

Table S5: Validation Results of Ion-ligand ipHMMs using generated Sequences

Domain	SMART Abr.	Sens <sup>1</sup>	Spec <sup>2</sup>	Acc <sup>3</sup>
Alkaline phosphatase homologues	alkPPc	0.67	0.55	0.58
Zinc finger	ZnFC2H2	0.55	0.56	0.55
Insulin / insulin-like growth factor / relaxin family.	IlGF	0.83	0.60	0.65
Trypsin-like serine protease	TrypSPc	0.38	0.75	0.69
Alpha-lactalbumin / lysozyme C	LYZ1	0.73	0.77	0.76
EF-hand, calcium binding motif	EFh	0.75	0.74	0.74
DNA polymerase A domain	POLAc	0.85	0.76	0.77
Zinc-dependent metalloprotease	ZnMc	0.50	0.78	0.74
ATPases associated with a variety of cellular activities	AAA	0.33	0.89	0.83
Immunoglobulin V-Type	IGv	0.52	0.79	0.76
Eukaryotic homologues of bacterial periplasmic substrate binding proteins.	PBPe	0.88	0.65	0.70
Alpha-amylase domain	Aamy	0.30	0.84	0.78
C-type lectin (CTL) or carbohydrate-recognition domain (CRD)	CLECT	0.23	0.83	0.77
Gelsolin homology domain	GEL	0.66	0.67	0.68
Bacterial periplasmic substrate-binding proteins	PBPb	0.52	0.65	0.63
Summary		0.58	0.72	0.71

<sup>1</sup>Sensitivity

<sup>2</sup>Specificity

<sup>3</sup>Accuracy=  $\frac{TP+TN}{P+N}$