terminus region of CETP showing sequences of peptides helix-*X* and helix-*Z*. The H466-D470 salt bridge and the hydrophobic cluster are shown. The structure was obtained from the Protein Data Bank, access code: 2obd.

In this study, we present a series of experiments which demonstrate that treatment of helix-*Z* with LPA and lysophosphatidylcholine (lyso-C_{12}PC), lipids that can be found on the surface of lipoproteins, promote a structural change from a β-chain to a native α-helix structure. Incubation of helix-*Z* with LPA concentrations above 2.5 mM completely inhibits the formation of amyloid fibrils, in a manner that interactions of peptide with specific hydrophilic/hydrophobic interfaces formed by this lipid, should retain peptide monomers at the surface and consequently prevent peptide self-assembly. These conditions might allow helix-*Z* to recover and maintain the functional α-helix conformation of the C-terminus domain of CETP and therefore warranty protein function.

2. Materials and methods

Cholesterol, cholesteryl-ester, L-α phosphatidic acid dipalmitoyl (PA), L-α-phosphatidylethanolamine dipalmitoyl (PE), L-α-phosphatidylcholine dipalmitoyl (DPPC) and thioflavin T (ThT) were obtained from Sigma–Aldrich (St. Louis, MO). L-α-Phosphatidylcholine (PC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC), 1-palmitoyl-2-oleoyl-sn-glycero-3-phospho-1-glycerol (POPG), 1-lauroyl-2-hydroxy-sn-glycero-3-phosphocholine (lyso-C_{12}PC) and 1-oleoyl-2-hydroxy-sn-glycero-3-phosphate (LPA) were obtained from Avanti Polar Lipids (Alabaster, AL).

2.1. Peptide synthesis and peptide preparation

Helix-*Z* (^{465}EHLLV*N*FLQSLS^{476}) and native peptide (^{465}EHLLVDFLQSLS^{476}) derived from the C-terminus of CETP were synthesized by GenScript (Piscataway, NJ) and dissolved in a carbonate buffer pH 9.5 (1 mg/ml). From this solution a further 1:5 dilution was carried out. To evaluate the structure at pH 7.2 in the different lipid environments, a sodium phosphate buffer was also used. Under the same conditions, the control peptide ^{460}DFGFPEHL^{46} was employed. Solutions were filtered through 0.22 μm membrane filters before carrying out the experiments. Purity of peptides was greater than 98% confirmed by mass spectrometry and HPLC analysis. Peptide concentration was determined by measuring the peptide bond absorbance at 205 nm.

Peptide samples at a concentration of 200 μg/ml were incubated with the different lipid preparations for 12 h at 25 °C before their structural characterization, employing circular dichroism, thioflavin T fluorescence, peptide bond spectroscopy and electron microscopy.

2.2. Circular dichroism spectroscopy

Circular dichroism (CD) spectra were recorded with an AVIV 62DS spectropolarimeter (AVIV Instruments) at 25 °C employing far UV wavelength (190–260 nm). Experiments were performed at a peptide concentration of 200 μg/ml in a 1.0 mm quartz path length cuvette, running AVIV software. Spectra were recorded with a 1 mm bandwidth, using 1 nm increments and 2.5 s accumulation time averaged over 3 scans. CD results are reported as mean molar ellipticity (Θ, deg cm^2 dmol^{-1}) considering the baseline correction.

2.3. Thioflavin T fluorescence and peptide bond spectroscopy

Employing 180 μg/ml of peptide, the absorbance was measured every 1 nm using a Perkin Elmer UV/Vis Lambda 2*S* spectrophotometer scanning from 200 to 240 nm. Peptide spectra were corrected by subtracting the corresponding control spectra obtained under identical conditions. Additionally, the β-structure was characterized with ThT fluorescence assay. Fluorescence emission spectra were registered at 25 °C from 470 to 540 nm with an excitation wavelength of 450 nm. A scan velocity of 60 nm/min using an Olis DM45 spectrofluorimeter was used. The concentrations of ThT and peptides were 10 μM and 36 μM, respectively.

2.4. Preparation of micelles formed by phosphatidylcholine/cholesteryl-esters

Lipids were mixed in chloroform and dried for 6 h under a gentle stream of N_2, and an additional period of 24 h in a SpeedVac concentrator (Savant). Lipid mixtures were prepared with a molar ratio of PC 2 mM and cholesteryl-ester 100 μM (20:1). After drying, lipids were resuspended in pH 6.8 buffer and subsequently sonicated 15 s on/30 s off pulses for 4 cycles of 10 min in an ice bath under a flow of N_2 using a Sonifier 250 ultrasonicator (Branson). Samples were left to equilibrate for 2 h and centrifuged at 13,000 rpm for 10 min before being used.

2.5. Preparation of micelles formed by lyso-C_{12}PC, LPA and PA

The required amounts of lyso-C_{12}PC dissolved in chloroform were placed under a gentle stream of N_2 for 4 h, complete solvent free treatment was achieved by an additional 22 h in a vacuum equipment. Samples were resuspended in a phosphate buffer pH 6.8 at 37 °C (50 mM). Samples were kept 2 h at 25 °C and subsequently centrifuged at 13,000 rpm for 10 min at 12 °C.

LPA samples in chloroform were placed under a gentle flow of N_2 for 6 h, and additional 12 h in vacuum equipment. The samples were hydrated in phosphate buffer and afterwards processed through 4 cycles of freezing in liquid N_2, and thawing at 37 °C. Solutions were left to equilibrate for 2 h and centrifuged at 13,000 rpm for 10 min. Under the same experimental conditions, PA vesicles were prepared with an additional step of sonication for 4 cycles of 10 min.

2.6. Preparation of micelles by phospholipids and LPA

PC and LPA were mixed in chloroform and dried for 6 h under a gentle stream of N_2 with an additional treatment using a SpeedVac concentrator 22 h in vacuum. Lipid mixtures were prepared with a molar ratio of PC 3.06 mM and LPA 0.92 mM. After drying, lipid mixture was resuspended in pH 6.8 buffer and subsequently sonicated for 4 cycles. Samples were left to equilibrate for 2 h and centrifuged at 13,000 rpm for 10 min. Employing the same methodology, micelles consisting of DPPC/LPA and PE/LPA were prepared. Under a ratio of POPC 75% and POPG 25%, negatively charged micelles were prepared with the addition of LPA.

2.7. Electron microscopy

Peptide samples incubated under different conditions were processed employing a negative staining technique and visualized using transmission electron microscopy (NS-TEM). Samples (10 μl) were placed on carbon-coated copper grids (400 mesh) for 10 min at 25 °C. Excessive liquid was removed and the grids were negatively stained with uranyl acetate solution (2%, w/v) for 5 min. Samples were dried for 20 min. NS-TEM images were acquired using a JEM-1200EX11 JEOL microscope at 70 kV with a magnification of 60,000×.

3. Results and discussion

Previous studies from our laboratory have shown that peptide helix-*Z* shows the formation of a β-type secondary structure dependent on pH and peptide concentration [5]. Conditions such as ionic strength did not modify the content of β-structure, and only temperatures above 70 °C promote a decrease in the percentage of this type of secondary structure [5]. In this study we evaluated the effect of several lipid arrangements upon helix-*Z* structure at pH 7.2 under physiological conditions. Specifically, we conducted a series of experiments by changing regional characteristics of lipid such as: polar head size, acyl chain length, electrostatic charge and degree of solvation, all of them able to modify the secondary structure of helix-*Z*.

Treatment with increasing incubation concentrations of lyso-C_{12}PC (0.01–40 mM) showed that lipid concentrations below 5 mM allow helix-*Z* to maintain a β-sheet conformation when monitored by CD (Fig. 2A). Incubation with 1 mM lyso-C_{12}PC, a concentration close to the critical micelle concentration (0.9 mM) for this lipid, increased values that correspond to a β-structure (Fig. 2A and B). Under this condition, interactions of helix-*Z* and lyso-C_{12}PC in an aqueous environment must have taken place in a dynamic equilibrium between lipid monomers as well as formed micelles. In this regard, it has been reported that molecules with a similar structure to lyso-C_{12}PC trigger the aggregation phenomenon in amyloidogenic proteins at concentrations equivalent to those used in this study [16]. In our hands, concentrations of lyso-C_{12}PC close to 10 mM induced a transition point between β-sheet structures and the formation of α-helical structures. This change was followed by evaluating the CD characteristics for a β-sheet conformation at 201 nm (Θ_{201nm}) (Fig. 2B). This phenomenon was also studied following changes in peptide bond absorbance at 218 nm (Fig. 2C) and by fluorescence coupled to ThT (Fig. 2D). Under treatment with lyso-C_{12}PC (10 mM), fibrillar structures were still identified in smaller quantities but more extended

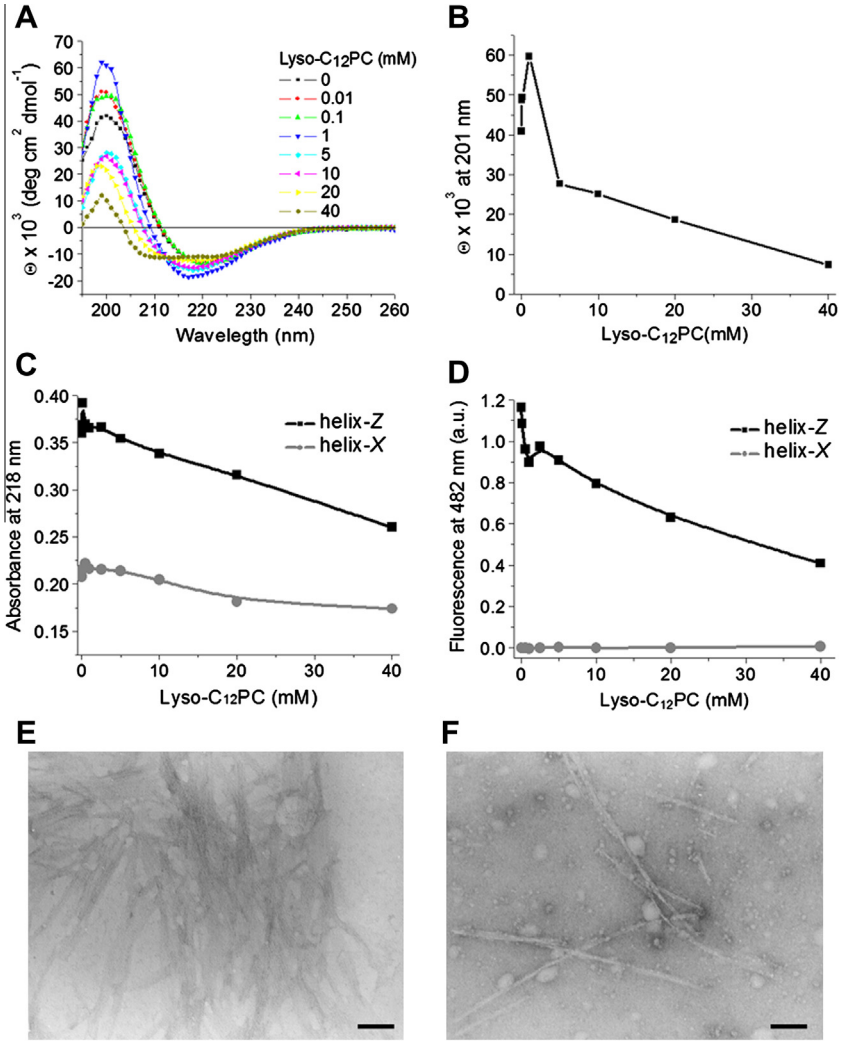

Fig. 2. Effect of lysophosphatidylcholine upon the structure of helix-*Z*. (A) CD spectra obtained under treatment with increasing concentrations of lyso-C_{12}PC. (B) Mean molar ellipticity values at 201 nm. (C) Under the same conditions, absorbance at 218 nm, (D) fluorescence coupled to ThT at 482 nm. Native peptide was used as control. (E) Amyloid fibrils formed by helix-*Z*. (F) Helix-*Z* incubated with lyso-C_{12}PC vesicles (10 mM). Bars correspond to 100 nm.

with respect to helix-*Z* samples not incubated with lipid (Fig. 2E and F). At higher concentrations of lyso-C_{12}PC (20 and 40 mM), although a residual signal for β-structures was detected following peptide bond absorbance and fluorescence coupled to ThT, CD measurements showed the formation of well-defined α-helix structures.

In another series of experiments, considering that the hydrophobic characteristics of the surrounding microenvironment are key conditions that favor structural changes in specific domains of lipid binding proteins, we evaluated several lipid molecules with structures similar to lyso-C_{12}PC. Using a concentration range between 0.1 and 10 mM LPA, a lipid with a small polar head close to the acyl chain, a series of experiments were carried out and the conformational changes from β-structures to α-helices studied. Spectra obtained showed an isodichroic point near to 215 nm associated with the presence of only two conformational states (Fig. 3A).

CD experiments show that this β to α transition was also identified by plotting the signal at Θ_{201nm}, where it was found that incubation with concentrations of LPA above 1 mM induces a drastic decrease in CD values associated with the loss of β-structure (Fig. 3B). In parallel, conformational changes were followed recording absorbance of peptide bonds at 218 nm (Fig. 3C) and by measurements of fluorescence coupled to ThT (Fig. 3D).

The present data indicate that LPA induces a well-defined structural transition in secondary structure from β-sheet towards an α-helix at concentrations above its cmc. In fact, after treatment with 2.5 mM LPA, ThT fluorescence was suppressed (Fig. 3D insert), indicating a complete loss of β-structure content. Fibrillar structures were not found in LPA samples analyzed below 10 mM and processed through NS-TEM (Fig. 3F). Our results suggest that conformational changes in secondary structure dependent of LPA are associated with a cooperative process, where helix-*Z* recovers the levels of an α-helical structure similar to what it is found when the native peptide is studied (Supplementary Fig. 1). However, this might not be considered a general phenomenon for lipids with a free hydroxyl groups at the polar head. At the highest lyso-C_{12}PC concentrations (20 and 40 mM), the fluorescence signal coupled to ThT was not completely abolished; therefore, incubation with lyso-C_{12}PC is associated with a partial transition towards the formation of α-helices.

Polar head size and the presence of a free hydroxyl group in position sn2 of the glycerol backbone, properties that should modify the degree of solvation at the surface of interfaces [7], should play a key role in the mechanisms that modulate lipid-dependent amyloid fibril formation [7,9]. In this case, the hydrophilic components of phospholipids such as a free hydroxyl group in LPA, may affect

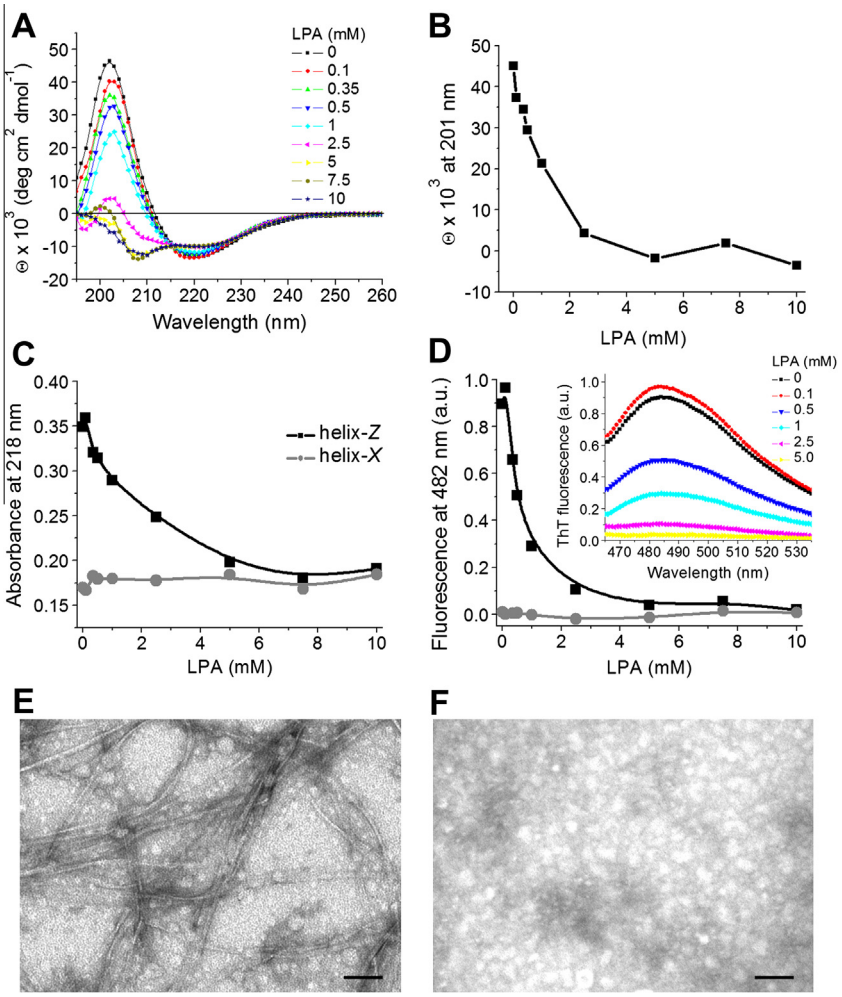

Fig. 3. Lysophosphatidic acid prevents the formation of amyloid fibrils by helix-*Z*. (A) CD spectra of helix-*Z* incubated with increasing concentrations of LPA. (B) Mean molar ellipticity values at 201 nm. (C) Absorbance values at 218 nm. (D) ThT-fluorescence at 482 nm. The native peptide was used as control. The insert shows the emission spectra of helix-*Z* at different concentrations of LPA. (E) Amyloid fibrils formed by helix-*Z*. (F) Effect of LPA treatment in the formation of fibrils. Four samples were processed on different days. Bars correspond to 100 nm.

the position and the array of the hydrophobic assemblies in relation to the interface [17]. We tested this possibility by treatment with increasing concentrations of PA, a lipid molecule with two acyl chains associated to the glycerol backbone, conditions that should not favor the conformational change from β-sheet structures to an α-helix. Employing spectroscopic techniques, this thesis was corroborated using a concentration range of 0.1–5 mM PA, when a β-sheet structure was maintained and the property to form amyloid fibrils was observed when peptide helix-*Z* was studied (Supplementary Fig. 2).

Considering that the electrostatic charge on lipid surfaces is a factor that could modulate the secondary structure of helix-*Z*, we studied the effect of a series of phospholipids mixed with LPA (76%/24%) (Fig. 4). Peptide treatment with micelles formed with POPC/POPG and LPA does not modify the profile of the β-secondary structure evaluated by CD and ThT fluorescence (Fig. 4A and B). This condition is maintained throughout the concentration range of 0.1–2.4 mM of these mixtures, showing micelle formation at the highest concentrations (data not shown).

When helix-*Z* was incubated with neutral vesicles composed of POPC (1.23 mM) and LPA (0.37 mM), CD spectra and fluorescence emission values were similar to the control values without the addition of lipids (Fig. 4A and B). A similar response was obtained when neutral micelles formed by phosphatidylcholine (PC) were studied, a condition in which the formation of well-defined amyloid fibrils is maintained (Fig. 4C and D). Since an extended incubation time (24 h) was used, the presence of oligomeric structures was reduced [5]. However, in these samples it was possible to identify amyloid fibrils located at the surface of lipid micelles (Fig. 4D insert), a condition that suggests there might be interactions at the surface of micelles without the presence of a structural change in helix-*Z*.

Treatment with increasing concentrations of lipids contained in mixtures composed of PC/cholesteryl-esters extensively used in a previous work employing CETP [18], did not modulate the structural changes described above for LPA and lyso-C_{12}PC and only a slight decrease in β-structure content was recorded (data not shown).

Under the same conditions, incubation with neutral micelles formed by DPPC and LPA maintains a β-sheet conformation in helix-*Z*. Nevertheless, in this case an increase in the fluorescence spectrum of ThT was registered, condition that is related to the presence of high concentrations of fibrils shown by samples processed for NS-TEM. Several characteristics related to the morphology of these fibrils showing a highly heterogeneous pattern, were registered (Fig. 4E).

Treatment with micelles composed of phosphatidylethanolamine (PE) and LPA presenting a positive charge at their surface and a small polar head group, induced a moderate decrease in the content of β-structures of helix-*Z* (Fig. 4A and B). Likewise, lower amounts of amyloid fibrils were recorded with respect to previous lipid treatments (Fig. 4F). Under our experimental conditions, at neutral pH helix-*Z* maintains a net negative charge (−1), in such a way that these results could be associated with a low electrostatic binding capacity at the surface of positive charged vesicles. Interestingly, when helix-*X*, the native C-terminus domain of CETP in a disordered state was evaluated in the presence of PE/LPA vesicles, the highest levels of α-helix are promoted (Supplementary Fig. 3).

A hydrophobic cluster at the C-terminus domain of CETP ^{467}LLVNFLQ^{473} originated by mutation $D_{470}N$ shares similar characteristics with the hydrophobic structural motifs for *steric zippers*, which have been described to integrate the molecular structure of amyloid fibrils [19,20]. In this sense, mutation $D_{470}N$ minimizes the electrostatic repulsion between peptide monomers, promoting the formation of hydrogen bonds in the backbone and triggering β-sheet and fibril formation in helix-*Z* [5]. These phenomena are restricted to the C-terminus end (residues 465–476), since peptide sequences that corresponds to ^{460}DFGFPEHL^{467}, do not show β-sheet formation, and even in the presence of lipids the peptide remains in a disordered state (data not shown).

The inhibition of fibril formation and stabilization of an α-helical structure in helix-*Z* seem to be directly associated with the specific physicochemical properties of LPA. The presence of a free hydroxyl group and a small polar head group may facilitate the molecular recognition for helix-*Z*, allowing the interaction of

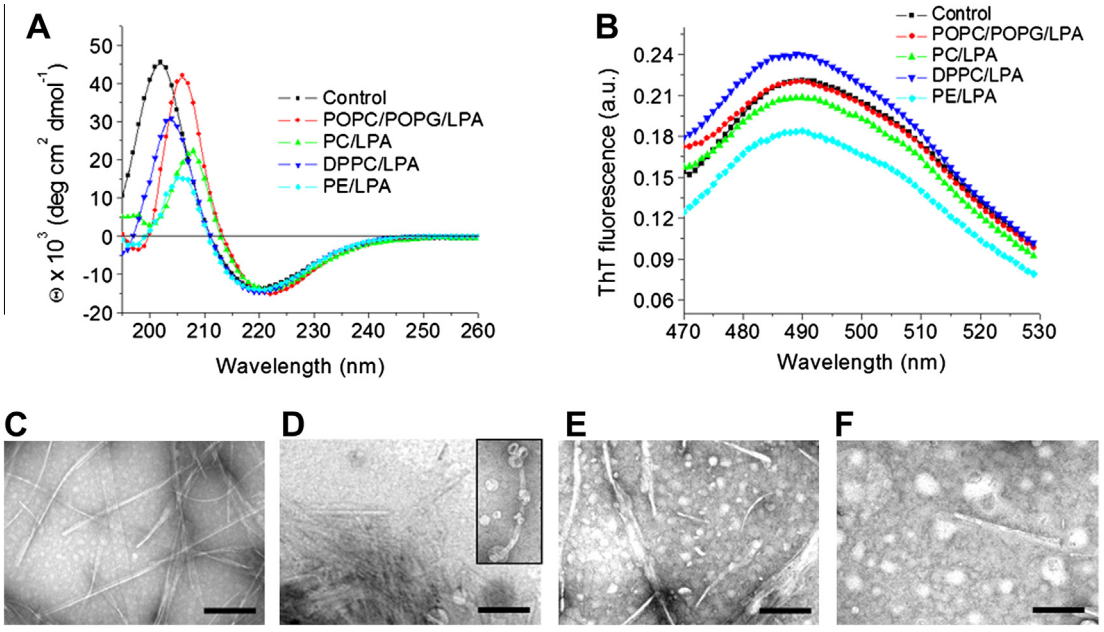

Fig. 4. Effect of lipid electrostatic charge upon the structure of helix-*Z*. (A) CD spectra of helix-*Z* incubated with lipid micelles of different composition. (B) Emission spectra ofThT-fluorescence. NS-TEM of helix-*Z* without lipid treatment (C), and with micelles composed of PC/LPA (D), DPPC/LPA (E) and PE/LPA (F). Bars correspond to 200 nm.

monomeric peptides at the surface of micelles. Therefore, nucleation and stacking of peptides, phenomena that lead to aggregation and ultimately to fibril formation are suppressed. In this sense, it has been reported that the stability of native folding is primarily determined by hydrophobic interactions between side chains, whereas the stability of amyloid fibrils is more dependent on backbone intermolecular hydrogen bonding interactions [21].

On the other hand, a large group of events occurring at the surface of lipids are influenced by hydrogen bonding networks [22], in such a way that binding of lipid/helix-*Z* at the surface of micelles or lipoproteins may involve the release of highly ordered water molecules located at the first layers of hydration, with the consequent reorganization of hydrogen bonds and hydrophobic interactions. Hence, conformational changes and modulation of secondary structure of peptides requires key conditions associated to the microenvironment, being key components the degree of solvation and the size of the polar head of lipids. In conclusion, our results suggest a regulatory role for LPA by modulating the mechanisms that maintain the C-terminus domain of CETP in a functional conformation directly associated to the presence of an α-helical structure for this segment.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.bbrc.2013.03.067.

References

[1] A.L. Alonso, A. Zentella-Dehesa, J. Mas-Oliva, Characterization of a naturally occurring new version of the cholesterol ester transfer protein (CETP) from small intestine, Mol. Cell. Biochem. 245 (2003) 173–182.
[2] S. Wang, P. Kussie, L. Deng, A. Tall, Defective binding of neutral lipids by a carboxyl-terminal deletion mutant of cholesteryl ester transfer protein. Evidence for a carboxyl-terminal cholesteryl ester binding site essential for neutral lipid transfer activity, J. Biol. Chem. 270 (1995) 612–618.
[3] S. Wang, X. Wang, L. Deng, E. Rassart, R.W. Milne, A.R. Tall, Point mutagenesis of carboxyl-terminal amino acids of cholesteryl ester transfer protein. Opposite faces of an amphipathic helix important for cholesteryl ester transfer or for binding neutralizing antibody, J. Biol. Chem. 268 (1993) 1955–1959.
[4] V.M. Bolaños-García, M. Soriano-García, J. Mas-Oliva, Stability of the C-terminal peptide of CETP mediated through an (i, i + 4) array, Biochim. Biophys. Acta 1384 (1998) 7–15.
[5] V. García-González, J. Mas-Oliva, Amyloidogenic properties of a D/N mutated 12 amino acid fragment of the C-terminal domain of the cholesteryl-ester transfer protein (CETP), Int. J. Mol. Sci. 12 (2011) 2019–2035.
[6] A. Andreola, V. Bellotti, S. Giorgetti, P. Mangione, L. Obici, M. Stoppini, J. Torres, E. Monzani, G. Merlini, M. Sunde, Conformational switching and fibrillogenesis in the amyloidogenic fragment of apolipoprotein A-I, J. Biol. Chem. 278 (2003) 2444–2451.
[7] P. Mendoza-Espinosa, A. Moreno, R. Castillo, J. Mas-Oliva, Lipid dependant disorder-to-order conformational transitions in apolipoprotein CI derived peptides, Biochem. Biophys. Res. Commun. 365 (2008) 8–15.
[8] A.M. Sheikh, A. Nagai, Lysophosphatidylcholine modulates fibril formation of amyloid beta peptide, FEBS J. 278 (2011) 634–642.
[9] P. Mendoza-Espinosa, V. García-González, A. Moreno, R. Castillo, J. Mas-Oliva, Disorder-to-order conformational transitions in protein structure and its relationship to disease, Mol. Cell. Biochem. 330 (2009) 105–112.
[10] E. Evangelisti, C. Cecchi, R. Cascella, C. Sgromo, M. Becatti, C.M. Dobson, F. Chiti, M. Stefani, Membrane lipid composition and its physicochemical properties define cell vulnerability to aberrant protein oligomers, J. Cell Sci. 125 (2012) 2416–2427.
[11] V.G. García-González, J. Mas-Oliva, El Concepto de Enfermedad Asociado a la Conformación de Proteínas, first ed., Universidad Nacional Autónoma de México and El Manual Moderno, Mexico, 2012.
[12] T. Ookoshi, K. Hasegawa, Y. Ohhashi, H. Kimura, N. Takahashi, H. Yoshida, R. Miyazaki, Y. Goto, H. Naiki, Lysophospholipids induce the nucleation and extension of beta2-microglobulin-related amyloid fibrils at a neutral pH, Nephrol. Dial. Transplant. 23 (2008) 3247–3255.
[13] H. Pál-Gábor, L. Gombos, A. Micsonai, E. Kovács, E. Petrik, J. Kovács, L. Gráf, J. Fidy, H. Naiki, Y. Goto, K. Liliom, J. Kardos, Mechanism of lysophosphatidic acid-induced amyloid fibril formation of beta(2)-microglobulin in vitro under physiological conditions, Biochemistry 48 (2009) 5689–5699.
[14] K. Nakanaga, K. Hama, J. Aoki, Autotaxin an LPA producing enzyme with diverse functions, J. Biochem. 148 (2010) 13–24.
[15] S. Okudaira, H. Yukiura, J. Aoki, Biological roles of lysophosphatidic acid signaling through its production by autotaxin, Biochimie 92 (2010) 698–706.
[16] S. Yamamoto, K. Hasegawa, I. Yamaguchi, S. Tsutsumi, J. Kardos, Y. Goto, F. Gejyo, H. Naiki, Low concentrations of sodium dodecyl sulfate induce the extension of beta 2-microglobulin-related amyloid fibrils at a neutral pH, Biochemistry 43 (2004) 11075–11082.
[17] D. Chandler, Interfaces and the driving force of hydrophobic assembly, Nature 437 (2005) 640–647.
[18] V. García-González, N. Gutiérrez-Quintanar, P. Mendoza-Espinosa, P. Brocos, Á. Piñeiro, R. Castillo, J. Mas-Oliva, Key structural arrangements at the C-terminus domain of CETP promote a mechanism for lipid-transfer activity, unpublished results.
[19] M.R. Sawaya, S. Sambashivan, R. Nelson, M.I. Ivanova, S.A. Sievers, M.I. Apostol, M.J. Thompson, M. Balbirnie, J.J. Wiltzius, H.T. McFarlane, A.Ø. Madsen, C. Riekel, D. Eisenberg, Atomic structures of amyloid cross-beta spines reveal varied steric zippers, Nature 447 (2007) 453–457.
[20] S.A. Sievers, J. Karanicolas, H.W. Chang, A. Zhao, L. Jiang, O. Zirafi, J.T. Stevens, J. Münch, D. Baker, D. Eisenberg, Structure-based design of non-natural amino-acid inhibitors of amyloid fibril formation, Nature 475 (2011) 96–100.
[21] A.W. Fitzpatrick, T.P. Knowles, C.A. Waudby, M. Vendruscolo, C.M. Dobson, Inversion of the balance between hydrophobic and hydrogen bonding interactions in protein folding and aggregation, PLoS Comput. Biol. 7 (2011) e1002169.
[22] M.Ø. Jensen, O.G. Mouritsen, G.H. Peters, The hydrophobic effect: molecular dynamics simulations of water confined between extended hydrophobic and hydrophilic surfaces, J. Chem. Phys. 120 (2004) 9729–9744.