

**Figure S3.** PLA2R CTLD domain alignment against CTLD1

**CTLD1-CTLD1**

| Score         | Expect | Method                       | Identities    | Positives     | Gaps      |
|---------------|--------|------------------------------|---------------|---------------|-----------|
| 247 bits(630) | 1e-91  | Compositional matrix adjust. | 118/118(100%) | 118/118(100%) | 0/118(0%) |

|       |    |   |     |
|-------|----|---|-----|
| CTLD1 | 1  | NSHICYQFNLLSSLWSSEAHSSCQMGGTLLSITDETEENFIREHMSSKTVEVWMGLNQL | 60  |
| CTLD1 | 1  | NSHICYQFNLLSSLWSSEAHSSCQMGGTLLSITDETEENFIREHMSSKTVEVWMGLNQL | 60  |
| CTLD1 | 61 | DEHAGQWSDGTPLNYLNWSPEVNFEPFVEDHCGTFSSFMPSAWRSRDCESTLPYICK   | 118 |
| CTLD1 | 61 | DEHAGQWSDGTPLNYLNWSPEVNFEPFVEDHCGTFSSFMPSAWRSRDCESTLPYICK   | 118 |

**CTLD1-CTLD2**

| Score          | Expect | Method                       | Identities  | Positives   | Gaps      |
|----------------|--------|------------------------------|-------------|-------------|-----------|
| 45.8 bits(107) | 2e-12  | Compositional matrix adjust. | 32/116(28%) | 53/116(45%) | 4/116(3%) |

|       |    |   |     |
|-------|----|---|-----|
| CTLD1 | 5  | CYQFNLLSSLWSSEAHSSCQMGGTLLSITDETEENFIREHMSSKTV-EVWMGLNQLDEH | 63  |
| CTLD2 | 5  | CYKLQK-EEKTWHEALRSCQADNSALIDITSLAEVEFLVTLGDNASETWIGLSSNKIP  | 63  |
| CTLD1 | 64 | AGWQWSDGTPLNYLNW-SPEVNFEPFVEDHCGTFSSFMPSAWRSRDCESTLPYICK    | 118 |
| CTLD2 | 64 | VSFEWSDSSVIFTNWHTLEPHIFPNRSQLCVS-AEQSEGHWKVKNCEERLFYICK     | 118 |

**CTLD1-CTLD3: No alignment**

**CTLD1-CTLD4**

| Score          | Expect | Method                       | Identities | Positives  | Gaps     |
|----------------|--------|------------------------------|------------|------------|----------|
| 43.1 bits(100) | 2e-11  | Compositional matrix adjust. | 26/73(36%) | 39/73(53%) | 7/73(9%) |

|       |    |  |    |
|-------|----|--|----|
| CTLD1 | 9  | NLLSSLWSSEAHSSCQMGGTLLSITDETEENFIREHMSSK-----TVEVWMGLNQLDE-  | 62 |
| CTLD4 | 13 | KVLMKRTWREAEAFCEEFGAHLASFAHIEEENFVNELLHSKFNWTEERQFWIGFNKRNPL | 72 |
| CTLD1 | 63 | HAG-WQWSDGTPL 74   |    |
| CTLD4 | 73 | NAGSWEWSDRTPV 85   |    |

**CTLD1-CTLD5**

| Score          | Expect | Method                       | Identities  | Positives   | Gaps       |
|----------------|--------|------------------------------|-------------|-------------|------------|
| 45.8 bits(107) | 3e-12  | Compositional matrix adjust. | 36/119(30%) | 54/119(45%) | 10/119(8%) |

|       |    |   |     |
|-------|----|---|-----|
| CTLD1 | 6  | YQFNLLSSLWSSEAHSSCQMGGTLLSITDETEENFIR---EHMSSKTVEVWMGLNQLDE   | 62  |
| CTLD5 | 6  | YLFHTFAS-EWLNFEFVCSWLHSDLLTIHSAHEQEFIHISKIKALSKYGASWWIGLQEERA | 64  |
| CTLD1 | 63 | HAGWQWSDGTPLNYLNWSPEVNFEPFVEDH---CGTFSSFMPSAWRSRDCESTLPYICK   | 118 |
| CTLD5 | 65 | NDEFWRWDGTPVIYQNW--DTGREERTVNNQSQRCGFIS-ITGLWGSEECVSMPSICK    | 120 |

CTLD1-CTLD6

| Score          | Expect | Method                       | Identities | Positives  | Gaps     |
|----------------|--------|------------------------------|------------|------------|----------|
| 53.9 bits(128) | 3e-15  | Compositional matrix adjust. | 26/67(39%) | 38/67(56%) | 3/67(4%) |

CTLD1 15 SWSEAHSSCQMGGTLLSITDETEENFIREHMSSKTVEVWMGLNQLDEHAGWQSDGTPL 74  
 +W+ A C +GGTL++I E E+ FI ++ +T VW+GL D W +G P+

CTLD6 19 NWTQAQHFCAEEGGTLVAIESEVEQAFITMNLFGQTTSVWIGLQNDYET---WLNKPV 75

CTLD1 75 NYLWSP 81  
 Y NWSP

CTLD6 76 VYSNWSP 82

CTLD1-CTLD7

| Score          | Expect | Method                       | Identities  | Positives   | Gaps      |
|----------------|--------|------------------------------|-------------|-------------|-----------|
| 45.4 bits(106) | 3e-12  | Compositional matrix adjust. | 30/103(29%) | 47/103(45%) | 5/103(4%) |

CTLD1 12 SLSWSEAHSSCQMGGTLLSITDETEENFIREHMSSKTVEVWMGLNQLDEHAGWQSDG 71  
 ++++W A +C M L+SITD+ ++F+ ++ W+GL D + WSDG

CTLD7 11 ANMTWYAAIKTCLMHKAQLVSITDQYHQSFLLTVLNLRLGYAHWIGLFTTDDNGLNFDWSDG 70

CTLD1 72 TPLNYLWSPPEVNFPEFVEDHCGTFSSFMPSAWRSRDCESTLP 114  
 T ++ W E E + C S W S CES L

CTLD7 71 TKSSFTFWKDE---ESSLLGDCVFADS--NGRWHSTACESFLQ 108

CTDL1-CTLD8

| Score          | Expect | Method                       | Identities  | Positives   | Gaps       |
|----------------|--------|------------------------------|-------------|-------------|------------|
| 56.6 bits(135) | 2e-16  | Compositional matrix adjust. | 38/122(31%) | 58/122(47%) | 12/122(9%) |

CTLD1 5 CYQFN-LLSLSWSEAHSSCQMGGTLLSITDETEENFIREHM---SSKTVEVWMGLNQL 60  
 CY F+ +L S+S+ AH C+ +G LL+I DE E F+ E + S VW+

CTLD8 5 CYSFSTVLDSMSFEAAHEFCKKEGSNLLTIKDEAENAFLLLEELFAFGSSVQMVWLNQAFD 64

CTLD1 61 DEHAGWQSDGTPLNYLW---SPEVNFPEFVEDHCGTFSSFMPSA-WRSRDCESTLPYI 116  
 + +W DGTP + NW P+ ++ F HC +P W+ C+ +I

CTLD1 65 GNNETIKWFDGTPDQSNWGIKPDY--FKPHHCVALR--IPEGLWQLSPCQEKKGFI 120

CTLD1 117 CK 118  
 CK

CTLD1 121 CK 122

The PLA2R domains were aligned using the blast program.

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