THE ROLE OF BIM-EL AND BCL2-α ON THE EFFICACY OF ERLOTINIB AND GEFITINIB IN LUNG CANCER

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Tyrosine kinase inhibitors erlotinib and gefitinib are small molecule inhibitors which are used for the treatment of lung cancer. Development of resistance to these drugs has been reported as one of the major setbacks in oncology. This study looked at the mechanisms leading to secondary resistance by assessing the gene expression of BCL2 family proteins which are associated with the intrinsic apoptotic signaling pathway. 8 genes were investigated in erlotinib and gefitinib treated cells by real time PCR and protein analysis by western blotting. The cells were exposed to the test drugs 48h prior to RNA or protein isolation. It was observed that BIM-EL a pro-apoptotic protein was up regulated in cells sensitive to the drugs but not in the resistant cells. BCL2-α an anti-apoptotic protein on the other hand was up regulated in the resistant cells and not in the sensitive cells. BCL2-α revealed a counter-regulation effect on BIM-EL and this effect is most likely one of the causes of secondary resistance to erlotinib and gefitinib.