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Integrated systems analysis of genomic and proteomic data to identify oncogenic mutations

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Secreted proteins encoded by mutated genes (mutant proteins) are a particularly rich source of biomarkers being not only components of the cancer secretome but actually implicated in tumorigenesis. One of the challenges of proteomics-driven biomarker discovery research is that the bulk of secreted mutant proteins cannot be identified directly and quantified by mass spectrometry due to the lack of mutated peptide information in extant proteomics databases. Here we identify, using an integrated genomics and proteomics strategy (referred to iMASp-identification of Mutated And Secreted proteins), 112 putative mutated tryptic peptides (corresponding to 57 proteins) in the collective secretomes derived from a panel of 18 human colorectal cancer (CRC) cell lines. Central to this iMASp was the creation of Human Protein Mutant Database (HPMD), against which experimentally-derived secretome peptide spectra were searched. Eight of the identified mutated tryptic peptides were confirmed by RT-PCR and cDNA sequencing of RNA extracted from those CRC cells from which the mutation was identified by mass spectrometry. The iMASp technology promises to improve the link between proteomics and genomic mutation data thereby providing an effective tool for targeting tryptic peptides with mutated amino acids as potential cancer biomarker candidates.

Biography

Suresh Mathivanan obtained his Ph.D. from Johns Hopkins University, USA and Institute of Bioinformatics, India in proteomics and bioinformatics. He undertook his postdoctoral studies at the Ludwig Institute for Cancer Research, Australia. He received a NH&MRC fellowship to study exosomes in cancer. He is currently a group head in La Trobe University, Melbourne, Australia. He has published more than 32 papers in international peer-reviewed journals and serving as an editorial board member of repute. His research articles have been cited at an average of more than 90 citations per article.

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