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Effects of fluid shear stress on the malignant characteristics and drug sensitivity of breast cancer

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Introduction & Aim: Recent studies have indicated that the dynamic stresses created by interstitial fluid flow/blood flow play important roles in tissue development, maintenance, function and pathogenesis. Increasing evidences also indicated that dynamic stresses, such as Shear Stress (SS), play roles in tumor cell survival and several malignant characteristics. SS in and around tumor tissue could affect the efficacy of anticancer agent delivery, tumor microenvironment, and metastasis/invasion capacity. In addition, SS also could affect the migration of Circulating Tumor Cells (CTCs) during metastasis. Our previous studies have shown that SS could increase the sensitivity of radiation and induce apoptosis on tumor cell through the inhibition of integrin β1/FAK pathway. Here, we want to clarify whether FAK also plays roles in controlling chemotherapeutic responsibility and regulating the malignant characteristics after SS stimulation in adherent tumor cells and CTCs.

Materials & Methods: Breast cancer cells (MDA-MB-231, MDA-MB-468 and MCF-7) were used in this study. Cells were seeded onto glass slides pre-coated with fibronectin or in suspension, and then subjected to 0, 1 and 12 dyne/cm2 of laminar shear stress for 0-24 hours. Cells were then collected to study the migration/invasion abilities, drug sensitivity and signaling transduction pathway by other assays.

Results: Our data showed that high shear stress (12 dyne/cm2) might inhibit the migration/invasion abilities of adherent and circulating tumor cells but not in low shear stress (1 dyne/cm2). Low shear stress could induce the Mesenchymal-Endothelial Transition (MET) in CTCs. In addition, high shear stress could also increase the cisplatin sensitivity in both adherent and circulating tumor cells. High shear stress could down-regulates FAK, p-FAK, p-AKT expression through integrin β1. Knockdown of FAK could increase the drug sensitivity and decrease the migration/invasion abilities induced by low shear stress in adherent and circulating tumor cells.

Conclusion: Our results suggest that mechanical forces applied on tumor cells may play important roles in tumor biology and the effects of shear stress could be taken into account in cancer therapy development.

Biography

Chi-Wen Luo has completed his PhD from Tamkang University, Taipei, Taiwan and Postdoctoral studies from National Institute of Cancer Research, National Health Research Institutes, Taiwan. He has been the Assistant Principal Investigator in Department of Pathology, Kaohsiung Medical University Hospital, Kaohsiung, Taiwan. He has published more than 20 papers in reputed journals.

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