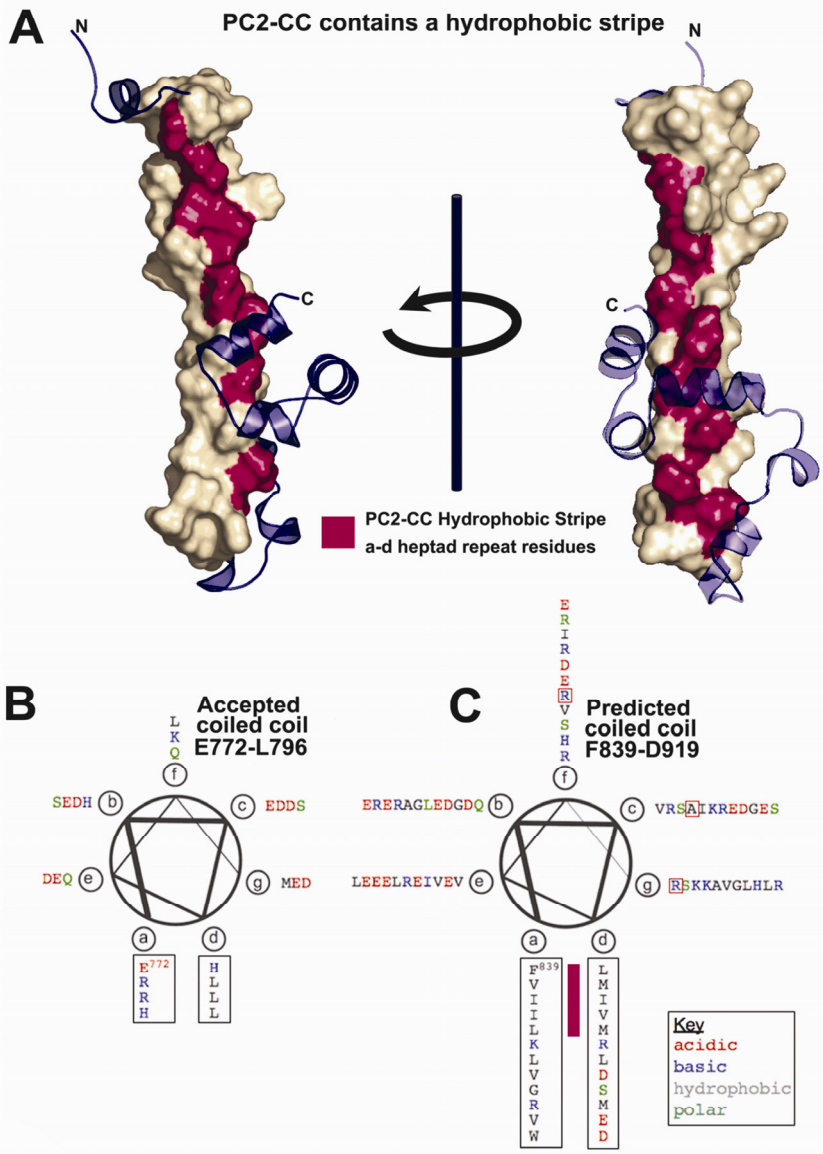
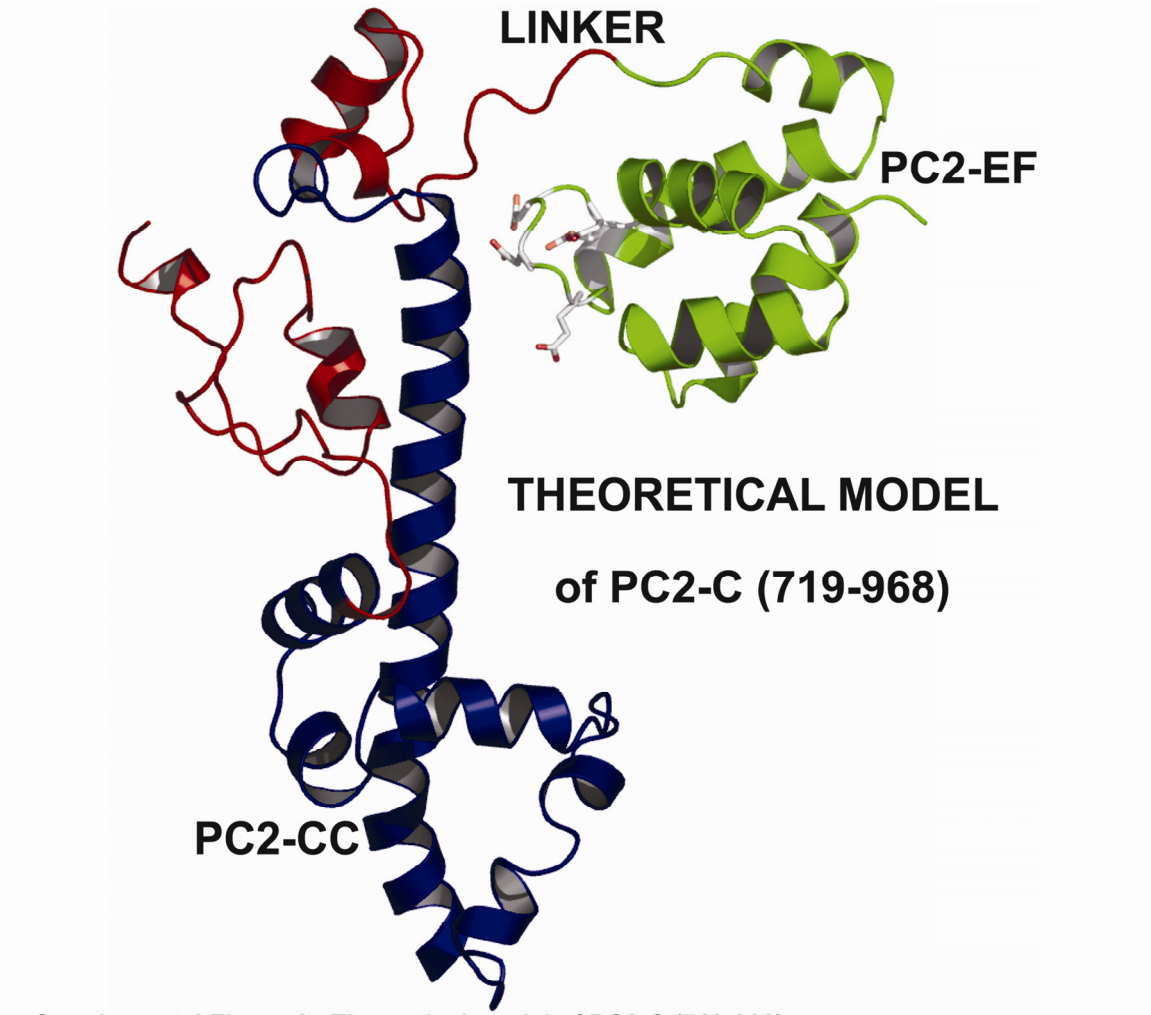
Supplemental Figure 1



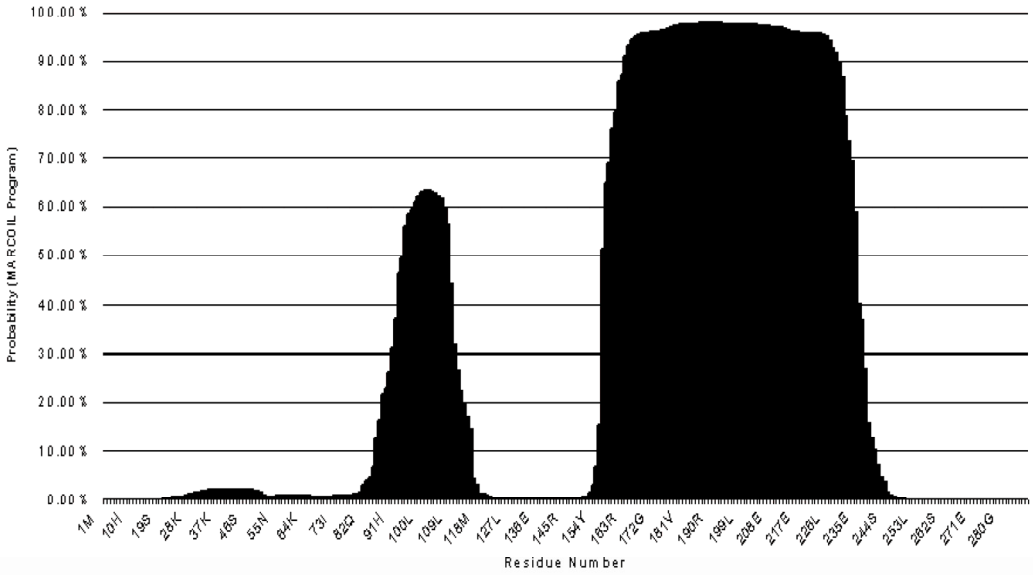
Supplemental Figure 1: PC2 contains a novel coiled coil domain with a hydrophobic protein-protein interaction surface. A) PC2-CC (G828-H927) is shown as cartoon and the central helix (F839-M870) depicted as surface. Heptad repeat 'a–d' residues predicted by MARCOIL are highlighted in pink. **B)** Helical wheel projection of PC2-C residues (E772-L796) previously reported to contain a coiled coil motif. Residues in the interface position 'a' and 'd' are hydrophillic or charged, making oligomerization at this site unfavorable. **C)** Helical wheel projection of PC2-C residues (F839-D919) proposed in this study to contain the coiled coil motif. Residues at the coiled coil interface 'a-d' are hydrophobic. The pink stripe corresponds to residues highlighted on the *de novo* model of PC2-CC and may serve as a PC2-C oligomerization or protein-protein interaction interface. PKD-associated truncations are boxed in red.

Supplemental Figure 2

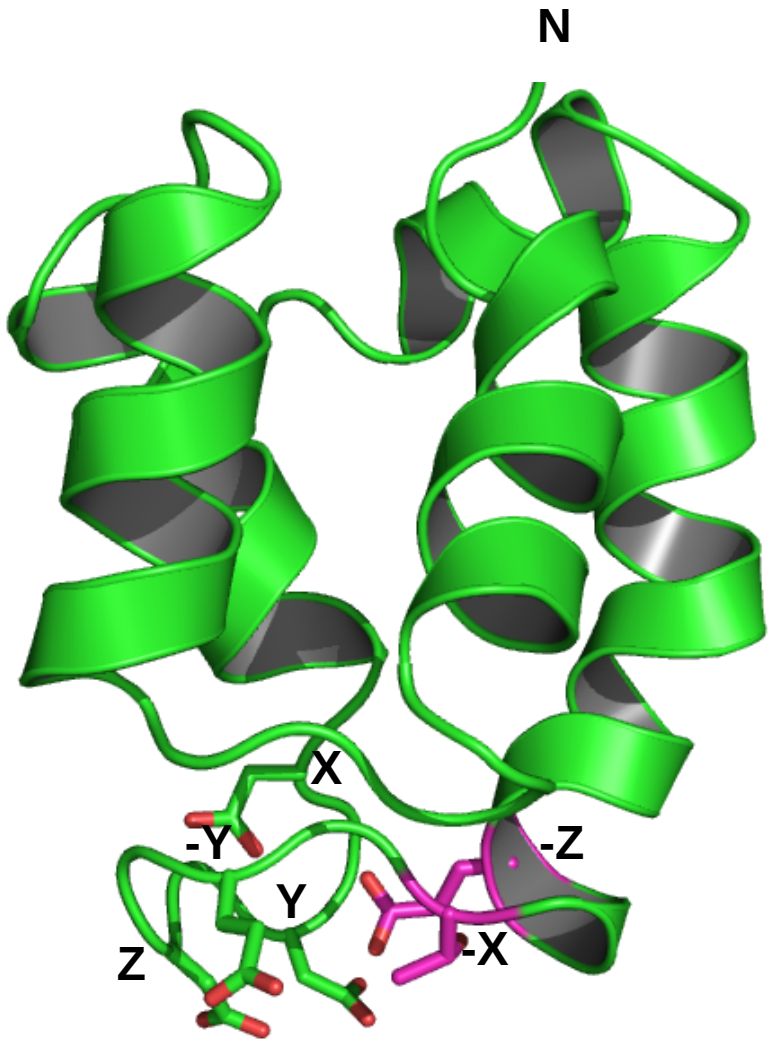


Supplemental Figure 2. Theoretical model of PC2-C (719-968)
ROBETTA models of PC2-C (703-968) and of PC2-EF (719-800) alone were analyzed to create a combined theoretical model of PC2-C. Coordinates for the ROBETTA model of PC2-EF (719-800) and coordinates of PC2-C (only residues 801-968) were combined and ligated using Swiss-PdbViewer followed by energy minimization. The combined model of PC2-C (719-968) was visualized using PYMOL. PC2-EF is shown in green and PC2-CC is shown in blue. Putative Ca^{2+} binding residues are shown as sticks. Flexible segments identified by limited proteolysis are shown in red. N-terminal residues 704-710 are not shown and were not included in the final model. Coordinates for ROBETTA models of PC2-EF, PC2-C and the combined theoretical model of PC2-C have been included as supplemental data.

Supplemental Figure 3

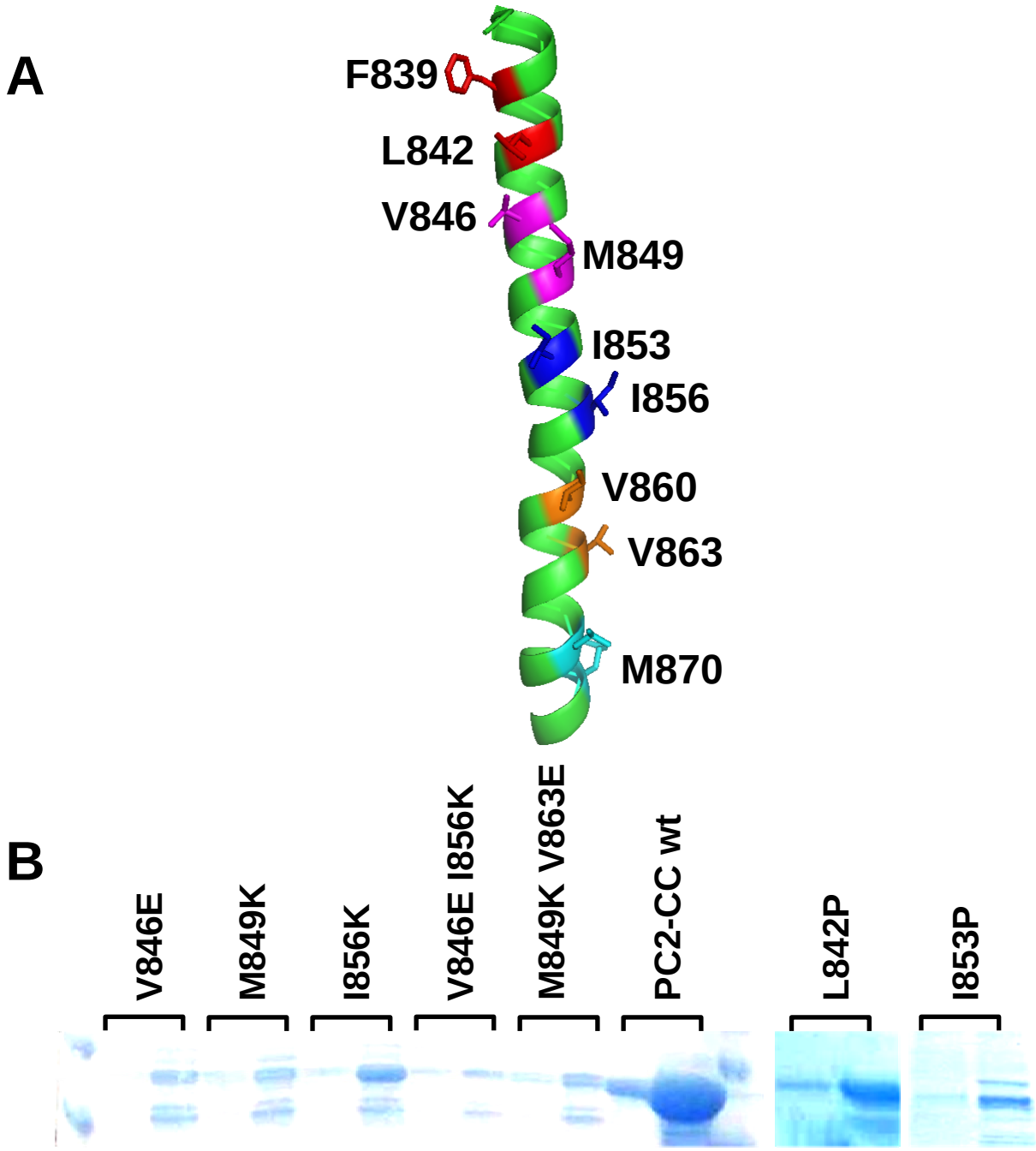


Supplemental Figure 3: MARCOIL output for PC2-C (M703-V968) suggests PC2 contains a previously unreported coiled coil domain (F839-D919). F839-D919 are predicted to have >90% propensity to form a coiled coil. Predicted coiled coil interface residues 'a' and 'd' are hydrophobic from F839-M870 and may serve as a oligomerization or protein-protein interaction interface. A shorter segment, Q776-D788, is predicted to have >50% propensity to form a coiled coil but the corresponding 'a' and 'd' interface residues are hydrophillic or charged.



Position	1	2	3	4	5	6	7	8	9	10	11	12
	X		Y		Z		-Y		-X			-Z
Residue	D763	Q764	D765	G766	D767	Q768	E769	L770	T771	E772	H773	E774
Mutation									T771A			E774A

Supplemental Figure 4. ROBETTA model of PC2-EF highlighting residues predicted to form a calcium binding loop. Residues in the –x position (T771) and –z position (E774), colored magenta, were mutated to alanine resulting in complete loss of calcium binding. PC2 residues predicted to form a canonical EF-hand calcium binding loop are listed in the above table.



Supplemental Figure 5. Site-directed mutagenesis of PC2-CC residues predicted to form the coiled coil oligomerization interface ('a-d' heptad repeat residues) to either a charged residue or proline induces non-specific aggregation and inclusion body formation upon recombinant expression in *E.coli*. **A.** ROBETTA model of the predicted PC2 coiled coil region highlighting the locations of heptad repeat residues 'a' and 'd'. **B.** SDS-PAGE of elution fractions following HisTrap Nickel column purification of individual charge or proline mutations of PC2-CC. Mutant PC2-CC varients were grown and purified in parallel and compared with wildtype PC2-CC for expression level, solubility and final yield. Only I856K and L842P yielded any protein (~20-fold less) in the soluble fraction, but these mutants rapidly precipitated. (note: minor bands visible on SDS-PAGE for mutations other than I856K and L842P are bacterial impurities)