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Máster en Métodos Computacionales en Ciencias

Project Nº 45 ASIGNADO

Título: *.Elucidating Abiraterone response on patients with Prostate Cancer via Machine Learning methods*

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Resumen

The mainstay of treatment for men with prostate cancer has been androgen depletion therapy (ADT), which is achieved by suppressing testicular production of androgens or countering androgen action with antiandrogens. In most cases, even though ADT is initially effective, >95% of patients on this treatment relapses, indicative of Castrate-Resistant Prostate Cancer (CRPC) development. The CYP17A1 inhibitor abiraterone (ABI) with prednisone or androgen receptor (AR) inhibitor enzalutamide (ENZA), becomes the first-line therapy for CRPC patients due to a significantly higher survival advantage. While encouraging, trials with ABI or ENZA have highlighted two major challenges: 1) pre-existing mechanisms of resistance preclude responses for nearly half of CRPC patients, and 2) resistance can develop rapidly in initial responders. The barrier to achieve the goal of identifying and understanding the resistance mechanisms and further selecting effective treatment to overcome resistance include: lack of appropriate clinical data that can be used to identify mechanism-based markers to understand resistance to next-generation AR-targeted therapies; as well as lack of innovative analytical tools that can find the right biomarkers for selection of additional therapies when standard therapy (AR signaling blocker) fails.

AR is a transcription factor that regulates many downstream genes upon ligand binding, followed by transporting to nuclear. The transcription activation also requires many other cofactors within the same protein complex, together with AR, to facilitate transcription regulation. Recently, it was also noted that there are co-factors specific to CRPC tumor, which can guild AR to specific gene regions to regulate gene transcription. **Therefore, it is critical to take a more comprehensive approach to focus on transcription regulatory network in this setting.**