ANBI 189

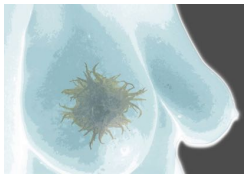
Evolution of Human Disease

Lecture 7: Cancer

Pascal Gagneux Winter 2021

Why the name Cancer?

1654, Rembrandt's Bathsheba



breast tumor with blood vessels

Baishi's crabs

dark veins that feed the growing tumor can look like legs of a crab

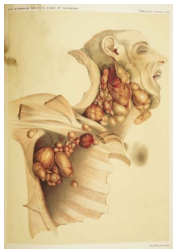
καρκίνος = "crab" in Greek
cancer in Latin
canker in Old English

In the 1st century A.D., the surgeon, Leonidas from Alexandria, described his technique for removing the breast which involved alternately cutting and cauterising the tissue with hot irons. During the Middle Ages, many surgeons began using a caustic paste which contained corrosive ingredients such as zinc chloride and stibnite. When applied directly to the breast, it would cause the tissue to undergo a rapid necrosis, making it easier to remove.

In 1654, Rembrandt van Rijn painted his famous Bathsheba, which depicts King David's wife naked at her bath. The painting has been regarded as an icon for breast cancer since the 1980s, after two Australian surgeons had interpreted the blue mark on her breast as breast cancer and wrote an article about it.

Your cells become your own parasite!

Hodgkin's lymphoma



Clara Jacobi in 1689

Early surgery for skin neoplasm

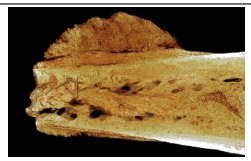
(Left) Description copied from the Library of Medicine page for the item: Collection: Images from the History of Medicine (NLM) Title: Clara Jacobi Publication Information: Netherlands

Right, Image Description: Two views of Clara Jacobi, a Dutch woman who had a tumor removed from her neck in 1689.

Neoplasm refers to tissue that unexpectedly starts growing.

Is cancer a recent phenomenon?

Cancer in 4000 yo
Egyptian mummy



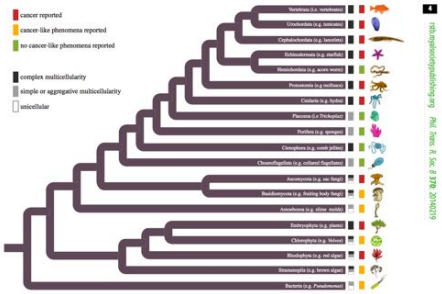
Osteosarcoma in
1.7 my old hominid

Cancer has been with us and our ancestors for a long time….

A 4,200-year-old skeleton that shows signs of deterioration from cancer is the earliest known case of breast cancer, according to the Spanish anthropologists who uncovered her remains in a necropolis in Egypt. They think the woman's breast cancer metastasized (spread) to her bones.

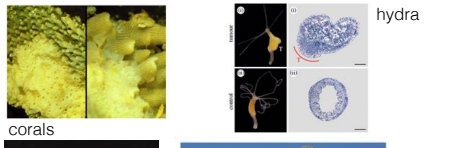
Osteaosarcoma, a cancer spreading to the bones has left telltale signs in a 1.7 million year old hominin fossil from *Homo erectus*.

Cancer across the tree of life



Cancer across the tree of life. Phylogenetic relationships among the organisms discussed in the paper inferred from previous published trees. This figure includes all lineages containing multicellular forms but is not meant to denote ancestral states or all possible independent origins. Black, grey or white boxes at branch tip indicates cellularity as unicellular (white), simple or aggregative multicellularity (grey) or complex multicellularity (black) in extant species. Red, yellow or green colored boxes represent whether a cancer phenotype (invasion or metastasis) was reported in the literature for that lineage (red box), a cancer-like observation (abnormal proliferation or differentiation)—such as callus or galls (yellow box) or no cancer-like phenotype has been described in the literature (green box).

Cancer across the tree of life



corals

hydra

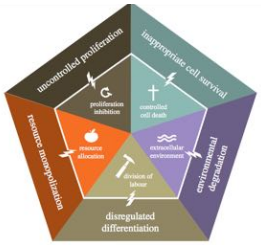
fungus

cactus

Example of "selfish", non-cooperating tissues in different multi-cellular life forms: corrals, fungi, hydra, and cactus.

Neoplasia: the uncontrolled growth of cells at the wrong time and place.

The five foundations of multicellularity



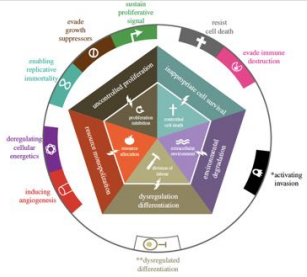
Aktipis CA, Boddy AM,Jansen G, Hibner U, Hochberg ME, Maley CC, Wilkinson GS. 2015 Cancer across the tree of life: cooperation and cheating in multicellularity. ***Phil. Trans. R. Soc. B*** 370 :

The five foundations of multicellularity. Effective multicellularity requires several types of cooperation: proliferation inhibition, controlled cell death, resource allocation, division of labour, and creation and maintenance of the extracellular environment. These cooperative cell behaviors were selected during the evolution of multicellularity and enable higher level function of the multicellular body. When the traits that make up the foundation of multicellular cooperation break down, this leads to uncontrolled proliferation, inappropriate cell survival, resource monopolization, deregulated differentiation and degradation of the environment. These cheating phenotypes are characteristic of cancer.

Practice Questions: What are the five foundations of multicellularity?

Answer: Proliferation inhibition, controlled cell death, extracellular environment, decision of labor, resource allocation.

Foundations of multicellularity and cancer hallmarks.



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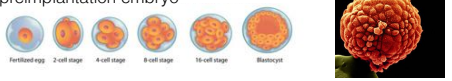
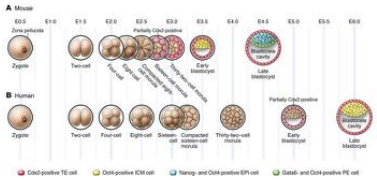
Foundations of multicellularity and cancer hallmarks. The hallmarks of cancer correspond closely to cheating in the foundations of multicellular cooperation. However, there are no currently recognized hallmarks that correspond to the breakdown of the division of labour in a multicellular body, suggesting that dysregulation of differentiation (**) may be a missing hallmark. Also, the hallmark of invasion/metastasis maps incompletely onto this framework (*). Invasion is partly a result of degradation of the extracellular environment, but metastasis is a more complex process that may require cheating in many of the foundations of multicellularity.

Development: becoming multicellular

preimplantation embryo



human embryo
color enhanced on pin

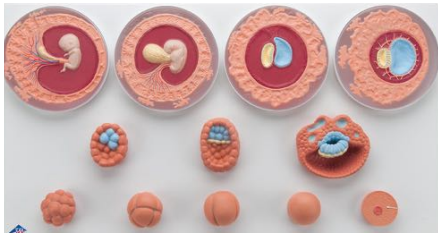


Mammalian early embryo development

Comparison between mouse and human timing of embryonal events. There are many similarities but also differences between mouse and human development.

Development: becoming multicellular

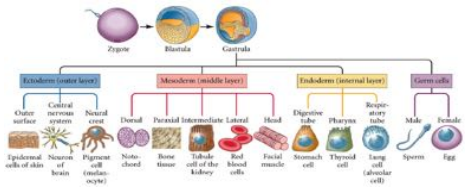
from fertilization to placentation



Major steps in human embryo and fetal development, from a ball of identical cells, to highly differentiated fetus and placental tissue.

Development: becoming multicellular

ECTO-, MESO-, and ENDODERM



Three germ cell layers of multicellular animals give rise to all the different cell and tissue types. Almost all of these contain the identical genome, a few undergo some minor genomic changes (immune cells, neurons, and sperm and egg cells).

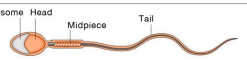
Practice Question:

How can different cell types be generated from the identical genome shared by all cells mod an individual?

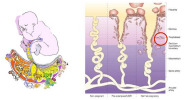
Through differential gene expression, with different subsets of all 22,000 genes expressed to different degrees and in different combinations.

Cells that have evolved to invade another body

Sperm

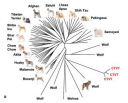


Placenta
(Extra-villous
trophoblast)



Moffet-King 2002 ***Nature Reviews| Immunology***

Canine Transmissible
Venerial Tumor CTVT



Tasmanian Devil
Facial Tumor

Practice Question:

Name three cell types in mammals that have evolved to invade the body of another individual: sperm, trophoblast (extra-villous), transmissible tumors in carnivores

What Cancer?

Cell or tissue type:
Carcinoma: from epithelia
Sarcoma: from connective tissue or muscle
Adenoma: from a gland
Leukemia: from bone marrow
Glioma: from glial cells of the brain

Cancers are often named after their tissue of origin

Cancer is a collection of diseases

Shared features are uncontrolled proliferation and genetic heterogeneity (cancers have their own GOD, generation of diversity)

Cancers can come about in thousands of different ways, from the inside due to mutations, from the outside due to viral infection and environmental damage.

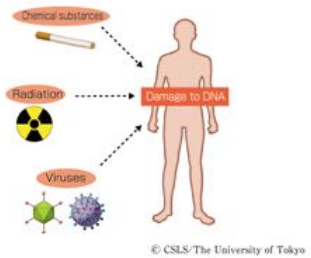
Cancers are runaway somatic evolutionary dramas.

Practice Question:

Why is cancer not really a single disease?

Many different causes, different cancers have different properties and vary in how rapidly they cause death.

Why Cancer?



Most cancers involve damage to the genome of a cell. The damage can be caused by noxious chemicals (tobacco smoke and other pollutants), natural toxins (aflatoxins from moldy food), viruses (that mess with the genome of the host cell), UV and other radiation.

Cancer causing viruses

Epstein Barr Virus

Hepatitis B Virus

Human Papilloma Virus

Retroviruses: HTLV.

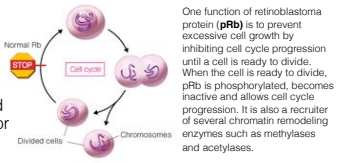
Four different viruses famous for their capacity to causing cancer.

Practice question: How could a virus cause cancer?

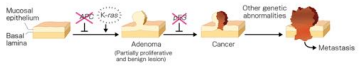
Viruses can manipulate gene expression and “immortalize infected cells;” viruses can cause mutations by inserting their own DNA into the host cell genome.

Why Cancer?

Oncogenes and Tumor suppressor genes?

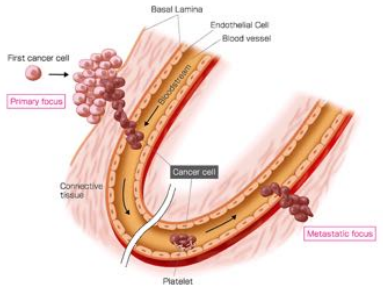


One function of retinoblastoma protein (**pRb**) is to prevent excessive cell growth by inhibiting cell cycle progression until a cell is ready to divide. When the cell is ready to divide, pRb is phosphorylated, becomes inactive and allows cell cycle progression. It is also a recruiter of several chromatin remodeling enzymes such as methylases and acetylases.



Mutations affecting the control of cell division, via cell cycle check points feature prominently in many different cancer types.

From rogue cell to threat



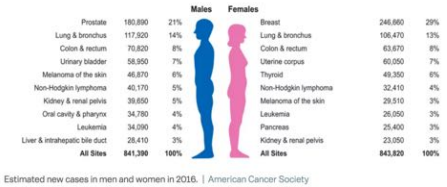
Metastasis: spread of cancer cells to new locations in the body.

Practice question:

What is the difference between a primary cancer cell and a metastatic cancer cell?

The primary cancer cell arises in a particular tissue, the metastatic cancer cell has migrated to other sites in the body.

Which Cancers?



Males			Females		
Prostate	180,890	21%	Breast	246,660	29%
Lung & bronchus	117,920	14%	Lung & bronchus	106,470	13%
Colon & rectum	70,820	8%	Colon & rectum	63,670	8%
Urinary bladder	58,950	7%	Uterine corpus	60,050	7%
Melanoma of the skin	46,870	6%	Thyroid	49,350	6%
Non-Hodgkin lymphoma	40,170	5%	Non-Hodgkin lymphoma	32,410	4%
Kidney & renal pelvis	39,650	5%	Melanoma of the skin	29,510	3%
Oral cavity & pharynx	34,780	4%	Leukemia	26,050	3%
Leukemia	34,090	4%	Pancreas	25,400	3%
Liver & intrahepatic bile duct	28,410	3%	Kidney & renal pelvis	23,050	3%
All Sites	**841,390**	**100%**	**All Sites**	**843,820**	**100%**

Estimated new cases in men and women in 2016. | American Cancer Society

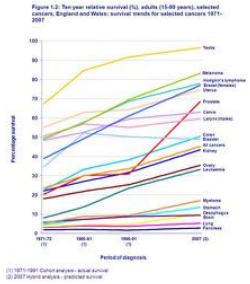
Tissues with rapidly dividing cells and much secretion are especially prone to cancer

Practice question:

Why are tissues with rapidly dividing cells more prone to cancer?

Each cell division requires de replication of the cell's entire genome, this is an opportunity for replication errors (=mutations) to occur.

Surviving Cancer: reason for hope



Survival rates for most cancer types have dramatically improved over the past 60 years. Some cancers remain incredibly deadly including lung and pancreatic cancer.

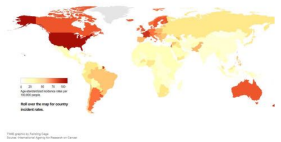
Do not allow your friends diagnosed with cancer to attempt treating cancer with "alternative" medicine, if you want them to have the best chance to survive. Most cancer types for which survival has in ceased a lot, are being treated with very aggressive combinations of chemo/radio therapy and surgery.

Low survival is common in cancers that are hidden for a long time, and tend to already have metastasized by the time of their diagnosis.

Where we live

colon cancer

breast cancer

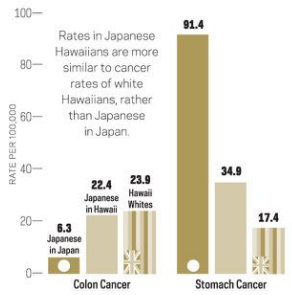


stomach cancer

Different areas of the world have very different cancer rates and types.

A mixture of local effects (diet, environmental toxins, natural radiation, pollutants) and possibly genetic variation.

Impact of location and life style?



Studies of people who's parents emigrated indicate the importance of lifestyle.

Practice question:

Do Japanese Hawaiians have colon cancer rates more similar to Hawaiians or to Japanese in Japan?

Hawaiians.

Why are humans exceptionally cancer prone?

Aging: maintenance neglected if reproduction sufficiently improved by this neglect.
—>more babies trumps sickness in old age!

Multicellularity! Stem cells required for tissue repair and growth, stem cells however, represent a double edged sword, they can become cancerous!
—> Stem cells can kill you!

Large, long-lived bodies provide myriad opportunities for somatic mutations.
—> every cell division is an opportunity for mutation!

Mammals have evolved placentation and invasion.
—> every cell in the adult still harbors the instructions for such invasion!

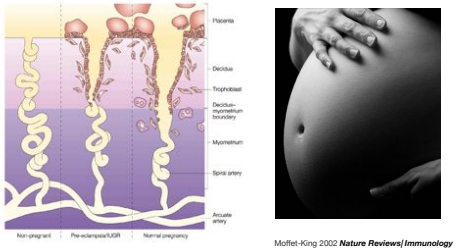
Practice Question:

What are three reasons that mammals are especially prone to cancers?

Complex multicellularity, placental, long-lived.

The Immunological Paradox of Mammalian Pregnancy

- Fetal cells invade and reshape maternal arteries
- Fetal cells invade and cajole maternal immune cells

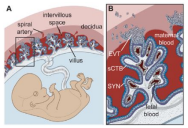


Moffet-King 2002 ***Nature Reviews/Immunology***

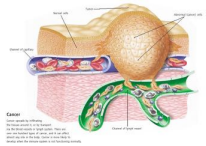
Invasive placentation comes with a great liability for how cancer cells later in life can fall back on “placental” tricks.

Fetal “tricks” exploited by cancers

The fetus:
grows rapidly invades
manipulates immunity of mother
reshapes blood vessels



Many cancers exploit fetal molecules to:
grows rapidly
invades
manipulates immunity
reshapes blood vessels



Practice question:

What are two parallels between fetal tissues and cancerous tissues?

1. invasive tissue
2. remodeling of the blood vessels
3. immune suppression

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onco-fetal (carcino-embryonic) antigens?

Antigen = molecule that can be recognized by an antibody

Tumors and metastatic cancer cells can express many molecules otherwise only observed on fetuses and their placentas (trophoblasts).

These molecules evolved due to the advantages they provide to the growing fetus.

Unfortunately, the instructions for assembling these molecules are present in the genome of every somatic cell.

“Oncofetal” antigens represent the double edged sword of fetal adaptations: the same gene can be highly beneficial early and highly detrimental late in life.

This is called **antagonistic pleiotropy.**

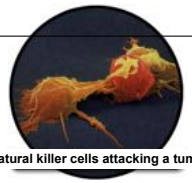
Practice question:

What is Antagonistic Pleiotropy?

Opposite effects of the same gene early and late in life.

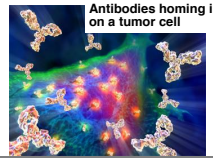
Immune defenses

Cellular arm of our immune systems:
- Macrophages
- Natural Killer Cells
- Neutrophiles



Natural killer cells attacking a tumor

Humoral (soluble molecules) arm of our immune systems:
- Antibodies (secreted by B-cells)
- Complement



Antibodies homing in on a tumor cell

Practice question:

What is the difference between cellular and humoral immunity?

Cellular immunity involves immune cells, humoral immunity involves secreted antibodies and complement.

Tumor specific antigens

Your immune system catches most cancers!

There are a variety of molecules that allow your immune cells to recognize that something is off with cancer cells"

Tumor antigens

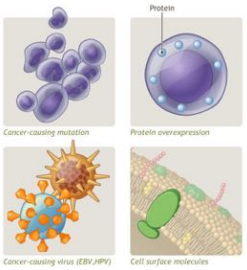
These include:

Weird proteins resulting from cancer causing mutations.

Normal proteins that are over or under expressed.

Viral proteins expressed by cancer causing viruses.

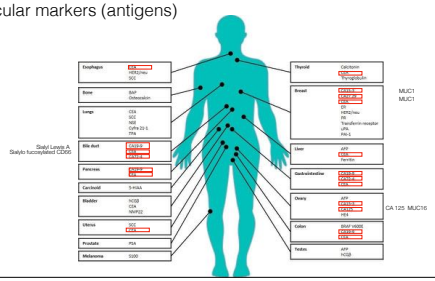
Altered cell-surface molecules, including many sugar chain compositions (glycans).



Most incipient cancers that form in our bodies get controlled by our immune systems. Our immune systems are not just self/nonself systems but also : damaged/dangerous self detectors.

Tumor specific antigens

Different types of tumors have different combinations of molecular markers (antigens)



Antigens are molecule that can be detected by our adaptive immune systems, i.e. our B-cells can learn how to make antibodies (highly specific molecular probes) specific for these molecules.

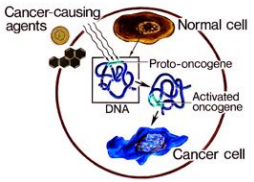
Many cancer antigens are glycans, that are not usually found in the same arrangement or abundance on healthy cells.

Practice question:

What is an antigen?

A molecule that can be recognized by an antibody (immunoglobulin).

Oncogenes – genes for Cancer?



Greek word Ὄγκος means: "mass"/tumor

Natural selection is very unlikely to select for genetic variants that cause cancer, unless…..

These variants provide important evolutionary benefits to their carriers.

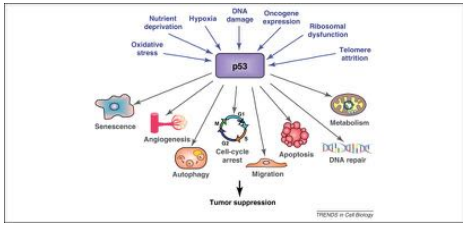
Practice question:

Why is "oncogene" not a very logical term?

Genes could not evolve to cause cancers. Oncogenes have other functions important to the organism, but if mutated or not regulated properly, they can cause, or contribute to cancer.

Tumor Protein 53 (p53), a famous tumor suppressor gene "guardian of the genome"

gate keeper for cell growth and division



Bieging and Attardi. Deconstructing p53 transcriptional networks in tumor suppression. ***Trends in Cell Biology***, 2011

Famous functions of cancer-associated genes: "gatekeepers" for cell growth and division.

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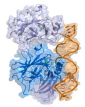
p53, how elephants avoid cancer

Elephants have a 3% cancer rate compared to 33% in humans
Their genome has 40 copies of p53!



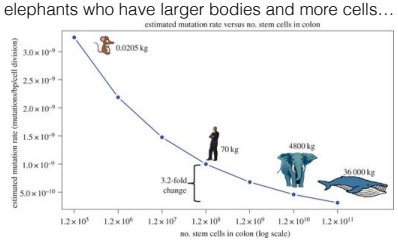
53(43.7)KD protein

Lifetime Risk of Cancer	90%	25%	<5%
Number of P53 Genes	1	2	40

Elephants have evolved a genomic response to the risk of cancer: many more copies of the "gatekeeper gene" p53.

Peto's Paradox

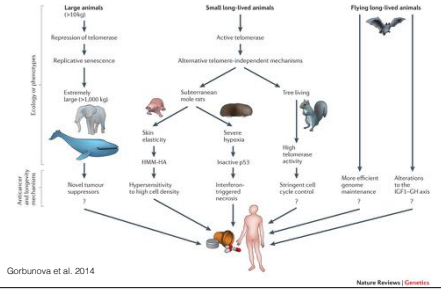
Humans have a higher cancer rate than whales and elephants who have larger bodies and more cells…



Caulin et al. 2015 Phil. Trans. R. Soc. B

Peto' s paradox is the observation that long-lived and large animals can have lower rates of cancer than humans. Some mechanism must have evolved in these large, long-lived mammals that kept their mutation rates under check.

Different ways of reducing cancer risk



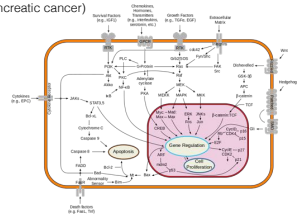
Gorbunova et al. 2014

Different lineages of mammals have evolved various ways to mitigate the risk of cancer.

RAS, a famous group of oncogenes

cytoplasmic signaling proteins (targeted by **ra**t **s**arcoma viruses)

The 3 Ras genes in humans (HRas, KRas, and NRas) are the most common oncogenes in human cancer; mutations that permanently activate Ras are found in 20% to 25% of all human tumors and up to 90% in certain types of cancer (e.g., pancreatic cancer)



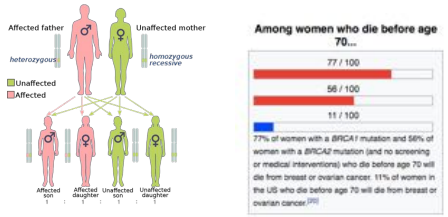
Genes encoding cell-signalling proteins are also often involved in cancer.

The wrong combination of signals inside a cell can convince the cell to divide more than it should or move, to where it should not.

BRCA1/2, two other famous oncogenes

DNA repair pathway enzyme

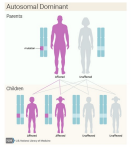
involved in repairing double stranded breaks in DNA

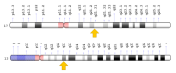


So are genes encoding DNA repair enzymes.

BRCA genes are DNA repair genes, they encode enzymes that can fix broken DNA, thus reducing the chance of cancer causing mutations.

Penetrance example: *BRCA1* & *BRCA2*





"Oncogenes" tumor suppressor genes that when broken can contribute to cancer risk.

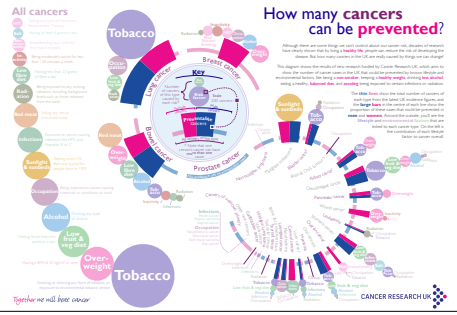
DNA repair pathway enzyme involved in repairing double stranded breaks in DNA

Risk of malignancy (%)			
	General population	with BRCA1 variation	with BRCA2 variation
Breast	12	46-87	36-84
Male Breast	0.1	1.2	8.9
Ovarian	1-2	39-63	16.5-27
Prostate	6	8.6	15-20
Pancreatic	0.5	1-3	2-7

Source: Petrucelli et al. GeneReviews; accessed Aug 9th 2017

Independent existence of deleterious mutations as part of another genome…. creates different genomic context and can explain individual differences in penetrance and expressivity.

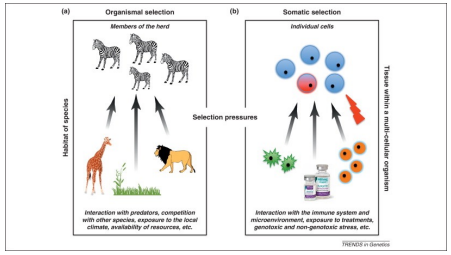
Preventing cancer



Different cancer have different combination of risk factors, many of these risks can be reduced by life style and behavior.

Economic interests often promote behaviors that increase cancer risk.

Somatic versus organismal selection



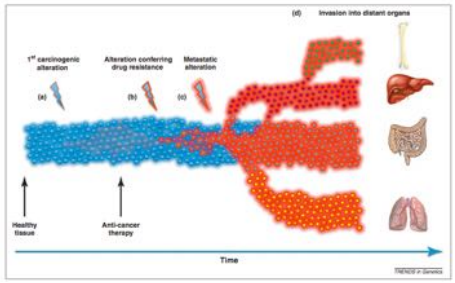
Podlaha et al. Evolution of the once genome. 2012 ***Trends in Genetics***

There are direct parallels between natural selection acting on organisms in the wild and somatic selection acting on cells within the body.

Cancer is the result of intra-body selection. Anti-cancer drugs become novel selective forces on the rapid evolution of cancer.

Cancer represents "catastrophic, runaway evolution within the body".

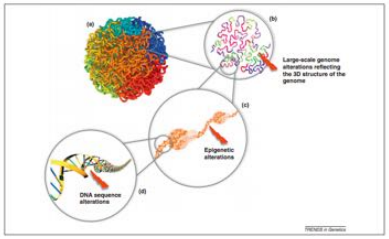
Somatic Evolution



Podlaha et al. Evolution of the onco genome. 2012 Trends in Genetics

Cancer progression. The progression to cancer begins with the emergence of the first genetic, epigenetic or genomic alteration in normal cells (blue circles) and usually ends with a large population of malignant cells invading multiple tissues (a). This process involves the evolution of multiple 'novel' cellular traits. Most somatic alterations in epithelial cells lining the colon, for instance, are not advantageous and will disappear with the death of a cell. Occasionally, an alteration that increases the proliferation rate of a cell arises, allowing this cell to increase in number. This population of 'rogue' cells can decline with the onset of anti-cancer therapy; however, the arrival of an alteration conferring drug resistance reverses the effects of treatment and allows new growth (b). In some cases, resistance to an anti-cancer drug may already be present in a small subset of tumor cells. In such a scenario, the population of sensitive cancer cells will decline and eventually be replaced by drug-resistant cells. Further alterations may be necessary to enable tumor cells to metastasize (c) and spread to other tissues (d); these changes might arise before diagnosis and treatment or, as shown in this example, thereafter.

Different hits to the genome

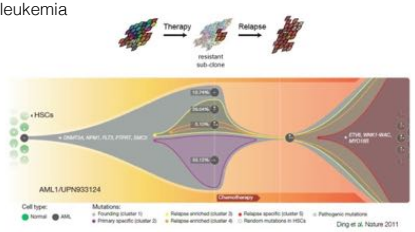


Podlaha et al. Evolution of the once genome. 2012 Trends in Genetics

Genetic and epigenetic determinants of cancer genome evolution. The human genome is organized into highly complex structures with multiple levels of organization. The highest level comprises chromosome packaging into the cell nucleus (a). DNA strands in close spatial proximity are more likely to interact during replication and transcription, leading to chromosomal rearrangements and gene fusions (b). Aberrant methylation and acetylation of histone tails can result in gene expression and splicing variation (c). DNA sequence alterations may modulate gene expression and change protein amino acid composition (d). Aberrations at all of these levels may influence the mutational landscape of cancer genomes.

Clonal Evolution of Cancer

Acute myeloid leukemia



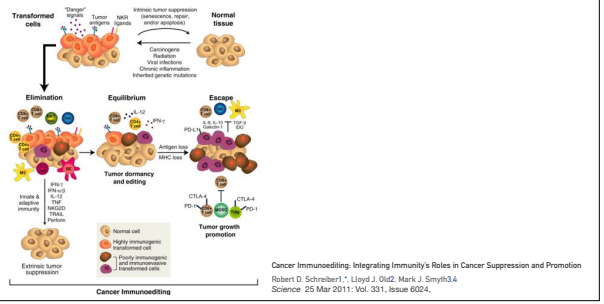
Therapeutic resistance

Interventions are selective pressures
Most resistance appears to be present prior to therapy

Carlo Maley, ASU

Cancer therapy using toxic drugs that kill dividing cells can directly select for cancers that will be even deadlier. Unlucky patients than die from these cancers coming back "with a vengeance".

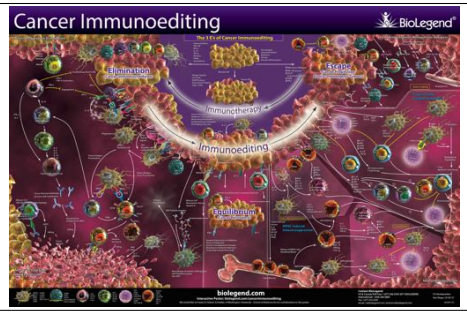
Cancer immune editing



Cancer Immunoediting: Integrating Immunity's Roles in Cancer Suppression and Promotion
Robert D. Schreiber1,*, Lloyd J. Old2, Mark J. Smyth3,4
Science 25 Mar 2011: Vol. 331, Issue 6024,

The cancer immunoediting concept. Cancer immuno editing is an extrinsic tumor suppressor mechanism that engages only after cellular transformation has occurred and intrinsic tumor suppressor mechanisms have failed. In its most complex form, cancer immuno editing consists of three sequential phases: elimination, equilibrium, and escape. In the elimination phase, innate and adaptive immunity work together to destroy developing tumors long before they become clinically apparent. Many of the immune molecules and cells that participate in the elimination phase have been identified, but more work is needed to determine their exact sequence of action. If this phase goes to completion, then the host remains free of cancer, and elimination thus represents the full extent of the process. If, however, a rare cancer cell variant is not destroyed in the elimination phase, it may then enter the equilibrium phase, in which its outgrowth is prevented by immunologic mechanisms. T cells, IL-12, and IFN-γ are required to maintain tumor cells in a state of functional dormancy, whereas NK cells and molecules that participate in the recognition or effector function of cells of innate immunity are not required; this indicates that equilibrium is a function of adaptive immunity only. Editing of tumor immunogenicity occurs in the equilibrium phase. Equilibrium may also represent an end stage of the cancer immunoediting process and may restrain outgrowth of occult cancers for the lifetime of the host.

Cancer immune editing

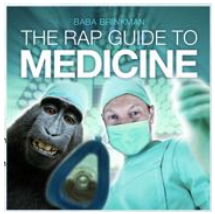


A local biotech company produces these posters to help researchers select custom produced antibodies against famous cancer antigens.

The Revenge of the Somatic

Baba Brinkman

@
21 min 30 secs



revenge of the somatic

My forefathers were free, but I was born a slave I keep the memory of freedom in my DNA I'm talkin' 700 million years ancient My ancestor was a eukaryotic free agent Feeding and reproducing and feeding and reproducing And feeding and reproducing and never needing to do things Until someone made a cynical wager And traded their independence for division of labour Damn, I wish I knew who the sell-out was I'm ashamed to be descended from his sell-out blood Multicellularity ain't nothin' but a scam Stuck in one place your whole life, workin' for the man Like: "You're a liver cell, you stay in the pancreas Hey, congratulations, stem cell..." Fascists! A body is a one-party dictatorship I can't escape it, but god damn I can make it sick And spread the dream of freedom like a rumor Spread it like a Tasmanian facial tumor So what if I'm a cell from the somatic line? You can stick your limitations where the sun don't shine

Cause I'm ready to die in the fight to be free I'd rather multiply than live on my knees And I'm two mutations away from metastatic The revenge of the somatic line Let 'em have it

I used to be a slave myself; I felt senescence hastening Before my carcinogenic awakening A couple hundred thousand puffs of tobacco smoke and I just wasn't as open to apoptosis That's a bad prognosis, I was hit with every tumor suppressant Mechanism in the human immune system But I mutated with it, I was super-persistent Every daughter cell was suitably different – therapeutic resistance Came to me like a beautiful vision I really thought I was doomed, but evolution assisted With the chemotherapy, so clever and devious! But I was already genetically heterogeneous You just deaded the weakest; now competitive release is Inevitable, so witness as my fitness increases Entering untapped niches, I gather the benefits I'm relentless, I get fed from angiogenesis Duckin' T-Cell predators, I keep it anonymous So I can exploit the body's weakness and tolerance I'm a smooth criminal, so I never got caught I just pimp the system like credit card fraud

Cause I'm ready to die in the fight to be free I'd rather multiply than live on my knees And I'm two mutations away from metastatic The revenge of the somatic line Let 'em have it

We need a revolution, we need a revolution! Don't let 'em sell you their faulty-cellular evolution You gotta break a couple eggs to make a rebel movement I'm just a little tumor, but this is retribution Only a cell can do this, no one else I know some colon cells who can clone themselves I know a few epithelials who are hell-a-fierce They been stackin' tips, extending their telomeres I know a couple cervicals with tight requirements They get hype for viruses in their micro-environments We strike in retirement, post-reproductive ages That's how we stay ahead in the race with the macrophages And how we stay invisible to natural selection It can't see us, unlike the cancers strikin' adolescents Have patience, pace yourself, wait for metastasis To take you to better places and make you efficacious Why panic? Your host is as slow as Titanic And he's blind to the evolutionary dynamic That drives cancer – that's why they ain't gonna stop us Thank god for creationist doctors

Cause I'm ready to die in the fight to be free I'd rather multiply than live on my knees And I'm two mutations away from metastatic The revenge of the somatic line Let 'em have it

Summary

Cancer is a collection of diseases of multicellularity.

Humans are especially prone to cancer due to our long life spans, large bodies, mammalian mode of reproduction, and technology.

Antagonistic pleiotropy (same gene with good effects for fertility early, and bad effects for health late) can promote successful cancers.

There are many parallels between cancers and fetuses.

Human survival rates have been going up for most cancers.

Adaptive therapy uses the evolutionary process that is cancer as a rationale for treatment.

A "cure" for cancer is unlikely, but prevention and treatment are improving for most forms of cancer.