Supplementary Material

**Structure of TRAF family: current understanding of receptor recognition**

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## Supplementary Figure1C:\Users\cau\Desktop\TRAF family sequence align.jpg

**Supplementary Figure 1.** Sequence alignment of TRAF family. TRAF domains are indicated by green high-right box. Red line indicates boundary between TRAF-N (N) and TRAF-C domain (C). Secondary structure was shown above the sequence.

## Supplementary Table1. Receptors with TRAF-binding motif

|  |  |  |  |
| --- | --- | --- | --- |
| TRAF family | TRAF1/2/3/5 | TRAF4 | TRAF6 |
| Receptors | TNFR2 | GPIb | CD40 |
|  | OX40 | GPVI | TACI |
|  | CD40 | TGFβR1 | RANK |
|  | CD30 | TGFβR2 | XEDAR |
|  | 4-1BB |  | TROY |
|  | RANK |  | BAFFR |
|  | HVEM |  | Fn14 |
|  | BCMA |  | IRAK |
|  | GITR |  | RIP2 |
|  | CD27 |  | OX40 |
|  | LMP1 |  | BCMA |
|  | RELT |  | TROY |
|  | LTbR |  | EDAR |
|  | TANK |  | p75 |
|  | TROY |  |  |
|  | EDAR |  |  |
|  | p75 |  |  |

## Supplementary Table2. Substrates of the E3 ligase activity of TRAFs

|  |  |  |
| --- | --- | --- |
| TRAF family | Substrates | References |
| TRAF2 | TRAF2 | (Habelhah et al., 2004) |
|  | TAK1 | (Fan et al., 2010) |
|  | RIP1 | (Alvarez et al., 2010) |
|  | TRIF | (Sasai et al., 2010) |
|  | cIAP1/2 | (Vallabhapurapu et al., 2008) |
|  | Smurf2 | (Carpentier et al., 2008) |
|  | Tristetraprolin | (Schichl et al., 2011) |
|  | DUSP14 | (Yang et al., 2016) |
|  | GβL | (Wang et al., 2017) |
| TRAF3 | TRAF3 | (Tseng et al., 2010) |
|  | TBK1 | (Netea et al., 2012) |
|  | ASC | (Guan et al., 2015) |
|  | IKK | (Netea et al., 2012) |
| TRAF4 | TRAF4 | (Wang et al., 2013) |
|  | Smurf1 | (Wang et al., 2013) |
|  | Smurf2 | (Zhang et al., 2013) |
|  | TAK1 | (Zhang et al., 2013) |
|  | TrkA | (Singh et al., 2018) |
|  | Akt | (Li et al., 2013) |
| TRAF5 | TRAF5 | (Tang and Wang, 2010) |
|  | RORγt | (Wang et al., 2015) |
| TRAF6 | TRAF6 | (Lamothe et al., 2008) |
|  | IL-17R | (Rong et al., 2007) |
|  | p75 | (Powell et al., 2009) |
|  | TGFβR1 | (Mu et al., 2011) |
|  | TAK1 | (Zhang et al., 2013) |
|  | IRAK1 | (Conze et al., 2008) |
|  | Akt | (Yang et al., 2009) |
|  | Fyn | (Liu et al., 2012) |
|  | NEMO | (Sebban-Benin et al., 2007) |
|  | NESCA | (Napolitano et al., 2009) |
|  | LAT | (Xie et al., 2013) |
|  | cIAP1/2 | (Tseng et al., 2010) |
|  | IRF5/7 | (Ning et al., 2008) |
|  | Beclin1 | (Shi and Kehrl, 2010) |
|  | NDP52 | (Inomata et al., 2012) |
|  | ECSIT | (West et al., 2011) |
|  | PIK3CA | (Wang et al., 2018) |
|  | PI3K (p85α) | (Hamidi et al., 2017) |

## Supplementary Table3. Current available structures of TRAF family with receptors

|  |  |  |
| --- | --- | --- |
| TRAF family | Peptide receptor | PDB ID |
| TRAF1(220-416) |  | 5E1T |
| TRAF1(220-416) | TANK(178-187) SVPIQCTDKT | 5H10 |
| TRAF2(327-501) |  | 1CA4 |
| TRAF2(327-501) | CD40(250-254) PVQET | 1D00 |
| TRAF2(327-501) | CD30(576-583) MLSVEEEG | 1D01 |
| TRAF2(327-501) | Ox40 (262-266) PIQEE | 1D0A |
| TRAF2(327-501) | m4-1BB (231-236) GAAQEE | 1D0J |
| TRAF2(327-501) | LMP1 (PQQATDD) | 1CZY |
| TRAF2(310-501) | CD40(250-254) PVQETLHGCQPVTQEDG | 1CZZ |
| TRAF2(310-501) | TNF-R2 (420-428) QVPFSKEEC | 1CA9 |
| TRAF3(341-568) |  | 1FLK |
| TRAF3(341-568) | CD40(247-268) TAAPVQETLHGCQPVTQEDG | 1FLL |
| TRAF3(377-568) | TANK(178-195) SVPIQCTDKTDKQEALFK | 1L0A |
| TRAF3(377-568) | TANK (171-191) IATDTQCSVPIQCTDKTDKQE | 1KZZ |
| TRAF3(377-568) | LTbR (385-408) PYPIPEEGDPGPPGLSTPHQEDGK | 1RF3 |
| TRAF3(377-568) | LMP1 (204-210) PQQATDD | 1ZMS |
| TRAF3(377-568) | BAFF-R (160-183) SVPVPATELGSTELVTTKTAGPEQ | 2GKW |
| TRAF3(377-568) | Cardif (138-158) PSCPKPVQDTQPPESPVENSE | 4GHU |
| TRAF4(290-470) TRAF4(292-466) |  | 4K8U, 4M4E |
| TRAF4(290-470) | GPIbβ (176-185) RRLRARARARA | 5YC1 |
| TRAF5(329-505) |  | 4GJH |
| TRAF6(346-504) |  | 1LB4 |
| TRAF6(346-504) | RANK (342-349) QMPTEDEY | 1LB5 |
| TRAF6(346-504) | CD40 (230-238) KQEPQEIDF | 1LB6 |
| TRAF6(346-504) | MAVS (450-468) GPCHGPEENEYKSEGTFGI | 4Z8M |

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