

## Validation of anticancer drug targeting RBBP6 and P53 pathways

Malungi Xaba

University of South Africa, Durban, South Africa

Retinoblastoma binding protein 6 is a 250kD multi-functional nuclear protein, found in humans. It is well known that RBBP6 promotes cell proliferation in several cancers by negatively regulating p53 via its E3 ubiquitin ligase activity alongside MDM2. Previous studies have shown RBBP6 to be involved in the regulation of cell cycle, carcinogenesis development, and apoptosis. Through alternative splicing and alternative promoters, RBBP6 encodes for four isoforms. RBBP6 isoform 1 is highly expressed in many cancers, whereas the RBBP6 isoform 3 is down regulated in some cancers, which suggest that RBBP6 is a potential target anti-cancer drug discovery. *In silico* studies show that plerixafor binds tightly to the E3 ligase site of the RBBP6 ring-finger domain. This suggests that plerixafor can potentially block the E3 ligase activity of RBBP6, resulting in the reactivation of p53 levels in cancer cells causing apoptosis. In this study, plerixafor was verified as a possible anti-cancer drug for the treatment of cancer *in vitro*. To validate plerixafor for its anti-cancer activity, MTT assay, real-time cell analysis and flow cytometry was used to determine cell viability in breast cancer (MCF-7), lung (A549) cancer and embryonic kidney (HEK293) cell lines. Plerixafor greatly reduced cell viability in cancer cells in a concentration and time dependent manner compared to untreated control and normal cells (HEK293). Moreover, flow cytometry revealed that plerixafor does not kill HEK293 normal cells at different concentrations. Interestingly, a significant increase in apoptosis was observed in A549 cells whilst only minimal apoptosis was detected in MCF-7 cells after treatment with plerixafor at different concentrations. Based on these findings plerixafor protects normal cells while it kills A549 cells in a concentration and time dependant manner. The effect on other cancer cell lines is currently being investigated. Plerixafor has the potential to be repurposed for cancer treatment.