Supplementary Figure Legends

Supplementary Figure 1 U266 cells, a myeloma cell line, were pretreated for 16 h without (medium) or with LBH589 (10 nM) (lanes 5-8) or depsipeptide (10 nM) (lanes 13-16) and then exposed to biotinylated TRAIL (bTRAIL) for 5 or 15 minutes. Cells were solubilized by 0.25% Triton-X100 containing DISC buffer. Lipid enriched fractions (Raft; corresponding to fractions 4 and 5 in Figure 1b) (lanes 1, 3, 5, 7, 9, 11, 13 and 15) and non-lipid fractions (Non-raft; corresponding to fractions 11 and 12) (lanes 2, 4, 6, 8, 10, 12, 14 and 16) were fractionated by discontinuous sucrose gradients and analyzed by western blotting.

Supplementary Figure 2 Expression of PKCα and β in different cells. Jurkat (clone E6.1), HeLa, DU145, HL-60, HL-525 (a PKCβ deficient clone from HL-60 cells) and CLL cells were examined by Western blotting for the expression of PKCα and β. A + sign indicates that the indicated cell type was either sensitive to TRAIL alone or that PMA abrogated the effect on HDACi-mediated TRAIL sensitization. Equal amounts of protein, as confirmed by Ponceau staining, were loaded onto the gels. HL-60 and HL-525 cells (Tonetti DA, Horio, M et al (1992) Cell Growth Differ 3, 739-45) were kindly provided by Dr. E.Huberman (Argonne National Laboratory, IL).

Supplementary Figure 3 PKCβ, Lyn and Syk are detected in the isolated DISC. Protein samples of lysate (lanes 1 and 2) and receptor pulled down from unstimulated (u/s) cells (lanes 3 and 4) from 2 CLL patients were analyzed by western blotting.

Supplementary Figure 4 Inhibition of tyrosine kinase activity does not reverse PMA abrogation of HDACi-mediated TRAIL sensitization. CLL cells were exposed for 16 h to depsipeptide (lanes 17-32) or for 2 h to either PP2 (lanes 5-8 and 21-24), SU6656 (SU; lanes 9-12 and 25-28) or piceatannol (lanes 13-16 and 29-32). Cells were then
exposed to PMA (20 ng ml⁻¹) for 30 min, followed by TRAIL (500 ng ml⁻¹) for 4 h and apoptosis assessed by loss of mitochondrial membrane potential. Error bar represents the Mean ± SD (n=5).

**Supplementary Figure 5.** Casein kinase1α (CK1α) but not casein kinase2α (CK2α) is detected in the isolated TRAIL DISC. CLL cells were exposed to depsipeptide (Dep; 10 nM) for 16 h followed by ST-TRAIL (500 ng ml⁻¹) for 5 or 15 min at 37 °C, and the TRAIL DISC was isolated. Protein samples of both lysate and the DISC were analyzed by Western blotting.
TRAIL-DISC is not detected in "raft-enriched fraction" following HDACi exposure of U266 cells.

**Table:**

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**Western Blot Images:**

- **TRAIL-R1**
  - Lane 1: 50 kDa
  - Lane 2: 50 kDa
  - Lane 3: 50 kDa
  - Lane 4: 50 kDa
  - Lane 5: 50 kDa
  - Lane 6: 50 kDa
  - Lane 7: 50 kDa
  - Lane 8: 50 kDa

- **Caspase-8**
  - Lane 1: 50 kDa
  - Lane 2: 50 kDa
  - Lane 3: 50 kDa
  - Lane 4: 50 kDa
  - Lane 5: 50 kDa
  - Lane 6: 50 kDa
  - Lane 7: 50 kDa
  - Lane 8: 50 kDa

**Supplementary Figure 1**
**Supplementary Figure 2**

**PKCa and PKCb**

- **Jurkat**
- **HeLa**
- **DU145**
- **HL-60**
- **HL-525**
- **CLL-1**
- **CLL-2**

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**Molecular Weight (kDa)**
- PKCa: 96 kDa
- PKCb: 96 kDa
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*Supplementary Figure 3*
Supplementary Figure 5