

Introducing Genetics & Genomics in Cancer Care

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Overview

- History of cancer
- Where we stand today
- Where we want to go



The Past

- Ancient Egyptian text, 1600 B.C. : world's oldest recorded case of breast cancer
- Cancer, word derived from *karkinos*, coined by Hippocrates (460-370 B.C.)
- Cradle of Human civilization, South Africa: osteosarcoma in foot bone of hominin, 1.6-1.8 million years ago



Old Theories on Cancer

- Contagious, spread by parasites
- Due to trauma, chronic inflammation



The Advent of Genetics & Genomics

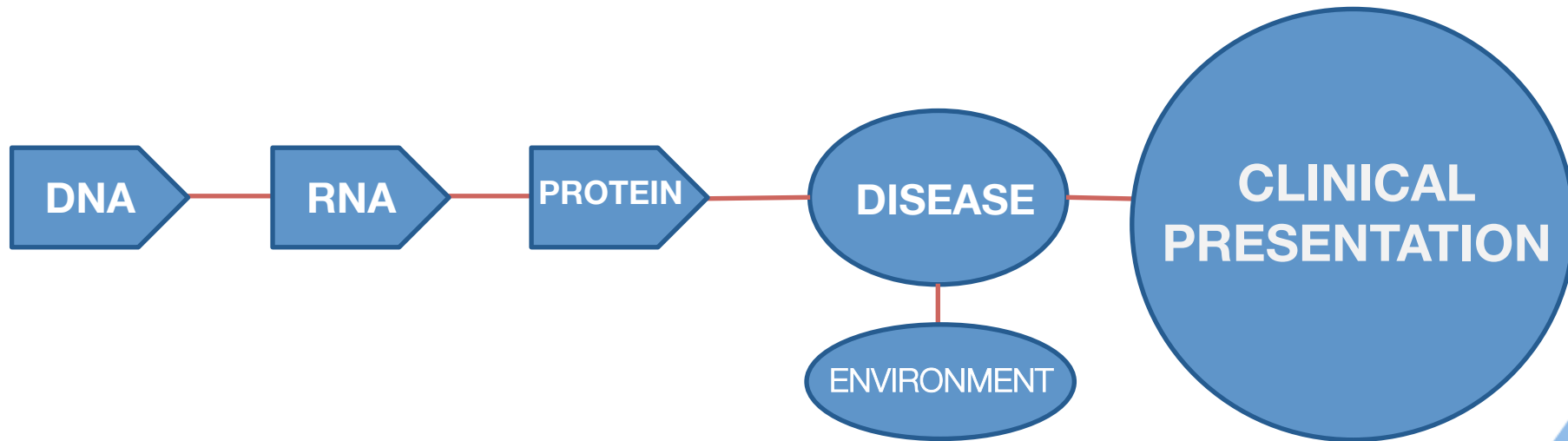
- DNA structure, Watson & Crick, 1962
- 1970's: the discovery of oncogenes & tumor



The Human Genome Project

- Goal was to complete a map of all our genes
- In 2001, 90% of human sequence published
- Completed in April 2003
- Complete genetic blueprint for a human being
- About 20,500 genes less than previously thought

The Basics of Genetics & Genomics



Definitions:

- **Genetics** is the study of genes and heredity and how the characteristics of living organisms are transmitted from one generation to the next.
- **Gene mutations** are permanent alterations in the DNA sequence that makes up a gene. Mutations are the basis of many cancers.
- **Cancer Genomics** is the study of DNA sequences and gene expression differences between tumor cells and normal cells

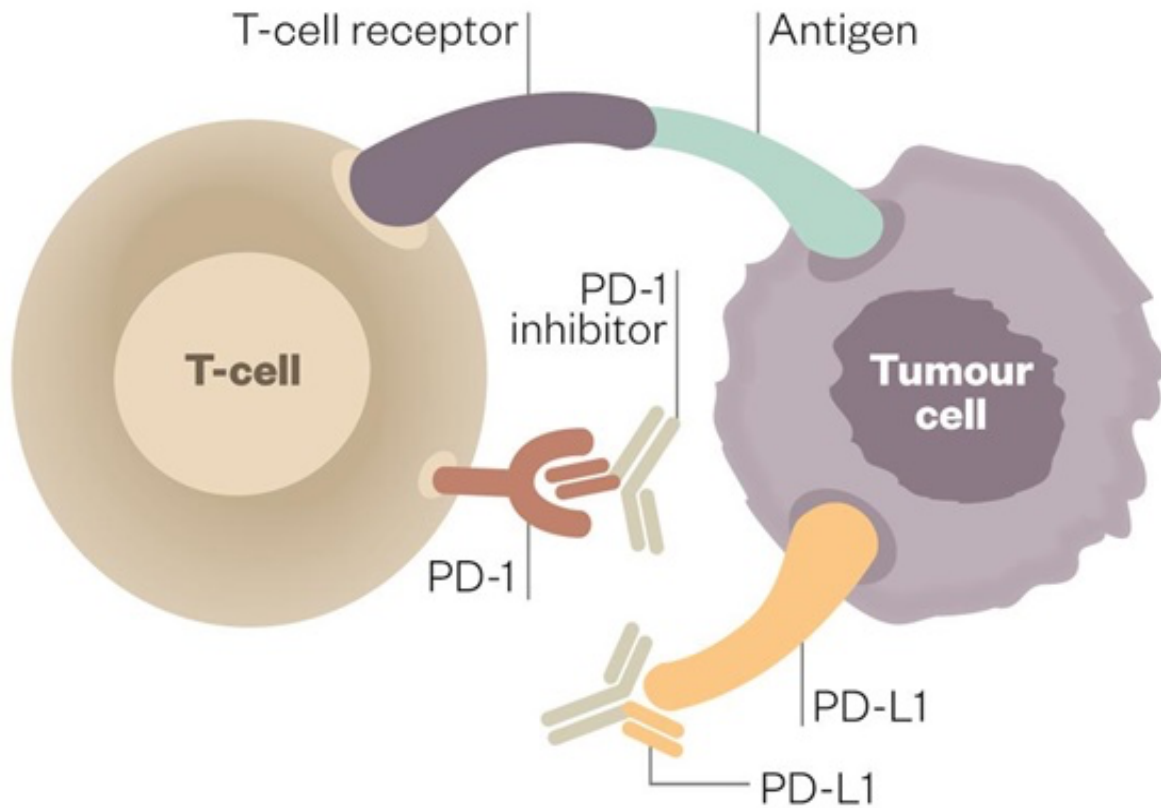
Now & the Future: Approaches to Treatment

- Traditional: surgery, chemotherapy, hormonal therapy, radiation therapy, adjuvant therapy
- Immunotherapy: use of biologic agents that mimic natural signals the body uses to control tumor growth (antigens, cytokines, etc)
 - example: Rituximab (monoclonal antibody, lymphoma & breast cancer)
- Vaccines
- Targeted Cancer Therapy: Immune check point inhibitors

Immune Check point Inhibitors

- The immune system's check points: allows the body to distinguish normal cells from foreign cells, thereby attacking the invading cells while leaving normal cells intact
- Checkpoints are molecules on immune cells that needs to be activated or deactivated to trigger an immune response
- Cancer cells use check points to avoid detection

PD-1/PDL-1 Inhibitors



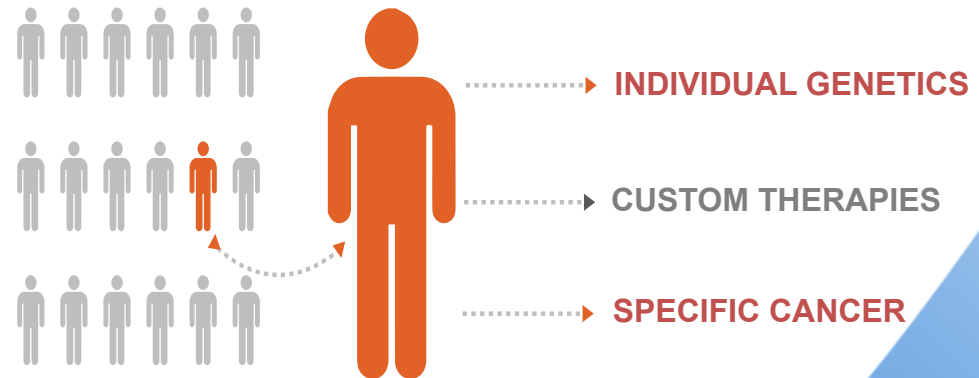
Precision Medicine in Cancer Treatment

- What is Precision Medicine?
- Administer the right drug to the right person at the right time
- NIH Precision Medicine Initiative
- *“You can match a blood transfusion to a blood type. That was an important discovery. What if matching a cancer cure to our genetic code was just as easy, just as standard? What if figuring out the right dose of medicine was as simple as taking our temperature? And that’s the promise of precision medicine -- delivering the right treatments, at the right time, every time to the right person.”*

Obama, January 30, 2015

Applying Precision Medicine to Cancer

- Using novel genomic technologies
- Identifying increased risk of disease and early intervention
- Maintaining health
- Getting the right treatment to the right patient at the right time
 - Beneficial treatment
 - Reduced side effects
 - Decreased cost



Tumor Profiling - Genomic Analysis of Tumor to Guide Treatment Decisions

The diagram illustrates the components of genomic analysis. It features three main categories, each with a hexagonal icon and a list of associated analyses:

- DNA** (blue hexagon with DNA double helix): Mutations, Indels & Copy Number Variants
- RNA** (red hexagon with RNA strand): Fusions & Variant Transcripts
- Protein** (brown hexagon with protein structure): Immunohistochemistry

Below these categories, a blue banner states: **CGP+** = Standard of Care + Clinical Trial Biomarkers


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Pharmacogenetics

- Administer the right drug at the *right dose* to the right person at the right time
- FDA has genomic considerations for efficacy and safety on labels of over 100 medications
- Every field of medicine
- Drug exposure and clinical response variability
- Risk for adverse events
- Genotype-specific dosing
- Mechanisms of drug action
- Polymorphic drug target and disposition genes

<http://www.fda.gov/Drugs/ScienceResearch/ResearchAreas/Pharmacogenetics/ucm083378.htm>





Where Are We Now?

- Developmental Therapeutics Program to bring new drugs to cancer patients
- Dedicated team of doctors and staff
- Molecular Pathology
- Genetics Program
- Early detection in high-risk for Pancreatic Cancer, Breast Cancer, Melanoma, Prostate Cancer Programs
- Alliance with USC Norris Comprehensive Cancer Center
- Caris Life Sciences Center of Excellence
 - Genomic testing of some cancer types
 - Integration of discussion of genomics into tumor board
- IT platform: Integration with Syapse

Pharmacogenetics Pilot Project

- 50 patients
- Buccal swab, 22 gene comprehensive panel
- Clinical and pharmacy history analyzed with genetic results
- Hypothesis is that Genetic testing will demonstrate 30% of patients are currently taking a drug for which there is a pharmacogenomics cautionary variant.





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LEAD, INNOVATE
& TRANSFORM

Hoag Family Cancer Institute

Thank You

Questions?

