

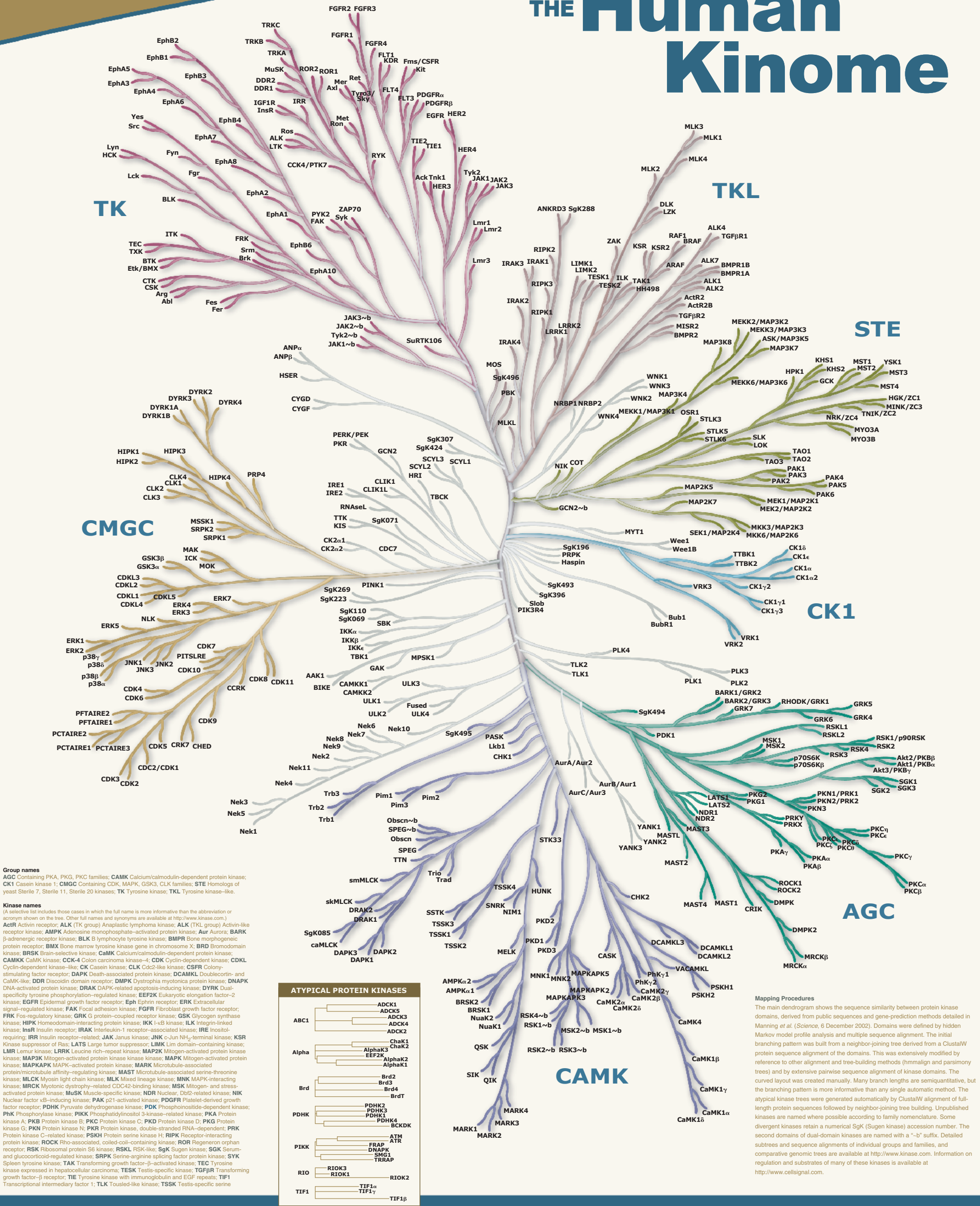
This phylogenetic tree depicts the relationships between members of the complete superfamily of human protein kinases. Protein kinases constitute one of the largest human gene families and are key regulators of cell function. The 518 human protein kinases control protein activity by catalyzing the addition of a negatively charged phosphate group to other proteins. Protein kinases modulate a wide variety of biological processes, especially those that carry signals from the cell membrane to intracellular targets and coordinate complex biological functions.

Most protein kinases belong to a single superfamily of enzymes whose catalytic domains are related in sequence and structure. The main diagram illustrates the similarity between the protein sequences of these catalytic domains. Each kinase is at the tip of a branch, and the similarity between various kinases is inversely related to the distance between their positions on the tree diagram. Most kinases fall into small families of highly related sequences, and most

families are part of larger groups. The seven major groups are labeled and colored distinctly. Other kinases are shown in the center of the tree, colored gray. The relationships shown on the tree can be used to predict protein substrates and biological function for many of the over 100 uncharacterized kinases presented here.

The inset diagram shows trees for seven atypical protein kinase families. These proteins have verified or strongly predicted kinase activity, but have little or no sequence similarity to members of the protein kinase superfamily. A further eight atypical protein kinases in small families of one or two genes are not shown.

THE Human Kinome



Group names
AGC Containing PKA, PKG, PKC families; CAMK Calcium/calmodulin-dependent protein kinase; CK1 Casein kinase 1; CMGC Containing CDK, MAPK, GSK3, CLK families; STE Homologs of yeast Sterile 7, Sterile 11, Sterile 20 kinases; TK Tyrosine kinase; TKL Tyrosine kinase-like.

Kinase names
(A selective list includes those cases in which the full name is more informative than the abbreviation or acronym shown on the tree. Other full names and synonyms are available at <http://www.kinase.com>.)
ActR Activin receptor; ALK (TK group) Anaplastic lymphoma kinase; ALK (TKL group) Activin-like receptor kinase; AMPK Adenosine monophosphate-activated protein kinase; Aur Aurora; BARK β -adrenergic receptor kinase; BLK B lymphocyte tyrosine kinase; BMPR Bone morphogenetic protein receptor; BMX Bone marrow tyrosine kinase gene in chromosome X; BRD Bromodomain kinase; BRSK Brain-selective kinase; CaMK Calcium/calmodulin-dependent protein kinase; CAMKK CaMK kinase; CCK-4 Colon carcinoma kinase-4; CDK Cyclin-dependent kinase; CDKL Cyclin-dependent kinase-like; CK Casein kinase; CLK Cdc2-like kinase; CSFR Colony-stimulating factor receptor; DAPK Death-associated protein kinase; DCAMKL Doublecortin- and CaMK-like; DDR Discoidin domain receptor; DMPK Dystrophin myotonic protein kinase; DNAPK DNA-activated protein kinase; DRAK DAPK-related apoptosis-inducing kinase; DYRK Dual-specificity tyrosine phosphorylation-regulated kinase; EEF2K Eukaryotic elongation factor-2 kinase; EGFR Epidermal growth factor receptor; Eph Ephrin receptor; ERK Extracellular signal-regulated kinase; FAK Focal adhesion kinase; FGFR Fibroblast growth factor receptor; FRK Fes-regulatory kinase; GRK G protein-coupled receptor kinase; GSK Glycogen synthase kinase; HIPK Homeodomain-interacting protein kinase; IKK I κ B kinase; ILK Integrin-linked kinase; InsR Insulin receptor; IRAK Interleukin-1 receptor-associated kinase; IRE Inositol-requiring; IRR Insulin receptor-related; JAK Janus kinase; JNK c-Jun N-terminal kinase; KSR Kinase suppressor of Ras; LATS Large tumor suppressor; LIMK Lim domain-containing kinase; LMR Lemur kinase; LRRK Leucine rich-repeat kinase; MAP2K Mitogen-activated protein kinase kinase; MAP3K Mitogen-activated protein kinase kinase kinase; MAPK Mitogen-activated protein kinase; MAPKAP MAPK-activated protein kinase; MARK Microtubule-associated protein/microtubule affinity-regulating kinase; MAST Microtubule-associated serine-threonine kinase; MLCK Myosin light chain kinase; MLK Mixed lineage kinase; MNK MAPK-interacting kinase; MRCK Myotonic dystrophy-related CDC42-binding kinase; MSK Mitogen- and stress-activated protein kinase; MuSK Muscle-specific kinase; NDR Nuclear, Dbp2-related kinase; NIK Nuclear factor κ B-inducing kinase; PAK p21-activated kinase; PDGFR Platelet-derived growth factor receptor; PDHK Pyruvate dehydrogenase kinase; PDK Phosphoinositide-dependent kinase; PhK Phosphorylase kinase; PIKK Phosphatidylinositol 3-kinase-related kinase; PKA Protein kinase A; PKB Protein kinase B; PKC Protein kinase C; PKD Protein kinase D; PKG Protein kinase G; PKN Protein kinase N; PKR Protein kinase, double-stranded RNA-dependent; PRK Protein kinase C-related kinase; PSKH Protein serine kinase H; RIPK Receptor-interacting protein kinase; ROCK Rho-associated, coiled-coil-containing kinase; ROR Regeneron orphan receptor; RSK Ribosomal protein S6 kinase; RSKL RSK-like; SgK Sugan kinase; SGK Serum- and glucocorticoid-regulated kinase; SRPK Serine-arginine splicing factor protein kinase; SYK Spleen tyrosine kinase; TAK Transforming growth factor- β -activated kinase; TEC Tyrosine kinase expressed in hepatocellular carcinoma; TESK Testis-specific kinase; TGF β R Transforming growth factor- β receptor; TIE Tyrosine kinase with immunoglobulin and EGF repeats; TIF1 Transcriptional intermediary factor 1; TLK Tousled-like kinase; TSSK Testis-specific serine