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Angiogenesis in carcinogenesis, focus on angiopoietins and tyrosine kinase receptors (Tie1 & Tie2): Current perspectives

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Angiogenesis still remains as one of the most promising therapeutic targets in cancer as it has been linked to tumor metastasis and other cellular processes. Angiopoietin induced angiogenesis through the angiopoietin pathway (Ang-Tie) involves Angiopoietin 1 (Ang1) and Angiopoietin 2 (Ang2) among others as stimulating ligands and Tyrosine kinase receptor 1 and 2 (Tie1 and Tie2) as receptors. Ang1 is involved in vessel-sealing effects, pro-survival signaling and promotion of vascular quiescence in mature vessels, the effects of Ang1 *in vivo* in a tumor setting suggests that manipulation of this ligand could have therapeutic potential. Ang2 has been implicated in tumor angiogenesis as it has been found to be highly expressed in tumors and has been associated with progressive tumor growth and development of metastasis in many types of carcinomas. This high expression has been shown to be inversely related to the decreased expression levels of miR-126, which in turn has been linked to increased metastatic potential and poor prognosis in cancers. Therefore, understanding the cross-talk amongst Ang1:Ang2 ratio, Tie1:Tie2 balance and how Tie1 cleavage and miR-126 regulate angiogenesis holds great promise to rationally understand the complex multilayered control during angiopoietin induce angiogenesis. Hence, this provides a rationale for developing novel antiangiogenics therapies and combinations targeting Ang-Tie pathway and other pathways such as VEGF-VEGFR with the potential of overcoming therapeutic resistance. Antiangiogenic therapies such as Ang2 and Tie1 inhibitors which have been found to inhibit tumor angiogenesis and growth can be tested in combination with other VEGF inhibitors and conventional chemotherapies

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