

## Computational predictive analyses of the substrate and drug specificities for 500 human protein kinases for assessment of genetic mutations

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About 538 protein kinases catalyze the phosphorylation of as many as 970,000 phosphosites in the human phosphoproteome. Over a third of global pharmaceutical R&D is focused on the discovery and development of protein kinases inhibitors, since defects in signalling from these enzymes has been linked to over 400 diseases. Using predictive algorithms based on training with over 22,000 kinase-substrate and 105,000 kinase-drug pairs along with the primary structures of the ~250 amino acid catalytic domains of 492 human protein kinases, we have defined many amino acid residues in these enzymes that are critical for determining their catalytic activity, substrate specificity and drug sensitivity. With the existence of about 60 million single nucleotide polymorphisms in human genomes, predictions based on this kind of information will be required to identify those individuals that harbour disease-causing mutations and the most effective drugs that may offer the best recourses in a personalized medicine strategy. We have also undertaken evolutionary analyses of the 970,000 phosphosites to identify the most conserved in 20 other diverse species to aid in the construction of a tissue and cell-specific atlas of high resolution maps of the interactions of the most critical nodes of communication in cell signalling networks. We have used this information to produce hundreds of antibodies against these protein and phosphosite targets that are deployed in high density antibody microarrays to permit wide scale monitoring of signalling systems in specific tissue and cell biopsy samples. The prediction and experimental data provided by these studies have been made freely available in a suite of open-access data- and knowledge-bases that are accessible from [www.kinexus.ca](http://www.kinexus.ca).

### Biography

Steven Pelech has been the president and chief scientific officer of Kinexus Bioinformatics Corp. for over 13 years. He was previously the founder and president of Kinetek Pharmaceuticals, Inc. for 6 years. Prior to this, he spent 5 years in post-doctoral training with Sir Philip Cohen at the University of Dundee and Nobel laureate Dr. Edwin Krebs at the University of Washington in Seattle. He is concurrently a full professor in the Department of Medicine at the University of British Columbia (UBC), where he has been on faculty since 1988. He received his B.Sc. (1979; Honours) and Ph.D. (1982) degrees in Biochemistry from UBC. He has authored over 200 scientific peer-reviewed publications about signal transduction and is one of the discoverers of the MAP kinases. He has served on grant review panels and as an ad-hoc reviewer for over 30 granting agencies and as an external reviewer for over 28 scientific journals.

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