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# GLYCOBIOLOGY & GLYCOPROTEOMICS

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## Nucleolin functions as a negative regulator of androgen receptor transcription

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Androgen receptor (AR) drives the development and progression of prostate cancer (PCa). Men who develop regionally advanced or metastatic prostate cancer often have long-term cancer control when treated with androgen-deprivation therapies (ADT), but their disease inevitably becomes resistant to ADT and progresses to castration-resistant prostate cancer (CRPC). ADT involves the use of potent competitive AR antagonists and androgen synthesis inhibitors. Resistance to these treatments often emerges through maintenance of AR signaling via ligand-independent activation mechanisms. There is a need to identify the molecular mechanism that regulates the AR signaling expression to develop novel therapies that enhance the efficacy of existing systemic therapies for CRPC patients. Here, we present evidence that implicates nucleolin (NCL) as a regulator of AR expression. The promoter of AR contains G-rich sequences that can form G-quadruplex structures (G4). We found that NCL binds to this G4 region within the AR promoter. A dual reporter assay showed that genetic knockdown of NCL increases the transcription activity of AR promoter only when the AR promoter G4 sequence is present. Genetic knockdown of NCL also increases the levels of both AR mRNA and protein in PCa cells but has no effect on AR mRNA stability. The ability of NCL to modulate AR expression was independent of AR activation. Moreover, compounds that stabilize G4 structures and increase NCL association with the G4 of the AR promoter decrease AR expression. These results indicate that NCL functions as a transcriptional repressor of the AR gene, and raise the important possibility that G4-stabilizing drugs can increase NCL transcriptional repressor activity to block AR expression. These findings contribute to a clearer understanding of the mechanisms that control the expression of AR and may be of significance for the development of alternative therapeutic options for men with CRPC.

### Biography

Elsa Reyes-Reyes has been working in the field of cancer biology for about 14 years. Her research focus has been to define signaling pathways that promote cancer progression using *in vitro* and *in vivo* models. Her research goal is to characterize and identify therapeutic targets with high clinical application potential for the treatment, diagnosis, and prognosis of cancer. During the past decade, she has acquired solid experience in drug development for the treatment of different types of cancer such as colon, lung, liver, and prostate. My research has led me to be co-inventor on five patents.

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