

Figure 4, supplement 1

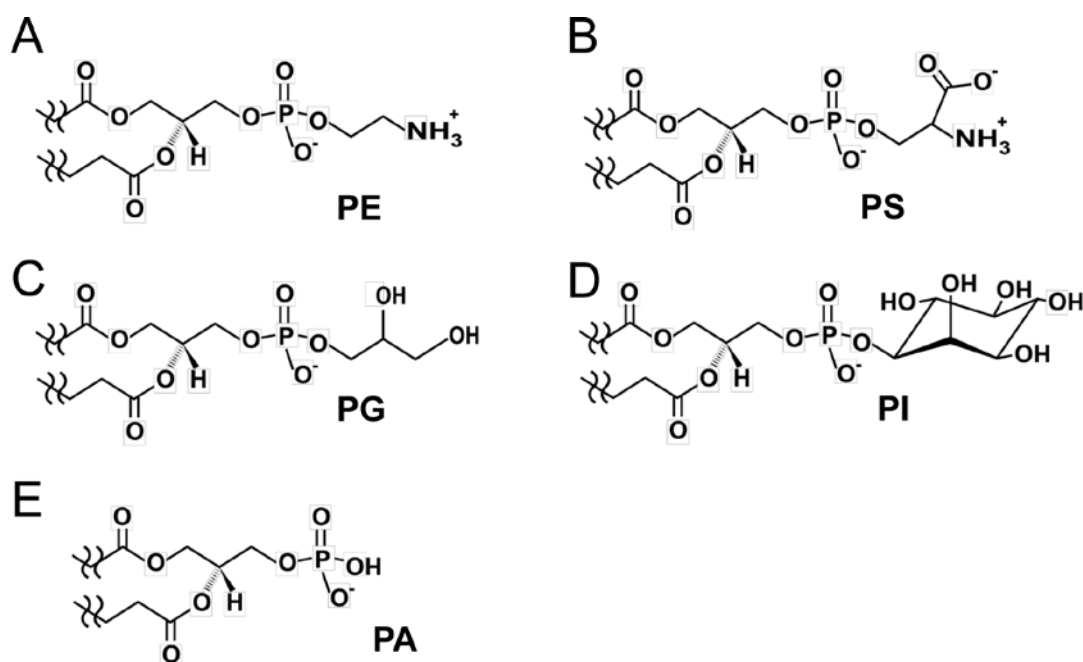


Figure 4-S1. Head group chemical formulas of various non-PC membrane phosphoglycerides (A) phosphatidylethanolamine PE, (B) phosphatidylserine PS, (C) phosphatidylglycerol PG (D) phosphatidylinositol PI, and (E) phosphatidic acid PA

Lipid specificity

Phosphoglycerol-based lipids have the same backbone topology but different head groups that define C2-domain binding specificity. Our findings reveal that the π -cation interaction is critical for binding to PC. PE (A) has a primary ammonium group replacing the $-\text{N}^+(\text{CH}_3)_3$ group in PC. Yet, earlier FRET data (Nalefski et al., 1998) and our SPR data (Fig 4B) indicate relatively weak binding of cPLA₂ C2-domain to PE. The electrostatic potential difference and diminished van der Waals contacts with Ala94, His62, and Asn64 could account for the binding affinity decrease for PE compared to PC. PS has a seryl group (B) replacing the $-\text{N}^+(\text{CH}_3)_3$ group in PC. Although the primary ammonium group in the seryl group would seem to be a candidate for undergoing π -cation interaction with Tyr96, binding by C2-domain is weak (Fig. 4B) suggesting steric clashing of the seryl carboxylate group with CBL residues. PG (C) and PI (D) are not suitable for interaction with cPLA₂ C2-domain due to lack of an ammonium group and steric clashing by their bulky head groups. PA (E) has only a phosphoryl moiety as its head group, which promotes weak interaction. Our SPR binding data showing much weaker binding of these phosphoglycerides compared to PC (Fig. 4B) are consistent with previous findings obtained using other techniques (Mosior et al., 1998; Nalefski et al., 1998; Six & Dennis, 2003).