

MINI Medical School

A 20/20 VIEW OF CANCER



Precision Cancer Therapy

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Disclosure

I have no actual or potential conflict of interest in relation to this program/presentation.



Objectives

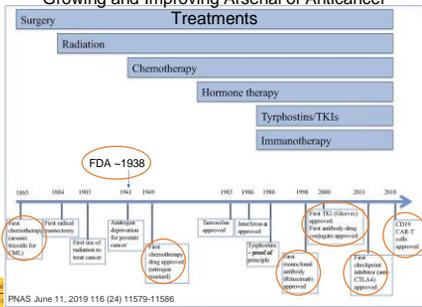
- Understand the types of treatments used to treat cancer
- Contrast precision medicine treatments and with traditional chemotherapy treatment
- Discuss the changes occurring in cancer treatments
- Understand the differences in side effects between precision medicine treatments and traditional chemotherapy
- Discuss how precision medicine applies to 2 cancer cases



Traditional Anti-Cancer Chemotherapy Treatments are Imprecise



Growing and Improving Arsenal of Anticancer Treatments



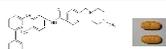
Precision Medicine Cancer Treatments Targeted Therapies

• Antibodies



- Rituximab (Rituxan)
- Bevacizumab (Avastin)
- Cetuximab (Erbix)
- Trastuzumab (Herceptin)
- Alemtuzumab (Campath)
- Many, many others

• Small Molecules



- Imatinib (Gleevec)
- Gefitinib (Iressa)
- Erlotinib (Tarceva)
- Dasatinib (Sprycel)
- Lapatinib (Tykerb)
- Nilotinib (Tasigna)
- Many others

Monoclonal antibodies target only certain cancer cells making treatment more precise

Approved Anti-Cancer Agent	Target on the Cancer
Rituximab	CD20
Bevacizumab	VEGF
Cetuximab	EGFR
Trastuzumab	HER2
Alemtuzumab	CD52
Pertuzumab	HER2
Panitumumab	EGFR
Olaratumab	PDGFR- α
Denosumab	RANKL

There are >100 monoclonal antibodies. Available mAbs are directed against a large number of antigens and also used for the treatment of immunologic diseases (e.g. IBD, MS), reversal of drug effects (e.g. anticoagulants), and cancer therapy (hematologic malignancies and solid tumors).

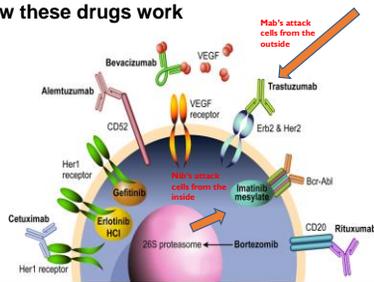


Small molecules target mutations in cancer cells making treatment more precise

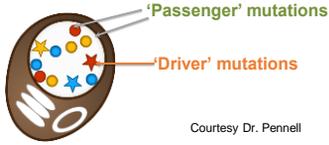
Approved Anti-Cancer Agent (e.g.)	Target on the Cancer
Imatinib	BCR-ABL, KIT, PDGFR β
Gefitinib	EGFR
Erlotinib	EGFR
Dasatinib	BCR-ABL
Lapatinib	HER2, EGFR
Nilotinib	BCR-ABL, KIT and PDGFR- α
Crizotinib	ALK
Dabrafenib	BRAF
Vemurafenib	BRAF



How these drugs work

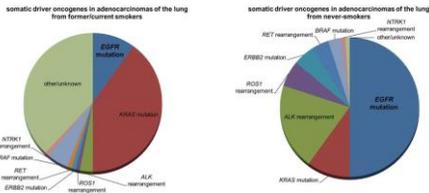


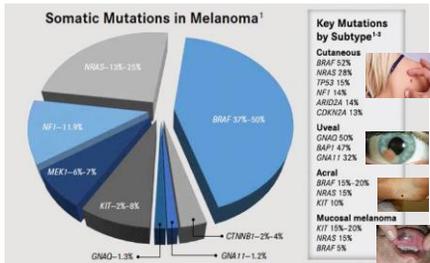
Identifying the “Driver” Mutation is Important in Controlling Cancer Growth



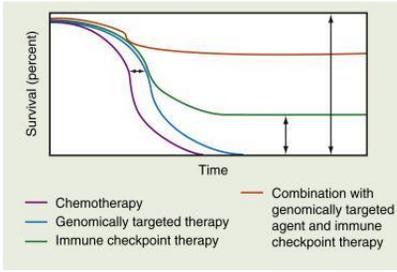


Genetic Mutations in Lung Cancer Cells









The promise of immunotherapy:
 Fig. 15.1. Adapted from Sharma P, Allison JP. Immune checkpoint targeting in cancer therapy: toward combination strategies with curative potential. *Cell* 161(2):205-214, 2015.

Case of Malignant Melanoma and Targeted Therapy Against a BRAF Genetic Mutation

Malignant melanoma

- Malignant cutaneous melanoma originates in melanocytes, specialized pigment cells, found in the skin.
- Melanoma accounts for 4-5% of all skin cancers but is responsible for 80% of deaths.
- Treatments for malignant melanoma in the past have been poor.

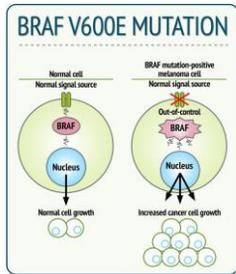


Advanced melanoma
 Image credit: National Cancer Institute

The BRAF Gene

- The BRAF gene encodes for a signalling protein.
- Mutations in the BRAF gene are present in many types of cancer, including malignant melanoma.
- Vemurafenib is an oral inhibitor of BRAF(V600E) kinase mutation.





Malignant melanoma before and after vemurafenib



38-year-old man with BRAF-mutant melanoma and miliary, subcutaneous metastatic deposits. Photographs were taken (A) before initiation of PLX4032, (B) after 15 weeks of therapy with PLX4032, and (C) after relapse, after 23 weeks of therapy. MEK mutation was identified. Wagie N et al. J Clin Oncol 2011;29:3085-3096.

Pharmacogenomic Markers are Mostly Related to Metabolism (how drugs are broken down in body)





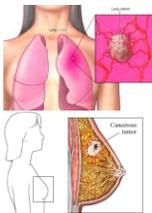
Advances in Cancer Therapy

- Unprecedented development of more powerful cancer therapies that target a specific gene or gene defect that maximizes efficacy.
- Identify the treatment that patient will most likely benefit.
- Harnessing of the immune system is key to control cancer.
- CAR-T therapies are the ultimate of personalized therapies.





Applications of Precision Medicine



Case 1 - Katherine – stage 4, nonsmoking lung cancer

Case 2 – Pamala – stage 1 breast cancer



Lung Cancer is the No. 1 killer of all cancers

Anyone with Lungs can get Lung Cancer

Research Matters

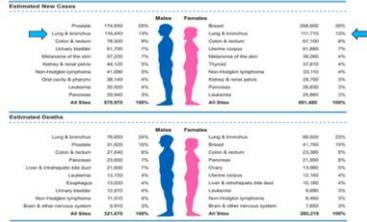
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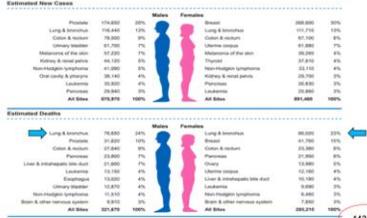


Cancer statistics, 2019



CA: A Cancer Journal for Clinicians, Volume 88, Issue 1, Pages 7-24. First published: 08 January 2019, DOI: 10.3332/caac.21081

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