**Step 1. Phylogenetic inference.**

(FASTA sequence file) \rightarrow \text{FastTree2} \rightarrow (phylogenetic tree) \rightarrow \text{expert clade annotation}

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**Step 2. Design LABEL module.**

(phylogenetic tree) \rightarrow (alignment hierarchy) \rightarrow (profile HMM hierarchy) \rightarrow perl, muscle, Jalview \rightarrow SAM's modelfromalign

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**Step 3. Train support vector machine (SVM).**

(SVM training data) \rightarrow \text{profile HMMs} \rightarrow \text{scores & annotations} \rightarrow (fully trained SVM) \rightarrow \text{Shogun}

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**Step 4. Annotate query sequences.**

(annotating pHMM training data) \rightarrow \text{query pHMM scores} \rightarrow \text{query sequence annotations}

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**Supp. Fig. 1:** The lineage partition in step 1 is used to design the annotation tree in step 2, giving rise to a hierarchy of profile HMMs. Step 3 is repeated at each internal node of the annotation tree, where profile scores of training data are used to train SVMs. For annotating query sequences, step 4 uses the pHMMs and SVMs from steps 2 & 3 to assign query sequence annotations in a root-to-tips fashion corresponding with the annotation tree.