Key Concepts in Cancer and Cancer Research

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Community Engagement and Education
Disclosure

• I have no actual or potential conflict of interest in relation to this program/presentation.
Cancer is the Leading Cause of Death in Minnesota
Cancers are Cells that **Accumulate Aberrantly** and Invade Local or Distant Tissues (**Metastasize**)

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To Better Answer the Question “What is Cancer?,” We Need to Discuss How our Bodies are Organized
Cells Follow **Instructions** Encoded in **DNA**
DNA (DeoxyriboNucleic Acid) is a Biochemical Information Storage and Retrieval System

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- Analogies for the genome include a hard drive, an owner’s manual, and a cookbook.
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One file/recipe = one gene (unit of information used to produce a discrete product: protein)
Receipt of **External Signals** by a Cell Causes It to **Access** Particular Genes (**Recipes**)
SNPs

(single nucleotide polymorphisms)
An average-sized human adult has $\approx 10,000,000,000,000$ (trillion) cells of >200 different types.
One Cell Generates One Person by **Differentiation**

**Shared**

**Unique**

---

**Housekeeping Genes**

**STEM CELL**

- Cardiac cells
- Enterocytes
- Fat cells
- Red blood cells
- Epithelial cells
- Chondrocyte

**Blastocyst**

**Stem cell**

**Neuron**

**Masonic Cancer Center**

**University of Minnesota**

Comprehensive Cancer Center designated by the National Cancer Institute
DNA Has Only **Four** “Letters” Called **Nucleotides**

- The molecules (nucleotides) that make up DNA are **A**, **C**, **G**, and **T**.
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- Nucleotides are linked in paired, coiled antiparallel strands.
- A always pairs with T and C always pairs with G.
- Each nucleated human cell has 12.9 billion letters (genome).
The Odds are Not in Our Favor

- $\approx 300\ \text{billion cells/day} \times 12.9\ \text{billion nucleotides/cell}$
  
  $\approx 3,870,000,000,000,000,000,000,000$ nucleotides/day

  $\approx 410\ \text{million miles of DNA/day}$
Cancers Are Genetic Diseases that Result from Alterations in DNA Sequence &/or Expression

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- Cancers are often genetically unstable.
  - DNA copying/repair machinery is compromised leading to **greater accumulations** of DNA mistakes during cell division.
Each DNA Strand is Copied During Replication
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Radiation Can Break DNA
Errors in DNA Repair Cause Mutations
Carcinogens Can Alter DNA

DNA ADDUCT
(add a duck)

CCTTAACCTTTGGGTCTTTGATATTGAT

ATTTGAAAC
Carcinogens Can Alter DNA

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All Mutations Are Not Created Equal

- Many mutations discovered in cancer cells are neutral passengers that merely accompany functionally important drivers that have been subject to selective pressure.
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- Many mutations discovered in cancer cells are neutral passengers that merely accompany functionally important drivers that have been subject to selective pressure.
- These mixtures of passenger and driver mutations together comprise the mutated gene sets of the tumors in question.
Driver Mutations Allow Cells to Overcome Barriers to Cancer
Cancers Primarily Strike Older Adults

Rates of new cases of all types of cancer, aggregated from 2004 to 2013.

https://apps.health.state.mn.us/mndata/cancer_all
How Do We Get Cancer?

- Age
  - Accumulation of DNA damage/change/mutations
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● Lifestyle
  ○ Intentional exposure to DNA damaging agents (carcinogens)
Why is Cancer Sometimes Deadly?
Cancer Compromises Organ Function

1. Starve, suffocate, squeeze healthy cells
   a. Reduces removal of toxins by kidneys
   b. Weakens the immune system which can lead to overwhelming, systemic infections (sepsis)
Cancers Can Block Vessels

1. Compromises healthy organ function

2. Blockages
   a. Excessive growths can block digestive track/blood vessels.
   b. Blockages can cause bleeds and can lead to other vascular problems such as aneurysms and strokes.
Cancers Can Cause Chemical Imbalances

1. Compromises healthy organ function
2. Blockages
3. Chemical imbalances
   a. Bone cancer can release excessive amounts of calcium.
   b. Liver cancer can perturb balances of enzymes.
   c. Cachectin-like substances tell the brain to stop feeling hungry and probably interfere with fat storage and utilization forcing the metabolic system to feed on normal tissue for energy.
Cancers are Like Weeds

http://www.aboutcancer.com/brain_met_mri_3.htm
Stages of Cancer: The Importance of Early Detection

Malignant (cancer) tumor cells invade local tissues and can metastasize to distant sites via the lymphatic and vascular systems.

Benign (not cancer) tumor cells grow locally and do not invade local tissue.
CANCER
>200 different diseases

Kaylee Schwertfeger, Ph.D.
The Anatomy of a Tumor
EVOLUTION OF CANCER THERAPY
The Evolution of Cancer Therapy

Conventional

Kills rapidly dividing cells
Exposed DNA is the Achilles' Heel of a Dividing Cell

Chromosome
Cell
- cytoplasm
- nucleus with 46 chromosomes

Tightly packed DNA

DNA sequence of a gene
DNA double helix

1/5000 inch
≈7 ft
Conventional
Kills rapidly dividing cells

Tumor-specific
Preferentially kills certain tumors

The Evolution of Cancer Therapy
Metastatic Colorectal Cancer

EGFR

Erbitux

DNA

Protein
The Evolution of Cancer Therapy

- Conventional
- Tumor-specific
- Patient-specific (precision medicine)

Preferentially kills certain tumors.
• Pharmacogenomics: Treatments tailored to the genetic changes in each person’s cancer and each person’s own genetics.

Cancer Immunotherapy

- Immunotherapy uses the immune system to treat a disease.
- Immunotherapy is a game changer for cancer because it is:
  - Specific
  - Potent
  - Long-lived
  - Adaptable
Immune System \textit{Constantly Removes} Nascent (Newly Formed) Tumors

\textbf{Immune Cells} \hspace{1cm} \textbf{Tumor Cells}
Clinically Apparent Tumors Have Escaped Immune Recognition

Immune Cells

Tumor-Induced Immune Suppression

Tumor Cells

Escaped
Overcoming Tumor-Induced Immune Evasion: Immune Checkpoint Blockade

Immune Cells

Tumor Cells
Overcoming Tumor-Induced Immune Evasion:

Engineered Immune Effector Cells (CAR)

CAR T-Cells

Tumor Cells

Tumor-induced Immune Suppression
Masonic Cancer Center’s Mission:
Reduce the Burden of Cancer in Minnesota

Masonic Cancer Center
® UNIVERSITY OF MINNESOTA
Comprehensive Cancer Center designated by the National Cancer Institute

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OFFICE OF ACADEMIC CLINICAL AFFAIRS
University of Minnesota
Driven to Discover®
Masonic Cancer Center is Minnesota’s Cancer Center

- Faculty research and testimony drive policy and legislation in MN
- Collaborate with other Non-Profits
  - Minnesota Cancer Alliance
  - MCA Cancer Health Equity Network
  - American Cancer Society Cancer Action Network
  - People’s Center, YMCA, Centro Tyrone Guzman
- Please contact us with questions, concerns, cancer issues you would like us to address, etc.
Types of Cancer Research

- Basic
- Lab
- Translational
- Clinical
- Clinic
- Standard of Care

How does it work?

How can this new knowledge be applied to cancer?

How does this new treatment compare to the current treatment?

Bench to Bedside

Bedside to Bench
The Masonic Cancer Center is a Comprehensive Cancer Center

The Cancer Continuum

etiology → prevention → screening → therapy → disparities → survivorship → palliative care

NCI Designated Comprehensive Cancer Center
Session 2: Mutations and Their Consequences

David Largaespada, Ph.D.
Cancer Genetics

Carol Lange, Ph.D.
When Good Cells Go Bad
Session 3: Causes and Prevention of Cancer

Robert Turesky, Ph.D.
Diet and Lifestyle Factors in Cancer Risk

Irina Stepanov, Ph.D.
E-cigarettes and Vaping: Chemistry and Toxicology Considerations
Session 5: Cancer in Minnesota

Doug Yee, M.D.
Clinical Trials and the Minnesota Clinical Cancer Trials Network

Rebekah Pratt, Ph.D.
Cancer in Minnesota
Session 6:
Cancer Survivorship

Tanya Bailey, MSW
A Heroic Journey Mindset

Anne Blaes, M.D.
Cancer Survivorship

Deborah Day Laxson, PMP
The Gray Zone
Cancer 101: Take Home Messages

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- The Masonic Cancer Center is **YOUR** cancer center.
Emily Whitehead
Complete Remission – Going Strong for 7.5 Years!
Acknowledgements

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- National Cancer Institute
- Randy Shaver Cancer Research and Community Fund