A Clinical Overview of Centrosome Amplification in Human Cancers

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Abstract:

The turn of the 21st century had witnessed a surge of interest in the centrosome and its causal relation to human cancer development - a postulate that has existed for almost a century. Centrosome amplification (CA) is frequently detected in a growing list of human cancers, both solid and haematological, and is a candidate "hallmark" of cancer cells. Several lines of evidence support the progressive involvement of CA in the transition from early to advanced stages of carcinogenesis, being also found in pre-neoplastic lesions and even in histopathologically-normal tissue. CA constitutes the major mechanism leading to chromosomal instability and aneuploidy, via the formation of multipolar spindles and chromosomal mis segregation. Clinically, CA may translate to a greater risk for initiation of malignant transformation, tumour progression, chemoresistance and ultimately, poor patient prognosis. As mechanisms underlying CA are progressively being unravelled, the centrosome has emerged as a novel candidate target for cancer treatment. This Review summarizes mainly the clinical studies performed to date focusing on the mechanisms underlying CA in human neoplasia, and highlights the potential utility of centrosomes in the diagnosis, prognosis and treatment of human cancers.

Key Word:
Boveri hypothesis, chromosomal instability, aneuploidy, centrosome, aurora kinase, p53