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Proteases and Protease Inhibitors: Implications in Antitumorigenesis and Drug Development

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ABSTRACT The role of proteases in cancer is far more complex than initially anticipated and include tumor promoting as well as suppressive effects and their inhibitors are emerging with promising therapeutics in cancer treatment. Proteases are involved in tumor growth both at the primary and metastatic sites. Inhibitors of all the five classes of proteases (serine, aspartyl, cysteine, metallo- and threonine) have been widely reported from plant, animal and microbial origin. Each protease exhibits a characteristics "recognition-specificity" and are specific to cleave proteins with a particular structure. Such a capability allows identifying signatures of protease activity in biological fluids. Individual pattern of protease expression help in easy prognosis and therapeutic administration of specific protease inhibitor. With the advance of surface enhanced laser desorption ionization time-of-flight (SELDI-TOF) mass spectrometry, proteomic technologies are directly applied into clinical diagnostic tests. The substrate phage technology can be used to develop protease profile signatures for all type of cancers. Recently, application of biomarkers in cancer treatment has become increasingly target-oriented. Gene expression signatures in cancer provide molecular phenotype that identifies tumor classification not evident by traditional histo-pathological methods. The current review deals with the role of proteases, their inhibitors in cancer especially in tumor progression, invasion/metastasis and also addresses the therapeutic approaches, viable strategy for cancer treatment and regime of the future drug development.