Role of Poly-Glutamine Repeats on Androgen Receptor Signaling in Prostate Cancer

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Androgen Receptor (AR) is a transcription factor and primary oncogenic driver in prostate cancer. Poly-glutamine (Poly-Q) repeats in AR are highly variable in different populations. Poly-Q length has been associated with the aggressiveness of prostate cancer. This study aims to determine how Poly-Q length influences AR signaling in prostate cancer cells. We have constructed plasmids carrying AR with different Poly-Q lengths: 12Q, 24Q (Wild-Type), and 48Q. The initial goal is to assess their expression in prostate cancer cell lines. 0.25ug of AR plasmids with different Poly-Q variants, and a vector control, were each transfected into the prostate cancer cell line PC3. Cells were allowed to proliferate for 2 days before treatment with 5nM DHT, the active form of testosterone, or a mock control for 2 hours. AR Expression was analyzed by Western blot, and its activity was quantified through dual-reporter luciferase assay driven by an AR promoter. It was found that between DHT and non-DHT treatment, Wild-Type AR showed a significant increase in expression of 10%. The 12Q and 48Q variants do not exhibit any significant difference; however, the 48Q variant is significantly lower in expression by 37% compared to the Wild-Type in the DHT treatment group. 12Q variants exhibit numerically higher expression in DHT than in non-DHT treatment groups, but this difference is insignificant. Because the Wild-Type AR polyQ length is similar to 12Q, this result is promising. Future optimization must be done to confirm this trend in PC3 and related cancer cell lines in vitro. Supported by NIH R25ES020721.