# 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

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## Abstract

Patients with aggressive breast cancer (BC) subtypes usually don't have favorable 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, we examined the expression of PARP protein in a large cohort of over 1000 Middle Eastern BC cases by immunohistochemistry. Correlation with clinico-pathological parameters were 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. We showed that 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. Our results revealed the role of PARP in Middle Eastern BC pathogenesis and prognosis. Furthermore, our 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.

## Recent Publications

Siraj AK, Pratheeshkumar P, Parvathareddy SK, Divya SP, Al-Dayel F, Tulbah A, Ajarim D, **Al-Kuraya K**. *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.* Oncotarget. 2018 – Accepted for Publication

Siraj AK, Pratheeshkumar P, Parvathareddy S, Qadri Z, Thangavel S, Ahmed S, Al-Dayel F, Tulbah A, Ajarim D, **Al-Kuraya K**. *FoxM1 is an independent poor prognostic marker and therapeutic target for advanced Middle Eastern breast cancer.* Oncotarget. 2018 Apr 3;9(25):17466-17482

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Pratheeshkumar P, Siraj AK, Divya S, Parvathareddy S, Begum R, Melosantos R, Al-Sobhi S, Al-Dawish M, Al-Dayel F, **Al-Kuraya KS**. *Downregulation of SKP2 in papillary thyroid cancer acts synergistically with TRAIL on inducing apoptosis via ROS.* J Clin Endocrinol Metab. 2017 Dec 28. doi: 10.1210/jc.2017-02178

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## Biography

Khawla Al-Kuraya, a distinguished physician-scientist, is the Director of the Research Centre at King Fahad National Centre for Children's Cancer, 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.

Dr. Al-Kuraya is a leader in the field of genomic cancer research. She is widely respected as Translational Scientist whose work bridges the laboratory and clinical settings. She has focused on identifying molecular signature of common Saudi tumors utilizing the recent technologies in the cancer genetic field.

An author of over 100 original research articles, editorials, review articles and book chapters. Dr. Al-Kuraya's professional memberships include the American Association for Cancer Research, College of American Pathologist and the American Society of Human Genetics. She also serves on numerous editorial boards.

Dr. Al-Kuraya 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.

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**Notes/Comments:**