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Tumor suppressive protein phosphatases in human cancer: emerging targets for therapeutic intervention and tumor stratification

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invited review for issue on 'New roles of phosphatases in cancer', edited by Jukka Westermarck and Nicolas Tonks

Abstract
Aberrant protein phosphorylation is one of the hallmarks of cancer cells, and in many cases a prerequisite to sustain tumor development and progression. Like protein kinases, protein phosphatases are key regulators of cell signaling. However, their contribution to aberrant signaling in cancer cells is overall less well appreciated, and therefore, their clinical potential remains largely unexploited. In this review, we provide an overview of tumor suppressive protein phosphatases in human cancer. Along their mechanisms of inactivation in defined cancer contexts, we give an overview of their functional roles in diverse signaling pathways that contribute to their tumor suppressive abilities. Finally, we discuss their emerging roles as predictive or prognostic markers, their potential as synthetic lethality targets, and the current feasibility of their reactivation with pharmacologic compounds as promising new cancer therapies. We conclude that their inclusion in clinical practice has obvious potential to significantly improve therapeutic outcome in various ways, and should now definitely be pushed forward.

Key words: protein phosphatase; tumor suppressor; phosphatase reactivation therapy; synthetic lethality; predictive marker; prognostic maker; PP2A; PPM1A; PPM1B; PPM1E; PPM1H; ILKAP; PDP; PHLPP; PTPRD; PTPRJ; PTPRK; PTPRM; PTPRO; PTPRR; PTPRS; PTPRT; PTPN2; PTPN6; PTPN9; PTPN12; PTPN13; PTPN14; DUSP1; DUSP2; DUSP4; DUSP5; DUSP6; DUSP9; DUSP10; DUSP16; CDKN3; CDC14; DUSP3; DUSP22; DUSP26; ACPP