

**List of prohormones used to build the binary logistics model for mammals.** Only portions of the prohormones for which experimental evidence of processing exist are used to build the model. The positions shown in columns 3-5 are for the preprohormones (i.e., including the signal sequence) derived from the Swiss-Prot database. For further information, consult Neuropred (<http://neuroproteomics.scs.uiuc.edu/neuropred.html>). Unusual processing sites include cleavage at non-basic sites or between basic residues. (This table can also be found in the supplemental section of *Amare et al. J. Proteome. Res., 2006.*)

Prohormone	Source	Prohormone Range Used in Model	Experimentally Verified Cleavage Sites	Unusual Processing Sites
Apelin	Rat	61-77	(60, 64) <sup>1</sup>	60 61, GRR KFR <sup>1</sup>
Brain natriuretic peptide (BNP)	Human	103-134	102 <sup>2</sup>	None
Calcitonin	Human	85-141	84 <sup>3</sup> , 120 <sup>3,4</sup>	120 121, KKR DMS <sup>3,4</sup>
Calcitonin gene-related peptide I (CGRP I)	Rat	83-119	(82, 100, 124) <sup>5</sup>	(124 124, RRRR DLQ; 100 101, NFV PTN) <sup>5</sup>
Calcitonin gene-related peptide II (CGRP II)	Human	82-119	(81, 123) <sup>6</sup>	119 120, RRRR DLQ <sup>6</sup>
Cholecystokinins (CCK)	Rat	46-115	45, <sup>7</sup> (81, 95, 106) <sup>8,9</sup>	None
Chromogranin B	Rat	21-40, 88-163, 202-227, 277-343, 454-573, 572-582, 615-634	(87, 201, 277, 453, 571, 584, 614) <sup>10</sup>	276 277, TKR RPR <sup>10</sup>
Cortistatin	Rat	84-112	(83, 98) <sup>11</sup>	None
Corticotropin releasing factor (CRF)	Rat	145-187	144 <sup>12</sup>	None
Dynorphin	Pig	175-184, 209-240	174, <sup>13</sup> 184, <sup>13,14</sup> 208, <sup>15</sup> 217, <sup>16</sup> 228, <sup>15,17</sup> 241 <sup>17</sup>	183 184, KYP KRS <sup>13</sup> 184 185, YPK RSS <sup>14</sup>
Galanin	Human	33-64	32, <sup>18,19</sup> 52, <sup>19</sup> 64 <sup>18,19</sup>	None
Galanin	Pig	24-64	32, <sup>20,21</sup> 64 <sup>20-22</sup>	36 37, WTL NSA <sup>20-22</sup>
Galanin-like peptide	Pig	23-82	84 <sup>23</sup>	(80 81, SQL ASK; 81 82, QLA SKR) <sup>23</sup>
Gastrin-releasing peptide	Pig	1-27	17 <sup>24,25</sup>	None
Glucagon	Human	53-83, 92-180	(52, 83) <sup>26</sup> (91,	None

			97,130, 180) <sup>27</sup>	
Glycoprotein hormones alpha (GLHA)	Human	25-116	None <sup>28, 29</sup>	None
Insulin	Human	25-110	(56, 89) <sup>30-32</sup>	None
Luteinizing hormone beta	Cow	21-139	None <sup>33</sup>	139 140, DIL FL <sup>33</sup>
Neuromedin U	Pig	1-25	17 <sup>34</sup>	None
Neurophysin I	Human	32-125	31 <sup>35</sup>	None
Neurophysin II	Cow	32-126	(31, 127) <sup>36</sup>	None
Neurophysin II	Human	32-164	32, <sup>37</sup> 125 <sup>38</sup>	None
Neurophysin II	Mouse	24-35, 141-166	(35,149, 166) <sup>39</sup>	(25 26, CY FQN; 140 141, QLD GPA; 150 151, LRL VQL; 152 153, LVQ LAG; 153 154, VQL AGT; 155 156, LAG TRE) <sup>39</sup>
Neurophysin II	Rat	36-128	(35, 129) <sup>40</sup>	None
Neurotensin/Neuromedin N	Rat	142-169	(142, 149) <sup>41</sup>	141 142, IKR KIP <sup>41</sup>
Neuropeptide B	Cow	25-53	55 <sup>42</sup>	None
Neuropeptide B	Human	25-48	48 <sup>42</sup>	48 49, GLR RSP <sup>42</sup>
Neuropeptide FFa (NPFFa)	Rat	72-83	(71, 84) <sup>43</sup>	(74 75, NPA FLF; 103 104, EFW SLA) <sup>43</sup>
Neuropeptide W	Human	32-57	57 <sup>44</sup>	53 54, LLM GLR <sup>44</sup>
Neuropeptide W	Pig	33-62	(57, 64) <sup>44</sup>	None
Nociceptin	Rat	135-151	(134, 153) <sup>45</sup>	None
Orexin	Rat	33-97	(68, 99) <sup>46</sup>	(68 69, GKR RPG; 70 71, RRP GPP) <sup>46</sup>

Pituitary adenylate cyclase-activating polypeptide (PACAP)	Rat	111-128, 131-168	110, <sup>47</sup> 130, <sup>47-49</sup> 160, <sup>49</sup> 171 <sup>48</sup>	None
Proenkephalin (PENK)	Mouse	100-106, 114-135, 188-262	(99, 106, 113, 135, 188, 197, 211, 218, 231, 238, 262) <sup>39</sup>	(199 200, RSP QLE; 200 201, SPQ LED; 244 254, SLP SDE) <sup>39</sup>
Prolactin-releasing peptide (PrRP)	Bovine	22-53	(32, 53) <sup>50</sup>	None
Pro-opiomelanocortin (POMC)	Cow	76-90, 106-234	90, <sup>51</sup> 105, <sup>52</sup> 131, <sup>52, 53</sup> 172, <sup>53</sup> 214, <sup>52, 54</sup> 232 <sup>54</sup>	75 76, NPR KYV <sup>51</sup> 162 163, DES AQA <sup>52</sup>
ProSAAS	Mouse	34-89, 129-142, 219-254	(41, 61, 142, 242, 254) <sup>55</sup> 90 <sup>56</sup>	128 129, DDP DAP <sup>55</sup>
RFamide-related peptide (RFRP)	Rat	108-127	(107, 127) <sup>57</sup>	None
Secretin	Human	28-54	(27, 57) <sup>58</sup>	None
Secretin	Pig	21-59	29, <sup>59, 60</sup> 59 <sup>59-61</sup>	None
Secretogranin II	Mouse	205-218, 269-299, 512-568, 598-612	(218, 286, 299, 526, 568, 612) <sup>39</sup>	(203 205, SVF GEL; 207 208, QEL QKL; 511 512, ARM LVK; 515 516, VKY PEL; 518 519, PEL LNR) <sup>39</sup>
Somatostatin	Pig	25-116	88, <sup>62, 63</sup> 102 <sup>64</sup>	56 57, AEL LSE <sup>65</sup>
Somatostatin	Rat	25-34, 89-116	88, <sup>66</sup> 102 <sup>47, 67</sup>	34 35, RQF LQK <sup>68</sup>
Tachykinin	Human	58-68, 98-126	58 <sup>69</sup> , 71, <sup>69</sup> 97, <sup>70</sup> 110, <sup>70, 71</sup> 129 <sup>71</sup>	57 58, IAR RPK <sup>69</sup> 100 101, HKT DSF <sup>70</sup>
Tachykinin	Rat	58-68, 98-126	(58, 71, 97, 110, 130) <sup>47</sup>	57 58, IAR RPK <sup>47</sup>
Thyrotropin beta	Human	21-132	None <sup>72</sup>	None
Thyrotropin-releasing hormone (TRH)	Rat	25-50, 154-233	52, <sup>73</sup> 153, <sup>74, 75</sup> 159, <sup>75, 76</sup> 171, <sup>74-76</sup> 177, <sup>76, 77</sup> 185, <sup>77</sup> 201, <sup>77, 76</sup> 207, <sup>73</sup> 233 <sup>73</sup>	None
Urocortin I	Rat	81-122	80 <sup>78</sup>	None

Vasoactive intestinal peptide (VIP)	Cow	81-155	80, <sup>79</sup> 110, <sup>79</sup> 124, <sup>80</sup> 155 <sup>80</sup>	None
Vasoactive intestinal peptide (VIP)	Human	81-155	80, <sup>81</sup> 110, <sup>82</sup> 124, <sup>81</sup> 155 <sup>82</sup>	None
Vasoactive intestinal peptide (VIP)	Rat	81-155	80, <sup>81</sup> 124, <sup>81,83</sup> 155 <sup>83</sup>	133 134, TDN YTR <sup>84</sup>

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**Table S2.**

<b>Model</b>	<b>Model 1</b>	<b>Model 2</b>	<b>Model 3</b>	<b>Model 4</b>	<b>Model 5</b>
True positive	26	20	19	22	24
False negative	8	7	5	5	6
False positive	3	6	8	9	4
True negative	49	53	54	49	51
Sensitivity	76.5%	74.1%	79.2%	81.5%	80.0%
Specificity	94.2%	89.8%	87.1%	84.5%	92.7%
Correct classification	87.2%	84.9%	84.9%	83.5%	88.2%
Positive predictive power	89.7%	76.9%	70.4%	71.0%	85.7%
Negative predictive Power	86.0%	88.3%	91.5%	90.7%	89.5%
Correlation	0.73	0.65	0.64	0.64	0.74