**Table S1:** Comparison of ADAM and BACE1 cleavage sites in described substrates. m: murine; h: human, aa: amino acids.

|  |
| --- |
| **ADAM cleavage sites** |
| **Substrate** | **Species** | **Cons. (m/h)** | **Distance to****TMD (aa)** | **P3** | **P2** | **P1** | **-Cleavage sites-** | **P1‘** | **P2‘** | **P3‘** |
| EpCAM | m | no | 35 | H | S | S | K | S | M |
| App | h | yes | 12 | H | Q | K | L | V | F |
| AREG | h | no | 14 | S | E | K | S | M | K |
| AREG | m | no | 11 | S | M | K | T | H | S |
| TNF-α | h | no | 20 | A | Q | A | V | R | S |
| TNF-α | m | no | 23 | T | L | T | L | R | S |
| **BACE1 cleavage sites** |
| **Substrate** | **Species** | **Cons. (m/h)** | **Distance to****TMD (aa)** | **P3** | **P2** | **P1** | **-Cleavage sites-** | **P1‘** | **P2‘** | **P3‘** |
| EpCAM | m | yes | 29 | L | I | Y | Y | V | D |
| App | h | yes | 20 | V | K | M | D | A | E |
| APLP1 | h | no | 29 | K | V | N | A | S | V |
| APLP2 | h | yes | 28 | K | E | M | I | F | N |
| CHL1 | h | yes | 20 | I | F | Q | D | V | I |
| IL1R2 | h | no | 9 | L | S | F | Q | T | L |
| L1 | h | no | 35 | T | D | Y | E | I | H |
| NRG1 | h | yes | 10 | I | E | F | M | E | A |
| NRG3 | h | yes | 10 | I | E | F | M | E | S |
| PSLG-1 | h | no | 17 | S | N | L | S | V | N |
| SCN1B | m | yes | 16 | I | H | L | E | V | V |
| SCN2B | h | no | 15 | I | H | L | Q | V | L |
| SCN2B | h | no | 12 | Q | V | L | M | E | E |
| SCN2B | m | no | 14 | I | Y | L | Q | V | L |
| SCN3B | m | yes | 32 | F | E | F | E | A | H |
| SCN3B | m | yes | 6 | E | D | F | T | S | V |
| SCN4B | m | yes | 13 | I | F | L | Q | V | V |
| ST6GAL1 | m | no | 11 | L | T | I | Q | A | K |
| SELPLG | h | no | 17 | S | N | L | S | V | N |