

SUPPLEMENTARY FIGURE 1: Sequence alignment of the N-terminal region of RAM from diverse Notch receptors. (A). The absolutely conserved WxP motif was used as an anchoring point in the alignment from which the other regions of conservation were determined. From the sequence alignment, three additional regions of conservation are readily apparent: (I) the basic region with a large bias for Arg at position six, (II) the HG motif, and (III) the GF dipeptide motif. Conserved residues are highlighted in green, highly conserved residues are bolded and highlighted in orange (R6, W14, and P16). In selecting Notch receptor sequences, closely related orthologs (e.g. mouse vs. human Notch1) were excluded to avoid bias in the alignment. (B). Sequence of the RAM consensus peptide displayed as the sequence entropy in a logos format (47).

A

| Organism (<i>Genus species</i>) | Notch | Sequence | Accession ID |
|--|-------|--|----------------|
| Mouse (<i>Mus musculus</i>) | N1 | R K R R R Q H G Q L W F E E G F K V | NP_032740.3 |
| Mouse (<i>Mus musculus</i>) | N2 | M A R K R K R K H G F L W L E E G F T L | NP_035058.2 |
| Mouse (<i>Mus musculus</i>) | N3 | R K R E H S T L W F E E G F S L | NP_032742.1 |
| Mouse (<i>Mus musculus</i>) | N4 | R R R R R E H G A L W L E P G F I R | NP_035059.2 |
| Chicken (<i>Gallus gallus</i>) | N1 | S R K R R R E H G Q L W F E E G F K V T E | XP_415420.2 |
| Chicken (<i>Gallus gallus</i>) | N2 | A K R K R K K H G S L W L E E G F I L R R | XP_001233596.1 |
| Frog (<i>Xenopus tropicalis</i>) | N | N K K R R R E H G Q L W F E E G F I P K | NP_001090757.1 |
| Zebrafish (<i>Danio rerio</i>) | N1A | S R K R K R E H C Q L W F E E G F K V N E | NP_571516.1 |
| Sea Squirt (<i>Ciona intestinalis</i>) | N | L T H R K R K R E T S T L W A E E G F N V T K | NP_001037825.1 |
| Sea Pineapple (<i>Halocynthia roretzi</i>) | N | R Q K R K R E N C T L W L E E G F G V P K | BAA25571.1 |
| Sea Urchin (<i>Lytechinus variegatus</i>) | N | A R K R F R T N G T W F E S N E V R T S | AAB82088.1 |
| Fruit Fly (<i>Drosophila melanogaster</i>) | N | S T Q R K R A H G V T W F E E G F R A P | NP_476859.2 |
| Worm (<i>Caenorhabditis briggsae</i>) | Lin12 | N R K R R I I N A P V W T P P M E N E D | XP_00166114.1 |
| Worm (<i>Caenorhabditis remanei</i>) | Lin12 | K R R M I T A K T W T P P M E N E D | AAP05764.1 |
| Worm (<i>Caenorhabditis elegans</i>) | Glp1 | R S R K R K M V N A T V W M P P M E S T | NP_499014.1 |
| Worm (<i>Caenorhabditis elegans</i>) | Lin12 | R T R K R R M I N A S V W M P P M E N E | NP_499007.1 |

B

