Systems Biology of Cancer Therapy Resistance

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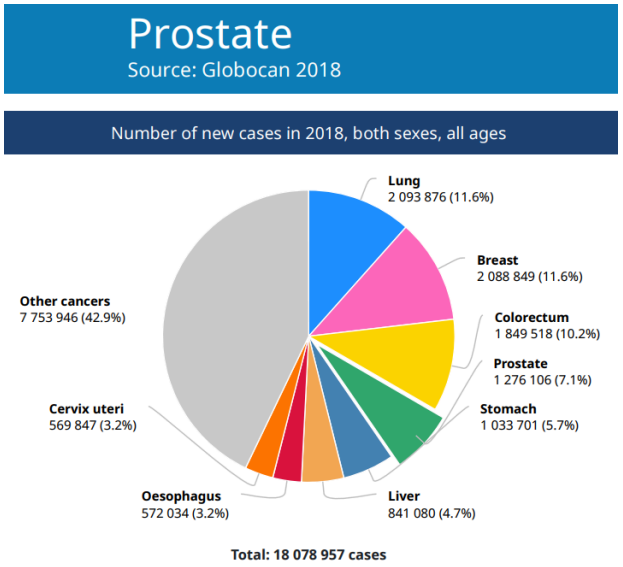
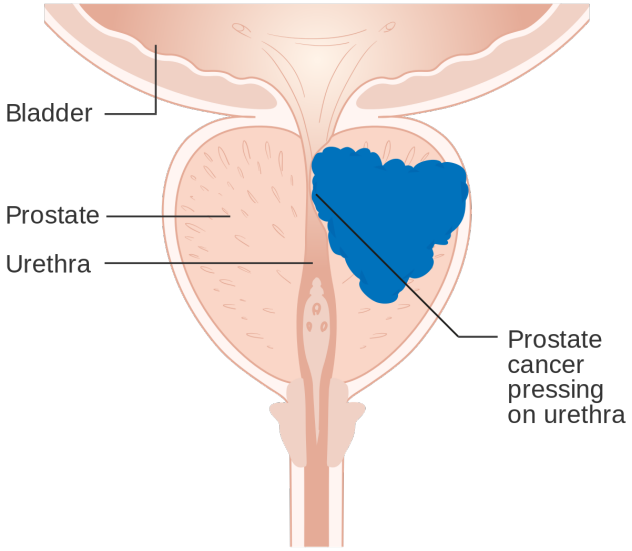
Drug resistance: an unsolved clinical challenge





- Prostate cancer among top 10 cancers in India; numbers expected to double in 2020
- Castration-resistant prostate cancer (CRPC): an incurable disease with a mean survival time of 1-2 years

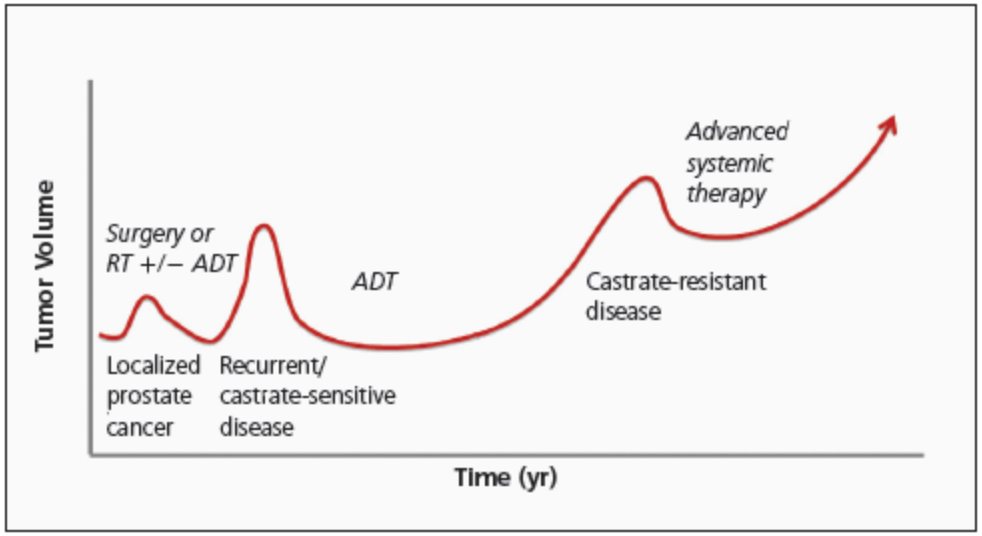


Figure: The Prostate Cancer Continuum. ADT = androgen deprivation therapy. RT = radiation therapy.

Dynamics of drug resistance in prostate cancer

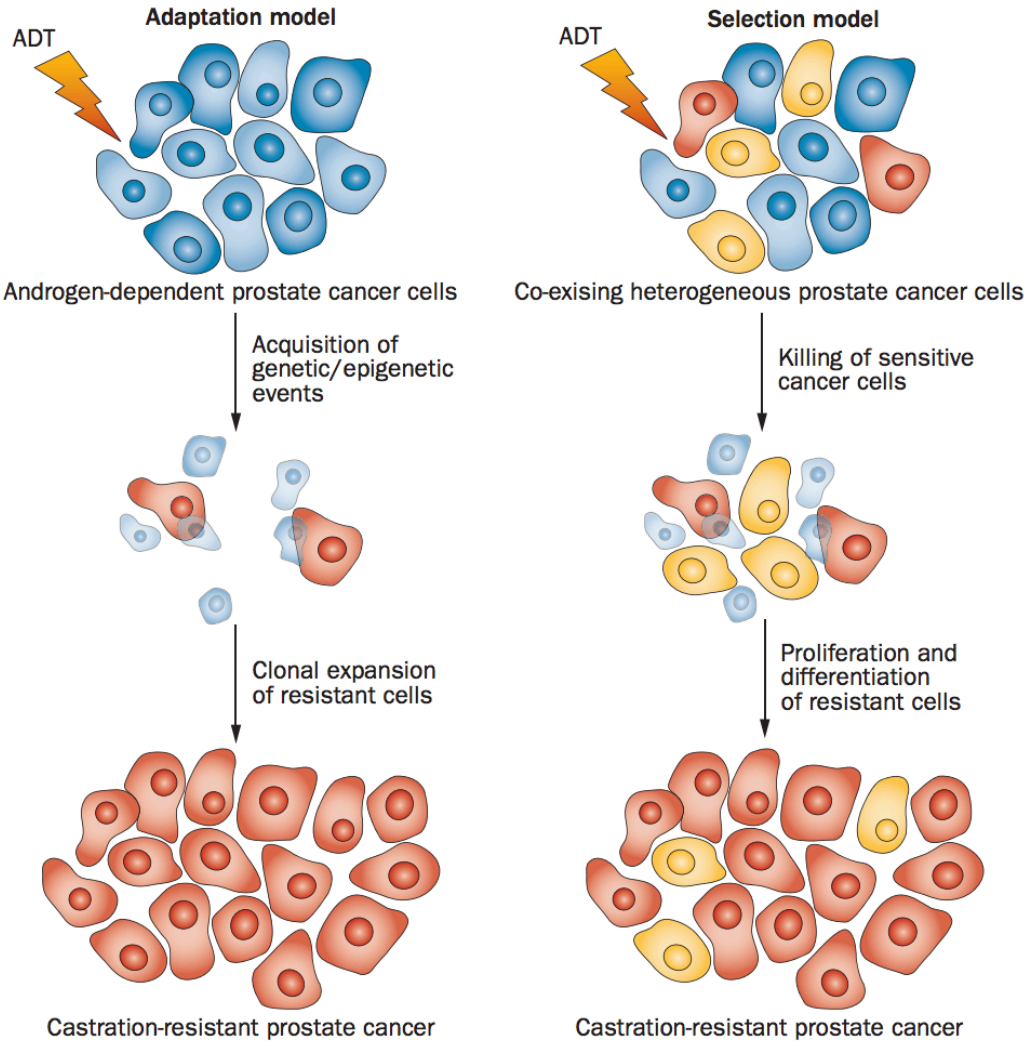
Mechanisms of drug/castration resistance are poorly understood.

Are cells selected for or do they adapt during therapy?

Is the selection and/or adaptation at a genetic/epigenetic/non-genetic level?

Is drug resistance determined in a cell-autonomous or a non-cell-autonomous manner (cooperation, competition among cells)?

Can we apply ‘adaptive therapy’ to cells to reduce drug resistance?



Zong & Goldstein, Nat Rev Urol 2012

Tools and techniques used

- Statistical/Computational tools to infer biological networks from dynamics
- Mechanistic mathematical modeling of biological regulatory networks
- Analyzing experimental transcriptomics/proteomics, and clinical data

Required background

- Basic understanding of ordinary differential equations and nonlinear dynamics (or the self-driven will to acquire them)
- Keen interest in pursuing interdisciplinary research (i.e. reading literature in both cancer biology and computational systems biology)
- **Note:** Students from physics/chemistry/mathematics/engineering background are welcome too, provided they show interest in acquiring the relevant understanding of biology

Further reading

Brady-Nicholls R *et al.* (2020) Prostate-specific antigen dynamics predict individual responses to intermittent androgen deprivation, Nat Comm, 11: 1750

Zong & Goldstein (2013) Adaptation or selection – mechanisms of castration-resistant prostate cancer. Nat Rev Urol, 10: 90-98