Cancer Vaccines

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Prophylactic

- Hepatitis B – Liver Cancer
- HPV – Cervical, Head and Neck, Anal

Therapeutic

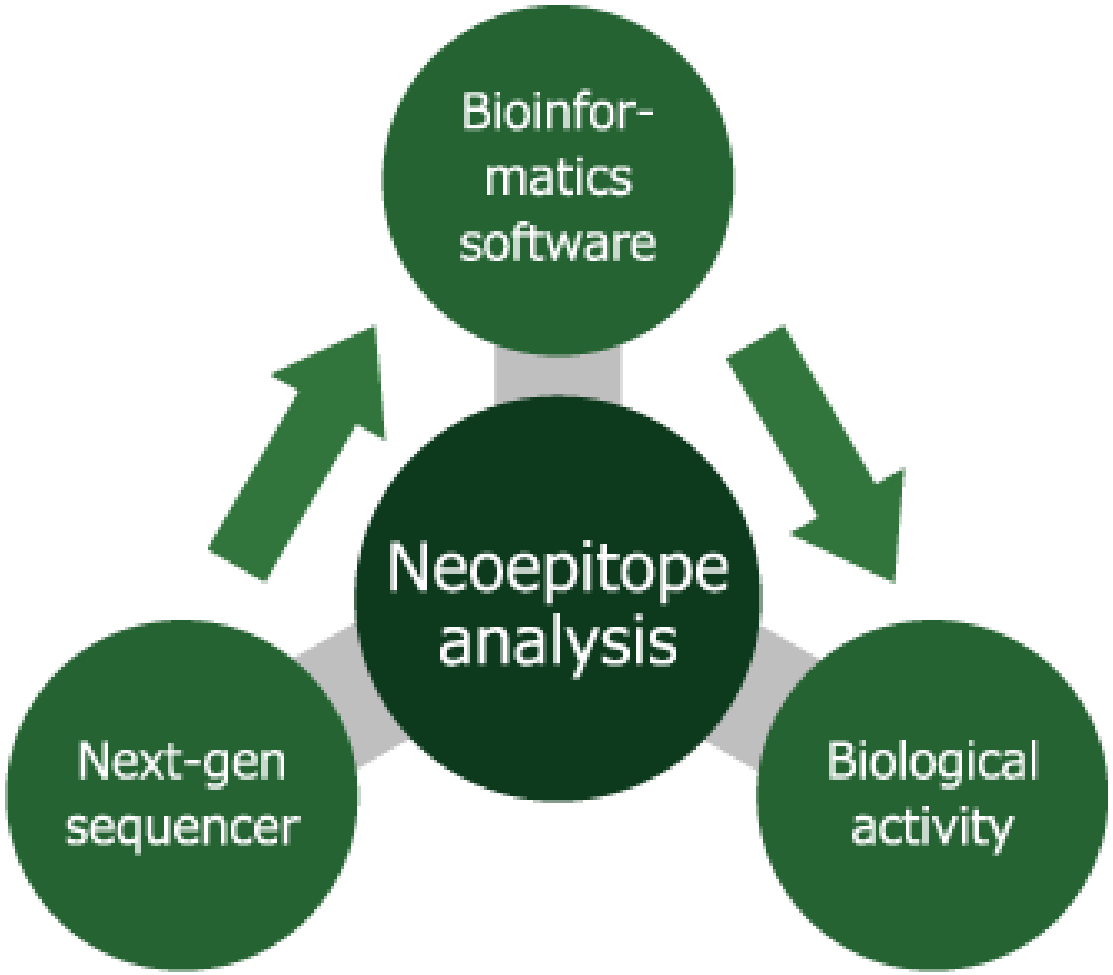
- Provenge (approved in 2010) for Prostate Cancer

Challenges to Effective Therapeutic Cancer Vaccines

- Antigen Selection
- Immune suppressive microenvironment

Tumour Antigens

- ***Oncofetal antigens*** – poorly immunogenic (MAGE, NY-ESO) - Lichty
- ***"Cancer Specific" post-translational modifications*** (e.g. glycosylation)
- ***Neoepitopes*** mutations that arise during tumour evolution



- Challenges to logistical generation of personalized vaccines (Neon, Gritstone, Genentech, BioNtech)
- Antigen loss variants leading to escape
- ***"Public"*** neo-epitopes e.g. K-Ras in pancreatic cancer

Autologous Tumour Cell Vaccines (Neo-epitopes?)

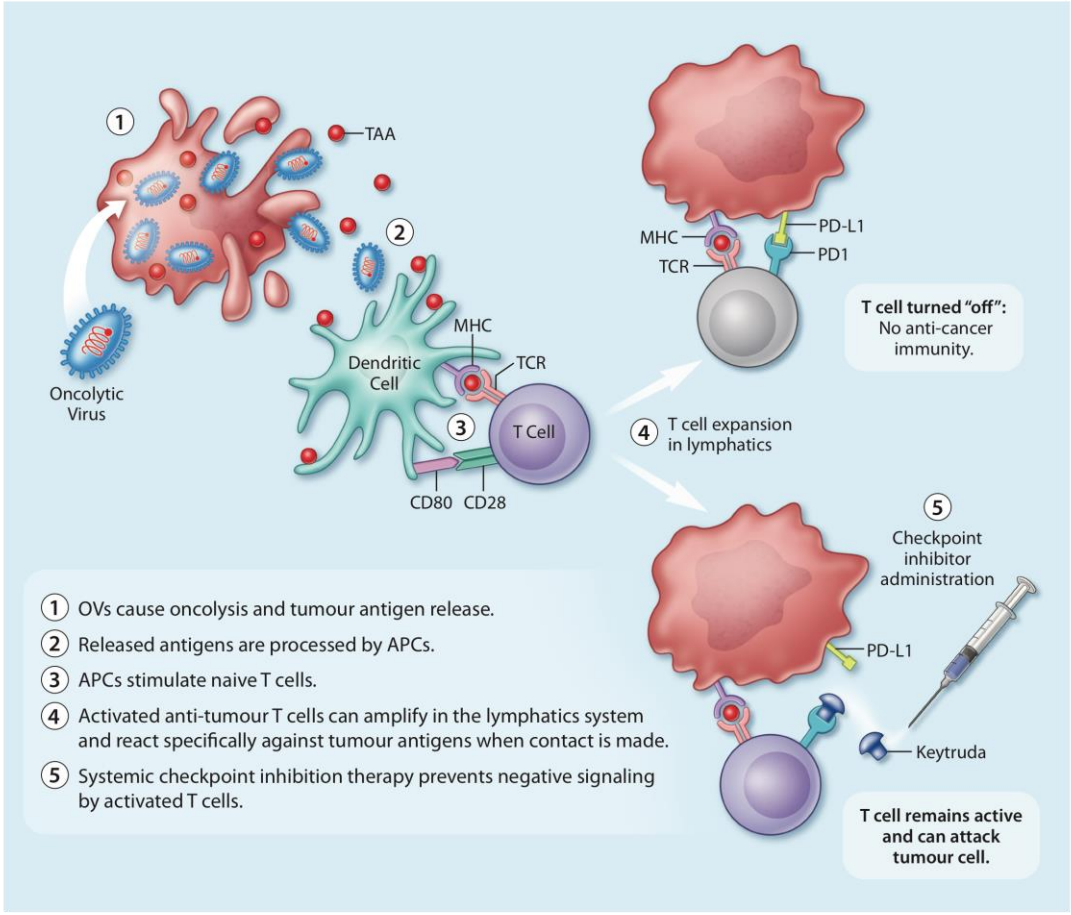
- ***Irradiated tumour cells + BCG*** (or Virus) Phase III studies in colorectal patients no overall survival benefit

- ***Autologous Dendritic Cells*** pulsed with TAA-GMCSF construct FDA approved for Prostate Cancer

- ***Engineered Autologous Tumour Cells*** – Gradalis developing a series of vaccines engineered to express GMCSF and block production of TGF beta, promising survival benefit in phase II studies with ovarian cancer patients

- ***Oncolytic Viruses –*** Creates an *in situ* vaccine effect, can be engineered to be a cancer vaccine, reverses local immune suppression, directly lysis tumor – Lichty, Kaufman, Evans

Immune Checkpoints Blunt Responses within the Tumour Microenvironment



Dr. Barakat

Rational Combination Therapy Approaches are the Future