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Proteomics and drug discovery in cancer

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Teaser: The field of proteomics has developed quickly over the past decade and its application to cancer research has considerable potential in the area of precision medicine.

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Author biographies

Leo K. Iwai

Dr Iwai received his undergraduate degree in chemistry, from the University of São Paulo in Brazil in 1995. He received his MSc and PhD in molecular biology from the Federal University of São Paulo in 1999 and 2004, respectively. After postdoctoral studies at the Harvard Medical School and at the Massachusetts Institute of Technology from 2005 to 2010 and at the Institute of Cancer Research in London from 2010 to 2012, he joined the Instituto Butantan in São Paulo as a research scientist in 2010. Dr Iwai studies snake venoms and their components as potential targets for diagnostics and therapy of cancer.

Eduardo S. Kitano

Eduardo Kitano graduated in pharmacy and biochemistry from the University of São Paulo, Brazil, in 2011. He is currently a PhD candidate at the Department of Biochemistry at University of São Paulo, developing his work at the Instituto Butantan. His current research focuses on the analysis of complex protein samples by mass spectrometry and sample preparation optimization with emphasis on peptide separation techniques, such as MudPIT and StageTip. Besides his active collaborative work with several different groups within the institute and at the University of São Paulo, he has focused on the characterization of protein expression patterns in sugarcane leaves at different stages of plant development.

Matheus Dias

Dr Dias graduated in biomedical sciences in 2005 from the Bandeirante University of São Paulo (Brazil). He received his PhD in biochemistry from the University of São Paulo in 2012, studying the mechanisms underlying growth factor signaling and cell cycle control in Ras-driven malignant cells. Since 2013, he has been a postdoctoral fellow at the Instituto Butantan in São Paulo, where he has been using an interdisciplinary approach, which includes proteomic techniques and computational modeling and/or simulation, to probe the network subjacent of Ras signaling in malignant cells to uncover potentially targetable vulnerabilities in Ras-driven malignant phenotypes.

Proteomics has emerged as an invaluable tool in the quest to unravel the biochemical changes that give rise to the hallmarks of cancer. In this review, we present the advances and challenges facing proteomics technology as applied to cancer research, and address how the information gathered so far has helped to enhance understanding of the mechanisms underlying the disease and contributed to the discovery of biomarkers and new drug targets. We conclude by presenting a perspective on how proteomics could be applied in the future to determine prognostic biomarkers and direct strategies for effective cancer treatment.

Introduction

The viability of multicellular organisms requires that individual cells must proliferate, differentiate, quiesce, senesce, and even die on behalf of organism homeostasis. The control of cellular fate involves many levels of complexity and organization, from hormonal signaling to cell cycle checkpoints. The foundation of several diseases lies in the malfunction and/or loss of this control, leading to the disruption of system homeostasis and, eventually, death. Cancers are the most frequent examples of such aberrations in the mechanisms that control cell fate.

Malignant transformation is a multistep process in which genetic and epigenetic alterations result in the malfunction of the normal checkpoints that control cell fate. Many different routes lead to a variety of malignant phenotypes observed in human cancers. However, it is a consensus that there is a defined collection of 'abilities' that all malignant cells must acquire to develop into a cancer. These include: sustained proliferative signaling; evasion of growth suppressive signaling; resistance to cell death; limitless replication; induction of angiogenesis; invasion; and acquisition of metastatic capability [1]. Underlying all these traits, known as the hallmarks of cancer, is the genomic instability that fuels the gradual acquisition of these capabilities through Darwinian natural

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