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OVEREXPRESSION OF PARP IS AN INDEPENDENT PROGNOSTIC MARKER FOR POOR SURVIVAL IN MIDDLE EASTERN BREAST CANCER AND ITS INHIBITION CAN BE ENHANCED WITH EMBELIN CO-TREATMENT

Khawla Al-Kuraya, Abdul Khalid Siraj, Pratheeshkumar Poyil and Fouad Al-Dayel

King Faisal Specialist Hospital and Research, Saudi Arabia

Patients with aggressive breast cancer (BC) subtypes usually don't have favourable prognosis despite the improvement in treatment modalities. These cancers still remain a major cause of morbidity and mortality in females. This has fostered a major effort to discover actionable molecular targets to treat these patients. Poly ADP ribose polymerase (PARP) is one of these molecular targets that are under comprehensive investigation for treatment of such tumors. However, its role in the pathogenesis of BC from Middle Eastern ethnicity has not yet explored. Therefore, the authors examined the expression of PARP protein in a large cohort of over 1000 Middle Eastern BC cases using immunohistochemistry. Correlation with clinico-pathological parameters was performed. Nuclear PARP overexpression was observed in 44.7% of all BC cases and was significantly associated with aggressive clinico-pathological markers. Interestingly nuclear PARP overexpression was an independent predictor of poor prognosis. PARP overexpression was also directly associated with XIAP overexpression, with PARP and XIAP co-expression in 15.8% (159/1008) of our cases. It was observed that the combined inhibition of PARP by olaparib and XIAP by embelin significantly and synergistically inhibited cell growth and induced apoptosis in BC cell lines. Finally, co-treatment of olaparib and embelin regressed BC xenograft tumor growth in nude mice. The results revealed the role of PARP in Middle Eastern BC pathogenesis and prognosis. Furthermore, the study data support the potential clinical development of combined inhibition of PARP and XIAP, which eventually could extend the utility of olaparib beyond BRCA deficient cancer.

Biography

Khawla Al Kuraya, a Distinguished Physician Scientist and is the Director of the Research Centre at King Fahad National Centre for Children's Cancer and Research, King Faisal Specialist Hospital and Research (KFSH) in Riyadh, Saudi Arabia. After receiving her Medical Degree from King Saud University School of Medicine in Riyadh, Saudi Arabia, she completed her Residency and Fellowship in Pathology at Georgetown University Hospital in Washington D C. She is an Expert in the field of Genomic Cancer research. She is widely respected as Translational Scientist whose work bridges the laboratory and clinical settings. Her research focusses on identifying molecular signature of common Saudi tumours utilizing the recent technologies in the cancer genetic field. She is an author of over 100 original research articles, editorials, review articles and book chapters. She is a Member of the American Association for Cancer Research, College of American Pathologist and The American Society of Human Genetics. She also serves on numerous Editorial Boards. She is the first Saudi female recipient of the prestigious First Rank King Abdulaziz Medal for her pioneering initiatives in cancer research and served as a Member of the Saudi Shura Council (Inter-Parliamentary Union) of the Kingdom of Saudi Arabia.

kkuraya@fkfshrc.edu.sa