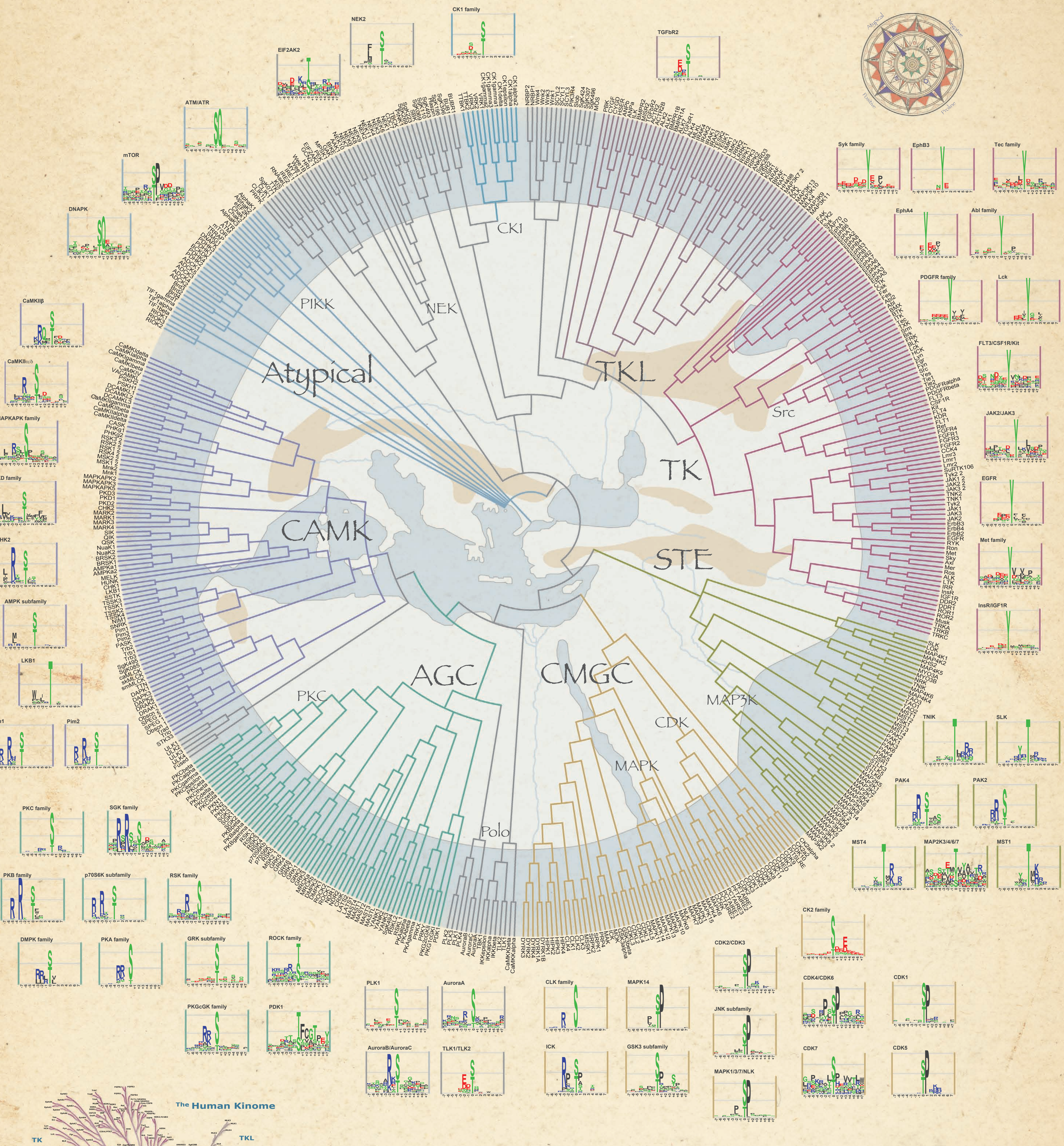
A Sequence-Specificity Atlas of the Kinase World



Finding the Targets of the Human Kinome

Protein kinases are enzymes that mediate cellular decision processes by catalyzing the addition of a negatively charged phosphate group to protein substrates, which can subsequently be recognized by phosphorylation-dependent binding domains in other proteins. The human genome encodes 518 protein kinases, which have been organized into a tree that represents evolutionary relationships. The substrate specificities of kinases are in part determined by the amino acid sequence of the phosphorylation sites, and comprehensively mapping the consensus sequence motif recognized by each kinase catalytic domain is thus crucial for understanding phosphorylation-mediated signaling networks.

NetPhorest (http://netphorest.info) is a community resource that uses phylogenetic trees to organize data from both in vivo and in vitro experiments to derive sequence specificities for individual kinase or phosphorylation-dependent binding domains or families of closely related domains. This poster presents the specificities of kinases as sequence logo plots around a phylogenetic map of the human protein kinases. The height of a stack of letters represents the information content of a particular position relative to a phosphorylation site, and the height of the individual letters is proportional to the frequency of the amino acid residue in question. The serine, threonine, or tyrosine phosphoacceptor residues are placed at the center of each logo plot. Closely related kinases typically have similar substrate specificities; however, distantly related kinases may not have divergent substrate specificities. The compass summarizes the major trends of the specificity atlas in the center; for example, most kinases that prefer positively charged residues are located in the lower left-hand part of the phylogenetic map.

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