Cancer: Emerging Research and Therapies

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IMA's Four Pillars

- Combating Chronic Disease
- Patient Empowerment
- Transparency in Medicine
- Building a Healthy Culture

Cancer: Pathology

Cause, Unknown?

Ryan N. Cole, MD AP/CP Board Certified

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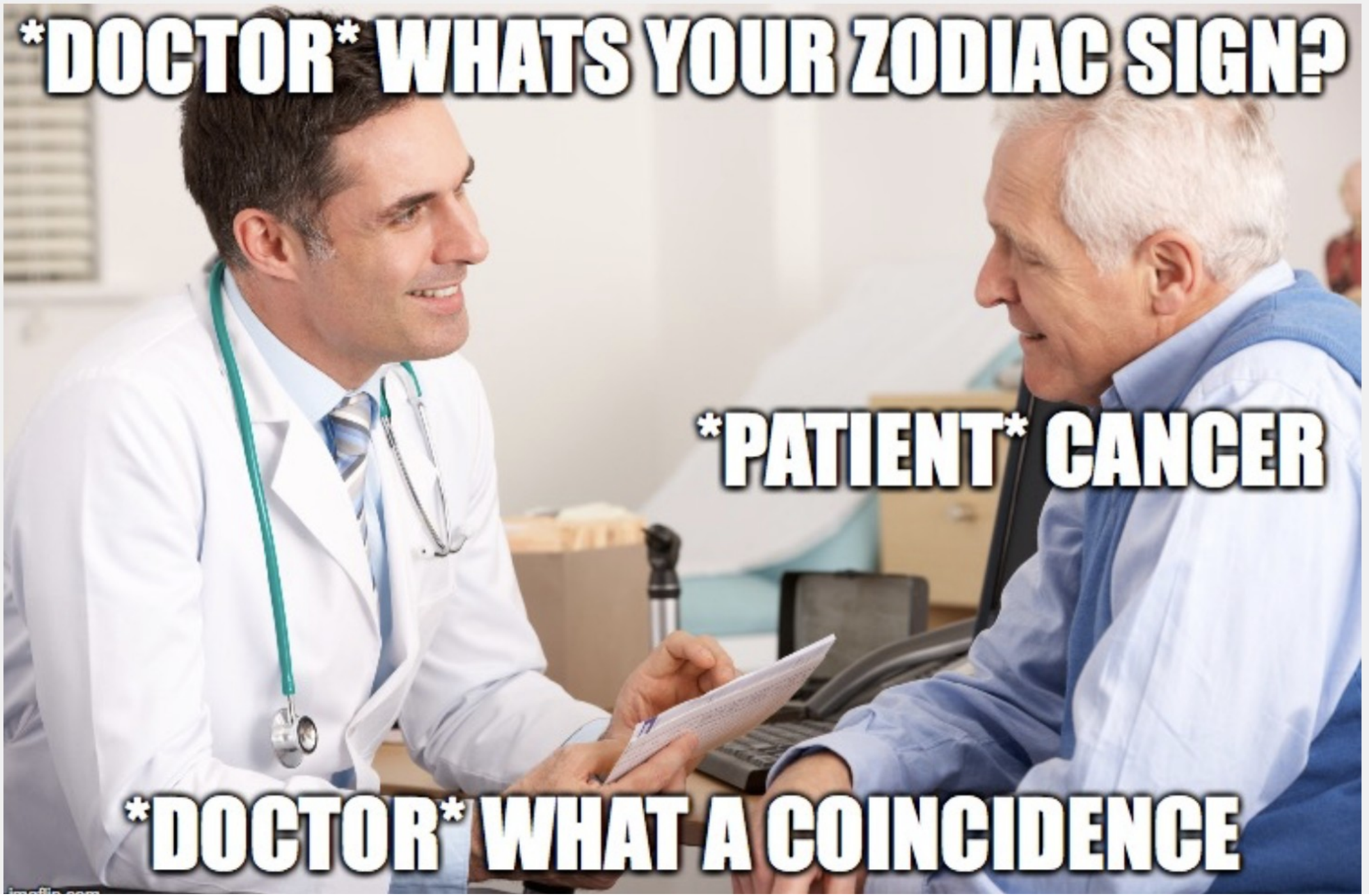

DOCTOR WHATS YOUR ZODIAC SIGN?
PATIENT CANCER
DOCTOR WHAT A COINCIDENCE

EMBRYOLOGY: CANCER

HOW DOES CANCER DEVELOP

LEADING CONSTRUCTS

- SOMATIC MUTATION THEORY (SMT)
- IMMUNOLOGIC THEORY
- STEM CELL THEORY
- TISSUE ORGANIZATION FIELD THEORY (TOFT)
- INTEGRATIVE (INCLUDING METABOLIC) THEORY
- CLONAL EVOLUTION AND BEYOND
- INFLAMMATION (CHRONIC)? INFECTIONS (MUTAGENIC VIRUSES, ETC.)?

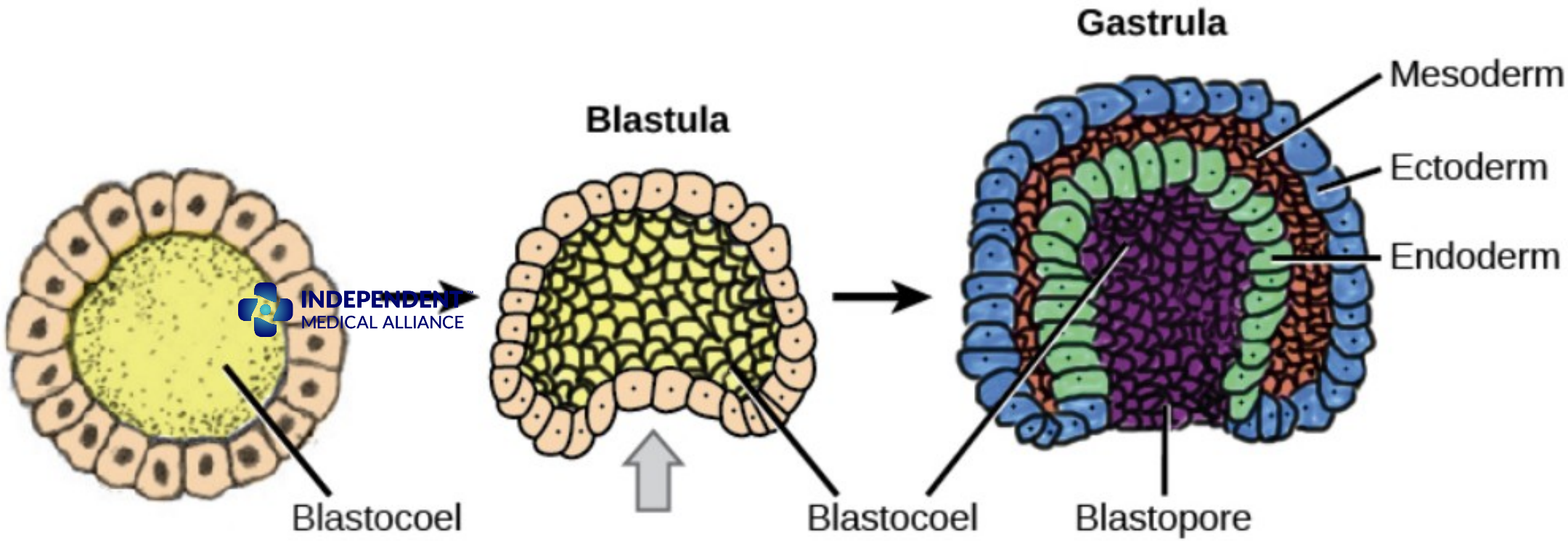
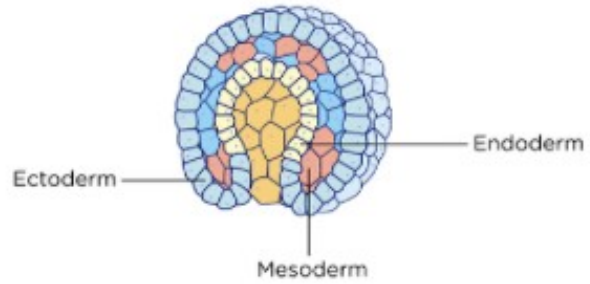
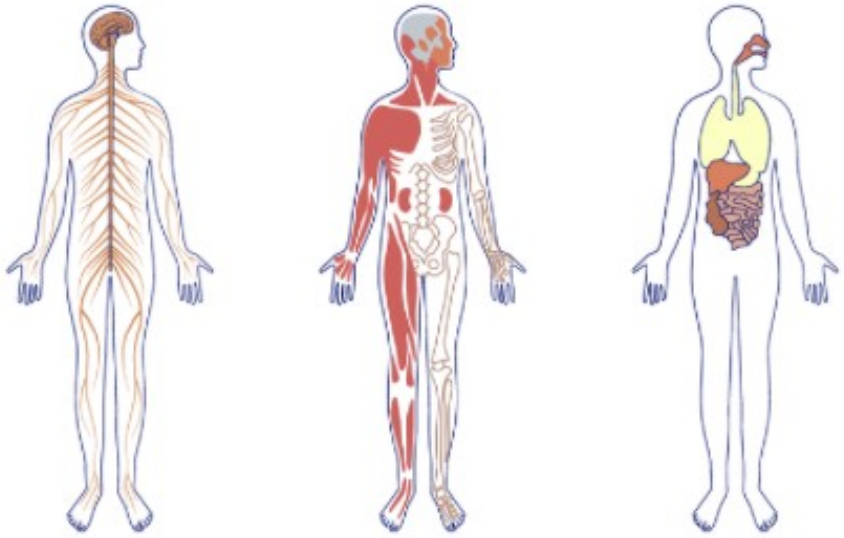


Figure 13.10 Gastrulation is the process wherein the cells in the blastula rearrange themselves to form the germ layers. (credit: modification of work by Abigail Pyne)





Ectoderm

- Epidermis of skin and its derivatives (including sweat glands, hair follicles)
- Epithelial lining of mouth and anus
- Cornea and lens of eye
- Nervous system
- Sensory receptors in epidermis
- Adrenal medulla
- Tooth enamel
- Epithelium of pineal and pituitary glands

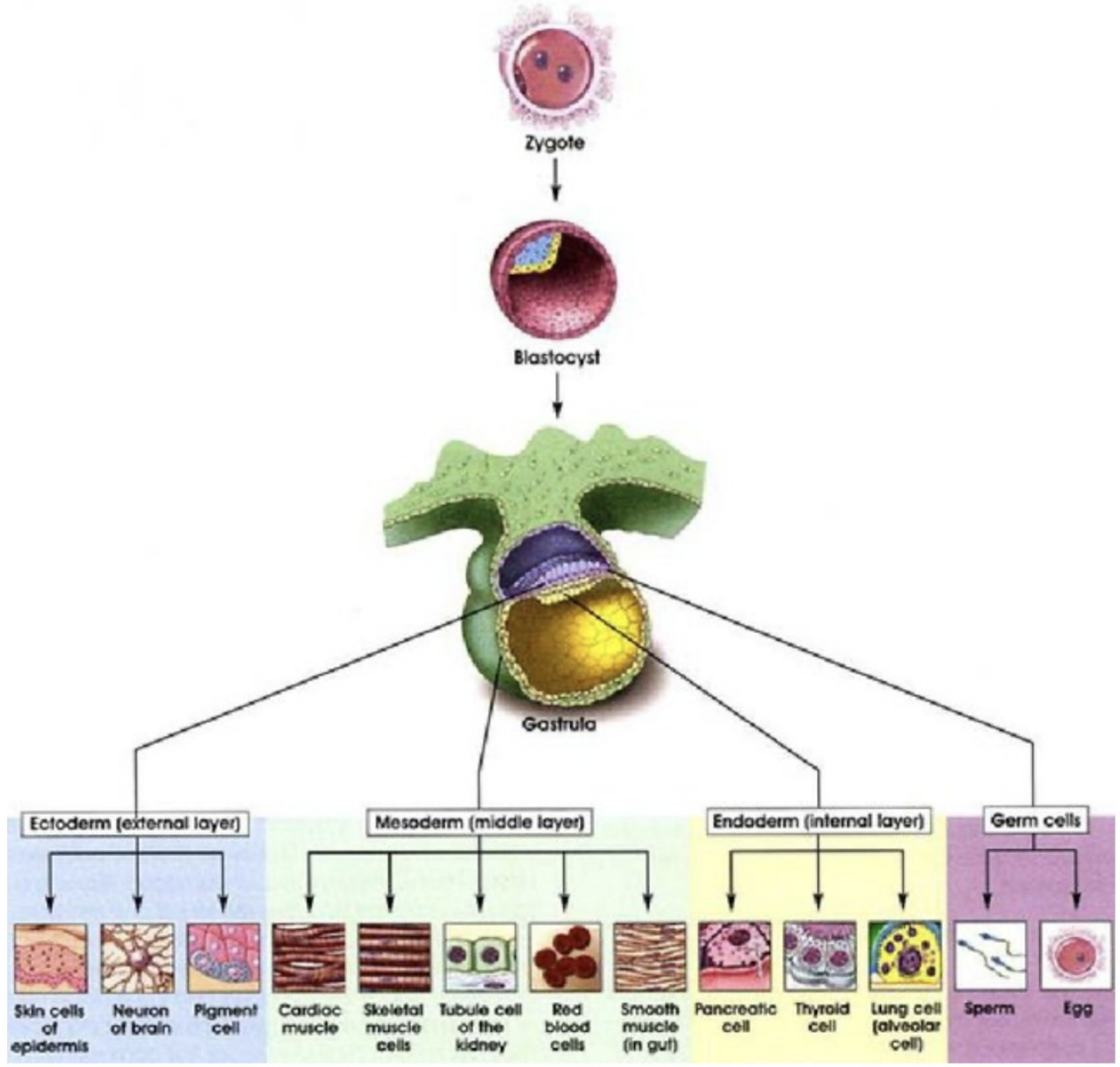
Mesoderm

- Notochord
- Skeletal system
- Muscular layer of stomach and intestine
- Excretory system
- Circulatory and lymphatic systems
- Reproductive system (except germ cells)
- Dermis of skin
- Lining of body cavity
- Adrenal cortex

Endoderm

- Epithelial lining of digestive tract
- Epithelial lining of respiratory system
- Lining of urethra, urinary bladder, and reproductive system
- Liver
- Pancreas
- Thymus
- Thyroid and parathyroid glands

Jack Westin



CANCER STEM CELLS

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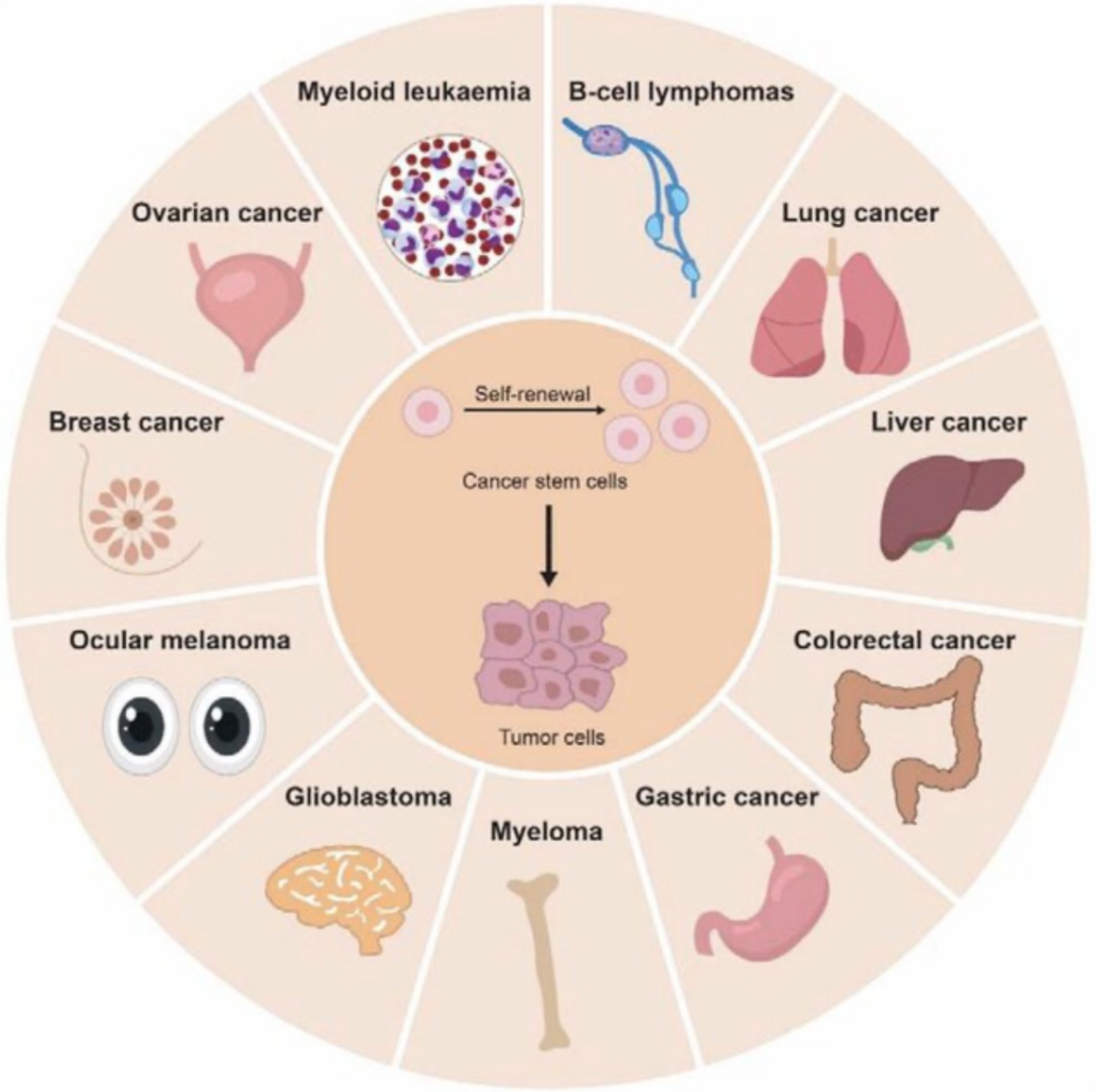

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Cancer Pleomorphism

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MODERN PATHOLOGY

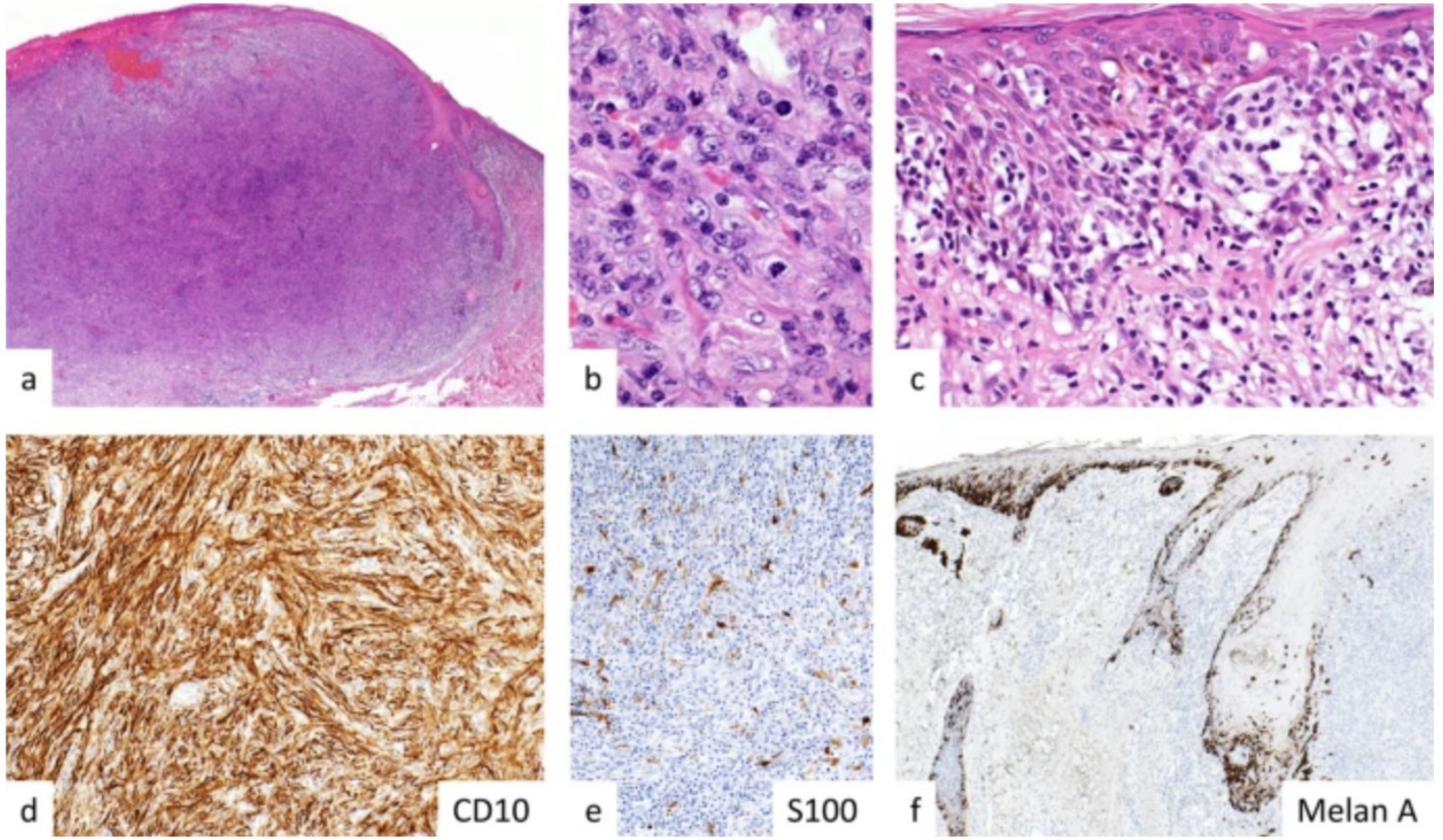
Article | Published: 21 June 2021

The clinicopathologic spectrum and genomic landscape of de-/trans-differentiated melanoma

Ingrid Ferreira, Alastair Droop, Olivia Edwards, Kim Wong, Victoria Harle, Omar Habeeb, Deepa Gharpuray-Pandit, Joseph Houghton, Katharina Wiedemeyer, Thomas Mentzel, Steven D. Billings, Jennifer S. Ko, Laszlo Füzesi, Kathleen Mulholland, Ivana Kuzmic Prusac, Bernadette Liegl-Atzwanger, Nicolas de Saint Aubain, Helen Caldwell, Laura Riva, Louise van der Weyden, Mark J. Arends, Thomas Brenn ✉ & David J. Adams

Modern Pathology **34**, 2009–2019 (2021) | Cite this article

Fig. 1: Dedifferentiated melanoma.



This ulcerated tumor shows a nodular growth pattern within the dermis (**a**). It is composed of sheets of pleomorphic epithelioid cells with brisk mitotic activity (**b**). The adjacent epidermis shows melanoma in situ (**c**). The invasive tumor expresses CD10 (**d**) but it is negative for S-100 protein (**e**) and Melan-A (**f**). Melan-A staining also highlights the background of melanoma in situ (**f**).

Fig. 2: Melanoma with rhabdomyosarcomatous transdifferentiation.

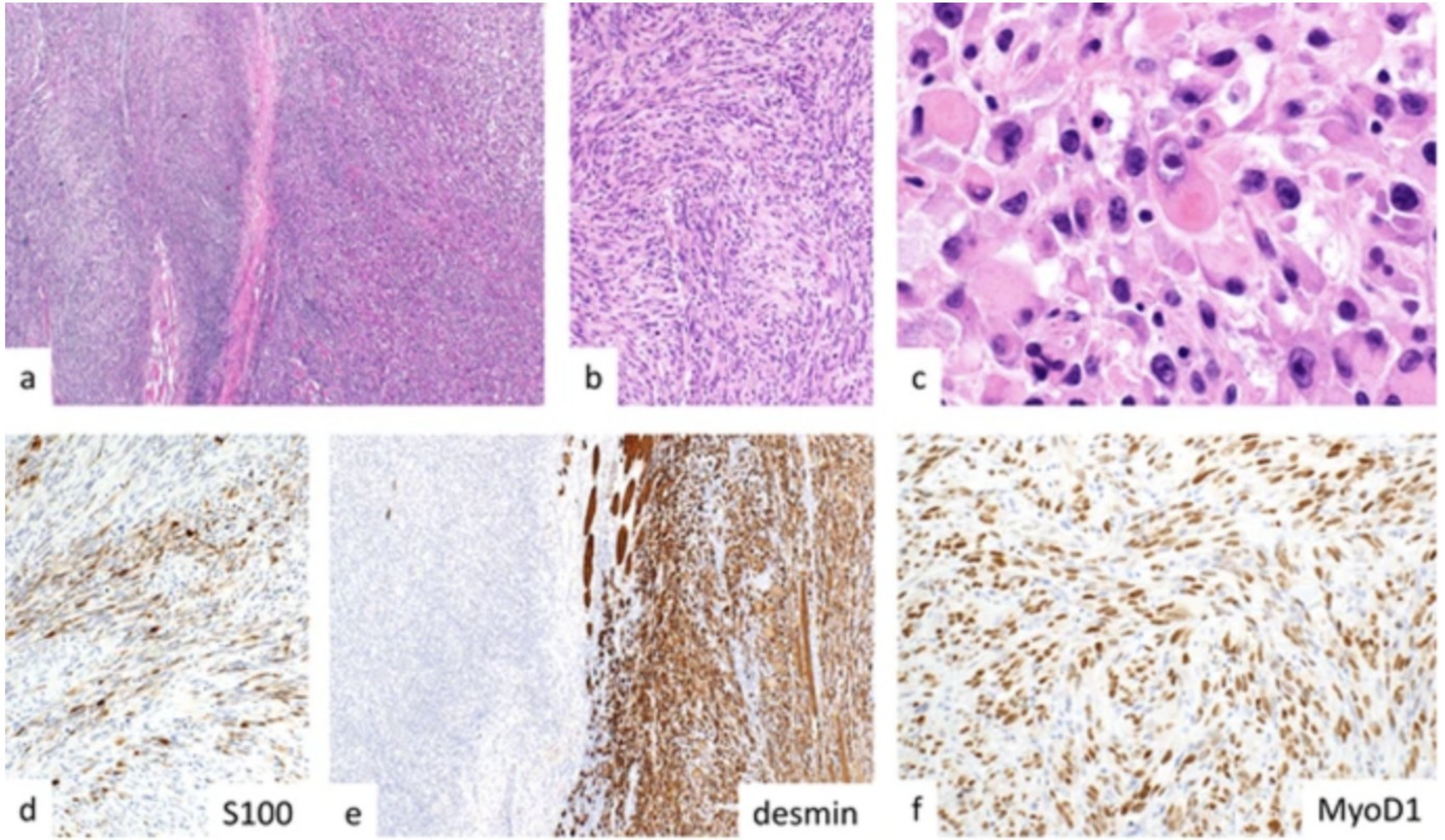
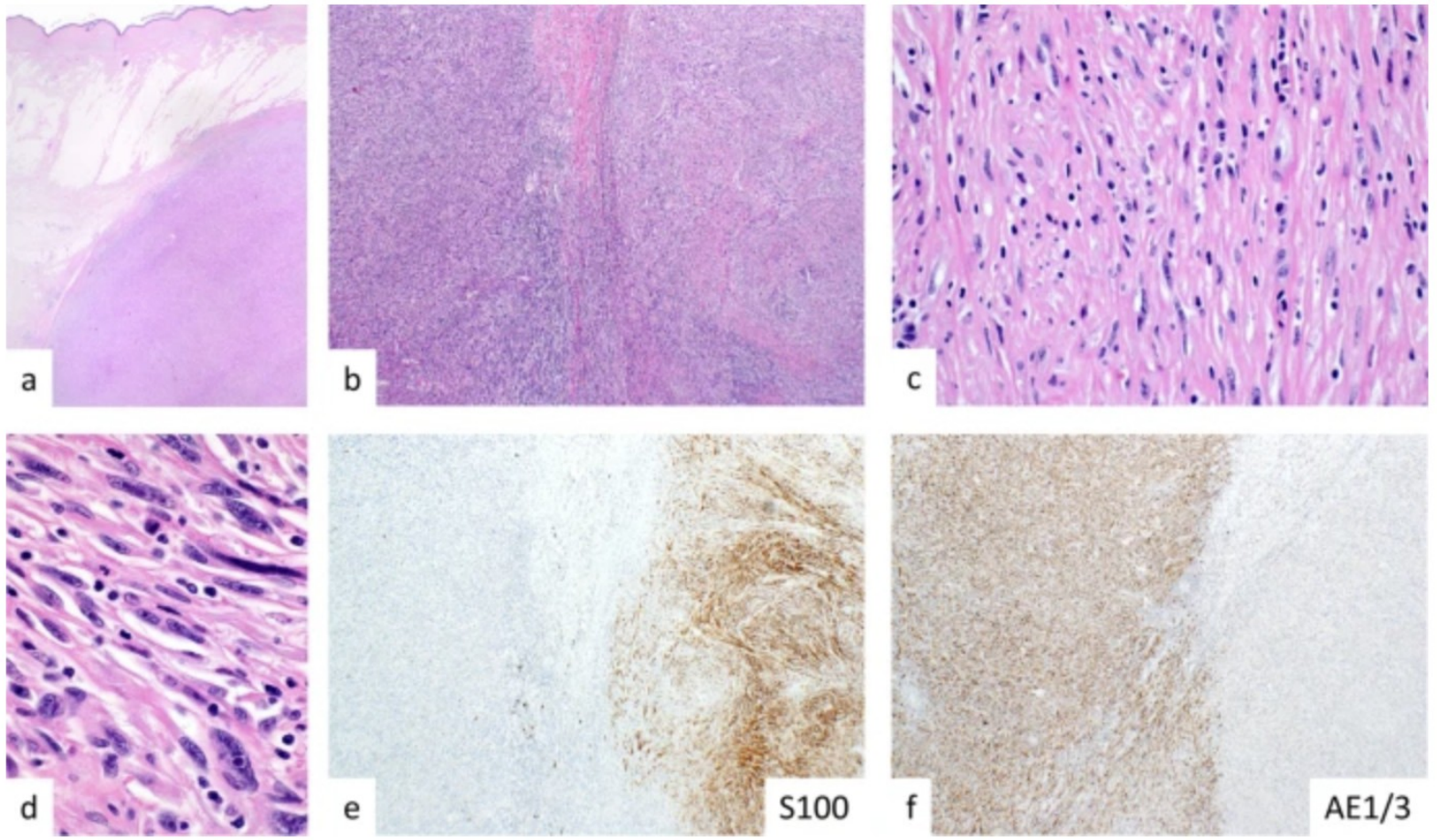


Fig. 3: Melanoma with epithelial transdifferentiation.



This large tumor invades subcutis and into the underlying fascia (**a**). It is composed of two morphologically distinct components (**b**) characterized by a spindle cell tumor in a desmoplastic stroma to the right (**c**) and a pleomorphic spindle cell tumor to the left (**d**). The desmoplastic spindle cell tumor expresses S-100 protein (**e**) and is negative for cytokeratin AE1/AE3 (**f**). In contrast, the pleomorphic component lacks S-100 protein expression (**e**) but is strongly and diffusely positive for cytokeratin AE1/AE3 (**f**).

OTHER EXAMPLES

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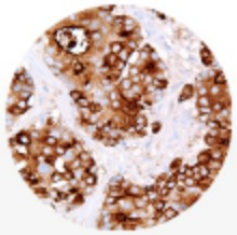
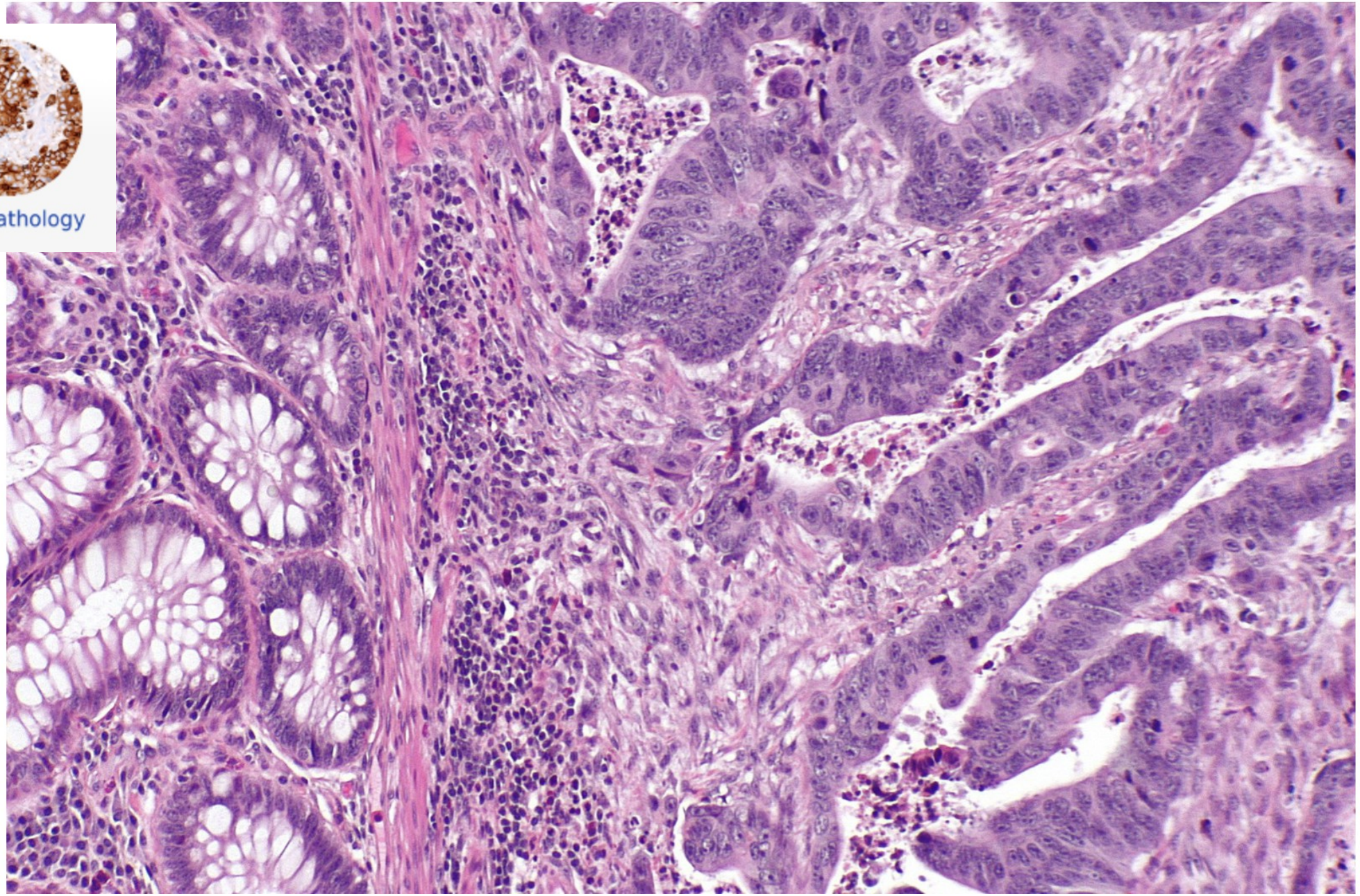


Libre Pathology



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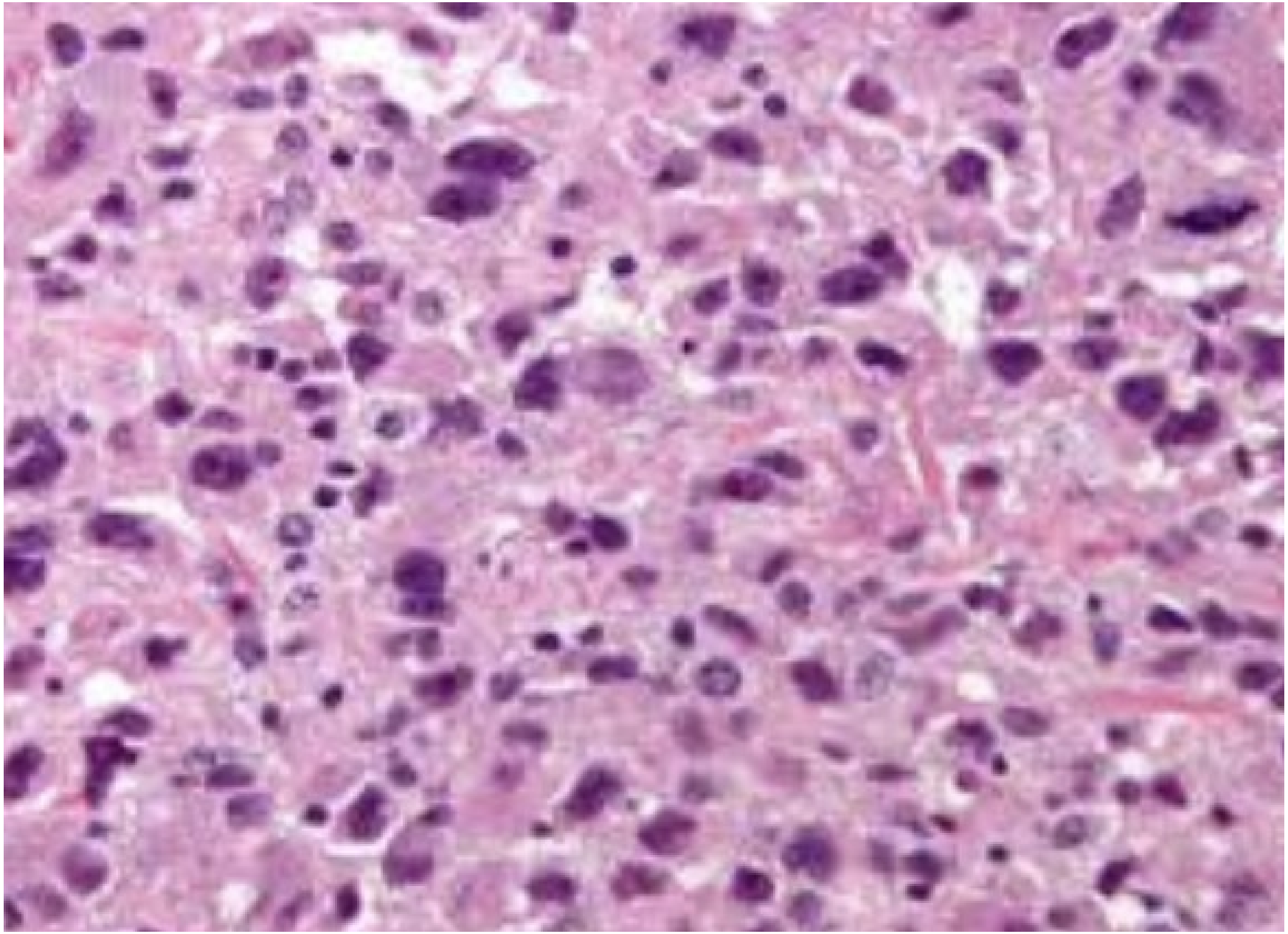

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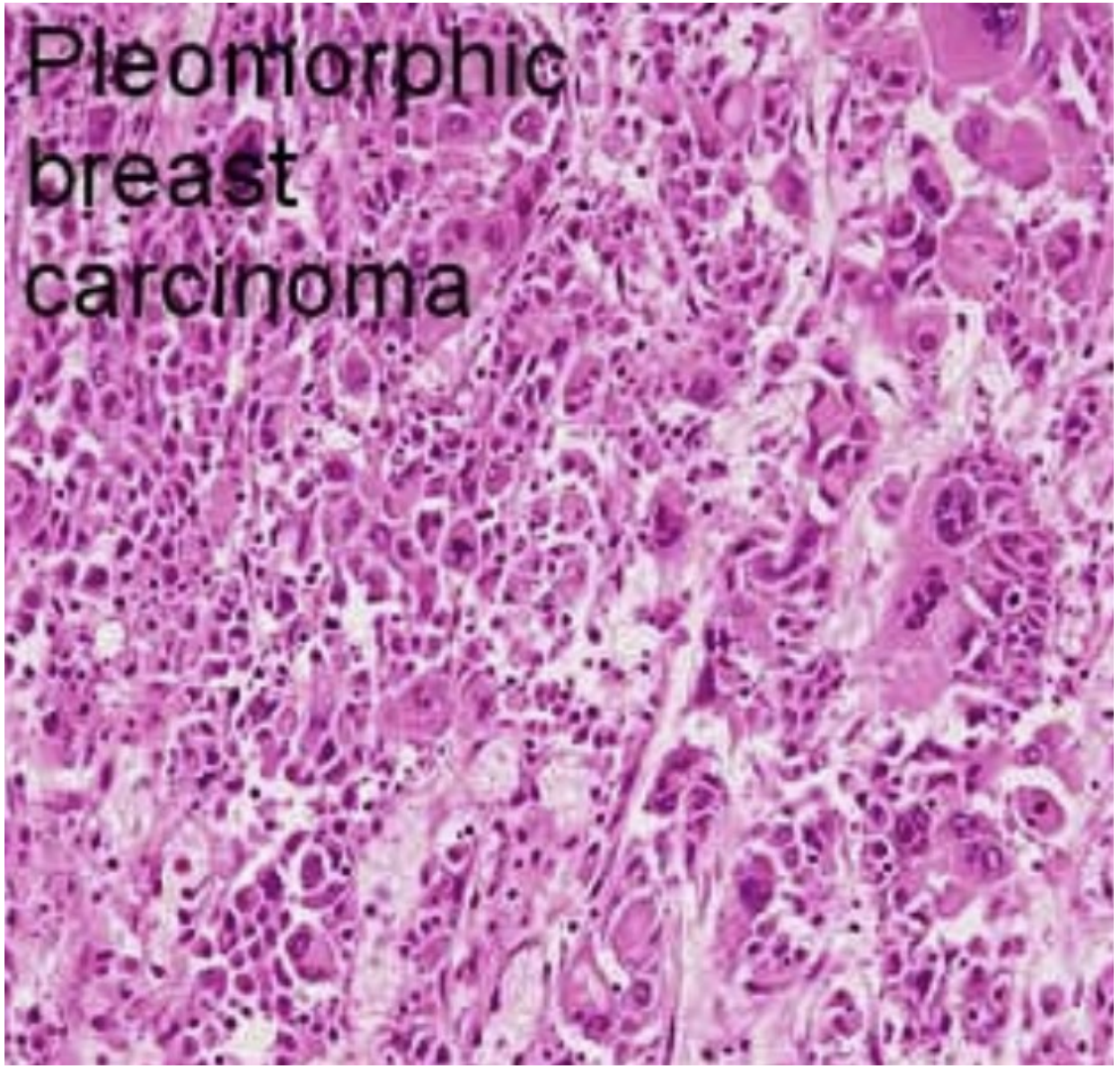
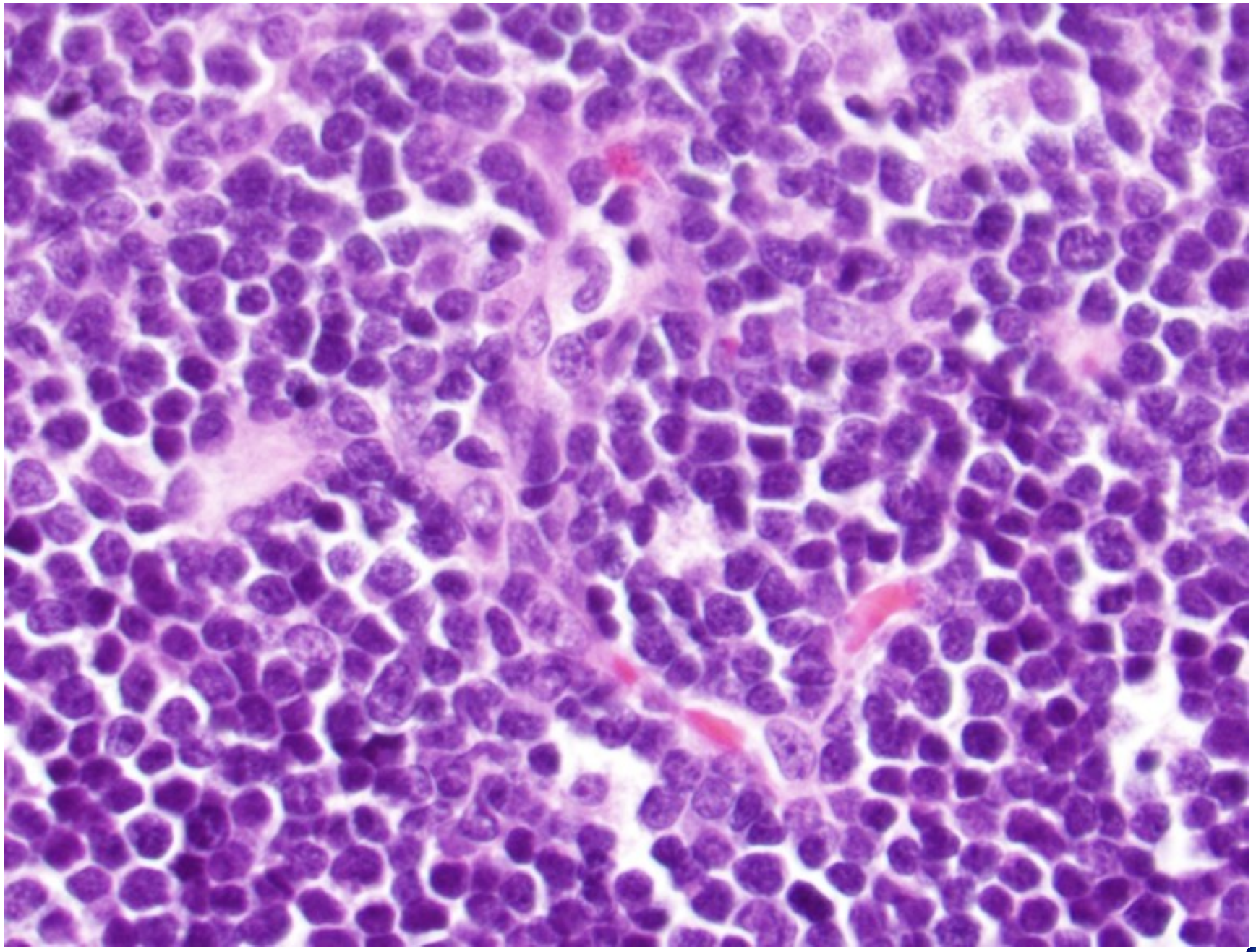
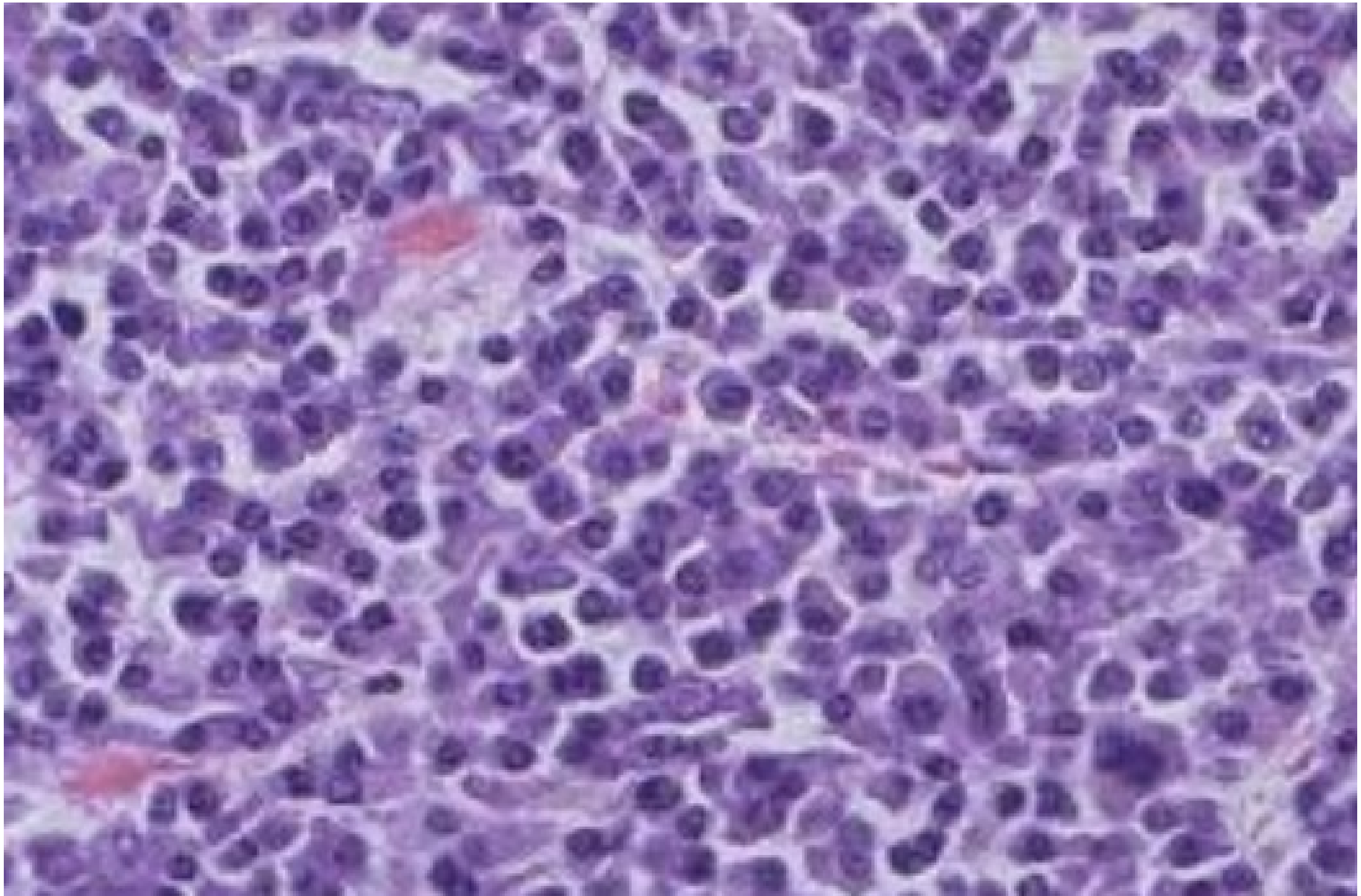


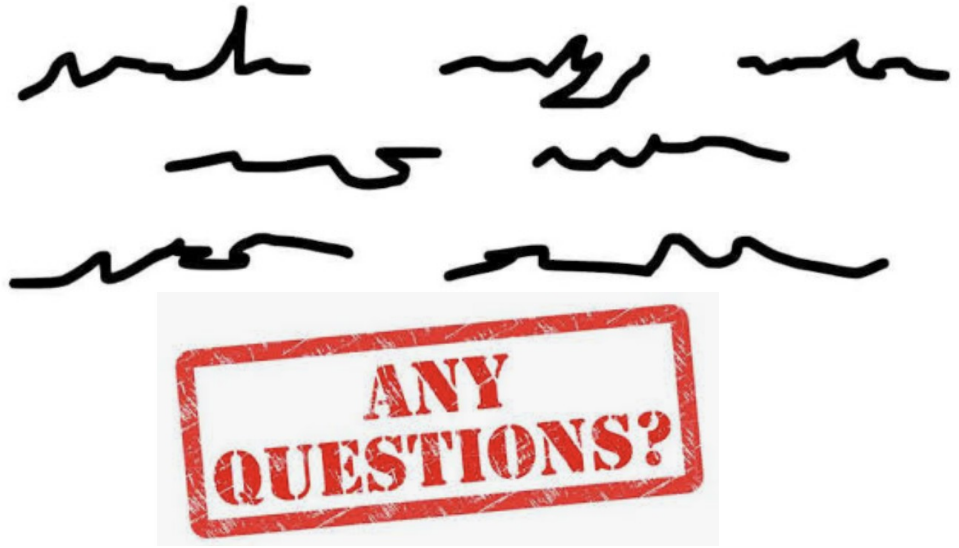
MONOMORPHIC TUMORS





- 8 billion humans
- 3 embryologic tissues
- 79 Organs (22 internal)
- Cells in the body approximately 28-36 trillion?
- Potential number of cancers?
- Text book Over 200 hundred
- Reality - Incalculable

A WISE DOCTOR ONCE WROTE



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Incidence of 17 cancers on the rise in younger generations!!!

- American Cancer Society analyzed data from 23 million people born between 1920 and 1990, 34 common types of cancer between 2000 and 2019.
- Attributed to obesity, insulin resistance, lack of exercise, and processed foods
- What's going on since 2019?

The Lancet Public Health: Volume 9, Issue 8E583-E593 August

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Personal Empirical Evidence of Hematological and Oncological Events in Association with Recent COVID-19 Vaccination

- Immediately - acute vascular events
- Then - unusual benign hematological processes
- Then - variety of unusual hematological malignancies
- Now - solid tumors on rise with change in patterns
  - Latent relapses after many year
  - Aggressive relapses
  - Unusual presentations of solid tumors
  - Younger onset of cancer
- Now over 1000 case reports in the literature

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Elephant in the Room

- **Are these COVID “vaccines” causing cancer???**

- It appears so…
  - As per published case studies and epidemiology reports (VAERS, CDC, MCR/MCD, States, Institutions, International, Insurance actuarials)

- But this is VERY complicated to discern
  - Epidemiological complexities

- Correlation does not imply Causation
  - Bradford Hill Criteria (temporality, analogy, consistency, plausibility, coherence, specificity, biological gradient, experimental evidence)

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Mechanisms of Carcinogenesis

- Metabolic
- Genetic (Germline and Somatic)
- Immune dysregulation
- Hormonal
- Inflammation/Autoimmune
- Infectious disease
- Exposures
- Diet
- Medications

Putative COVID vaccine causes of cancer

- T cell dysregulation, CD4 & CD8 downregulation
  - “T-cell exhaustion”
  - Loss of immune surveillance and control
- IgG switch to IgG4
- Amplification of Inflammatory cytokines – Toll-like receptors (TLRs)
- Interaction with p53, BRCA1/2
- SV40 DNA and other DNA contamination
- modmRNA reverse transcription
- Antigenic mimicry, autoimmunity
- Ribosomal frame shifting – nonsense proteins, prions
- **NGS testing archives may give a clue...**

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SARS-CoV-2 Vaccination and the Multi-Hit Hypothesis of Oncogenesis

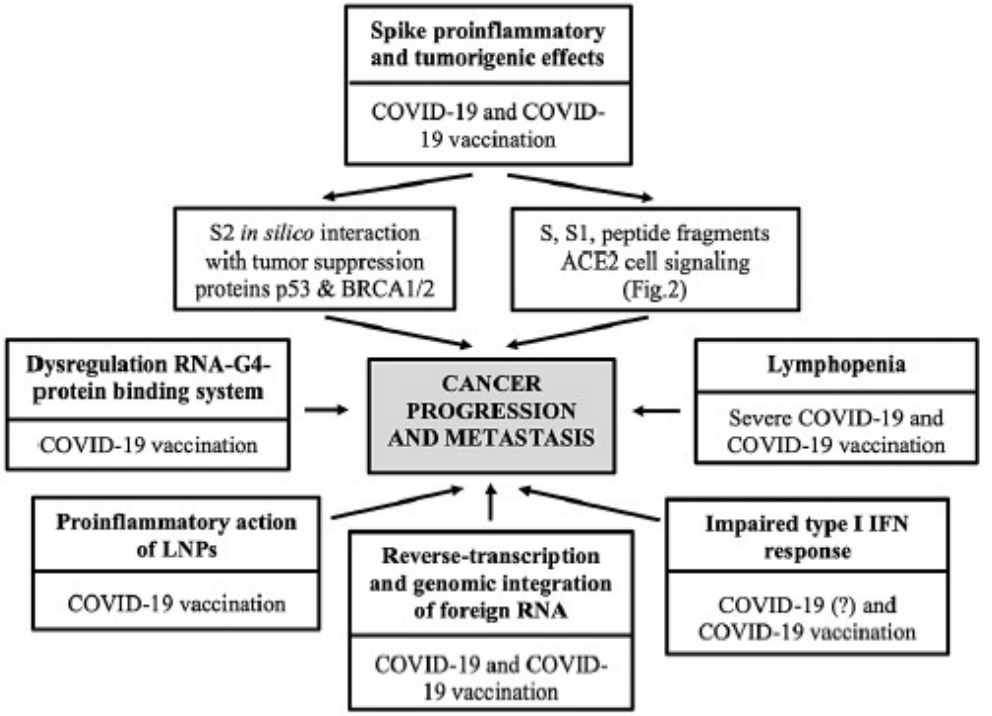

FIGURE 1: Cancer-promoting molecular mechanisms and pathways potentially mediated by SARS-CoV-2 and/or certain COVID-19 vaccines

SARS-CoV-2: severe acute respiratory syndrome coronavirus 2, COVID-19: coronavirus 2019, BRCA1/2: breast cancer 1/2, ACE2: angiotensin-converting enzyme 2, LNPs: lipid nanoparticles, RNA: ribonucleic acid, IFN: interferon

2023 Valdes Angues et al. Cureus 15(12): e50703. DOI 10.7759/cureus.50703

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Transformation of Cancer Therapeutics (old)

- Radical Surgery
- High dose radiation therapy
- Maximum dose combination chemotherapy
- Hormone removal/blockade
- Ablative chemo with autologous STEM cell transplant

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Transformation of Cancer Therapeutics (new)

- Minimally Invasive Surgery
- Stereotactic radiation therapy, Radiopharmaceuticals
- Monoclonal Antibody Targeted therapy
- Molecularly Targeted Therapy
- Better Hormonal Therapies
- Antibody Drug Conjugates – ADC
- Immunotherapy – Checkpoint inhibitors, CTLA4
- BiTE therapy (Bispecific T-cell engager)
- CAR T Cell therapy (Chimeric Antigen Receptor)

Final thoughts going forward

- You need to take great scrutiny with EVERYTHING you put in your body! EVERYTHING! That includes:
  - Chemotherapy drugs
  - **Any** drug with FDA approval
  - **Any** repurposed drug with off-label use
  - **Any** beverages
  - **Any** foods
  - **All** health and nutrition products
  - Vaccinations
- Do not ever take any modified gene product pushed as a vaccination or prevention of ANY infection or disease!!!

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Find a doctor you can trust

- Public trust in physicians and hospitals plummeted
  - 71.5% in April 2020 to 40.1% in January 2024
  - 50-state survey of U.S. adults led by Northeastern University
- Physicians have lost patient trust
  - Pandemic cemented that
  - Nurses and pharmacists are more trusted.
- Develop a relationship with a physician you trust!

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CANCER CARE

THE ROLE OF REPURPOSED DRUGS
AND METABOLIC INTERVENTIONS
IN TREATING CANCER

2ND EDITION

Paul E. Marik, MD, FCCM, FCCP

FOCUS ON THE CANCER STEM CELL

The Current Cancer Epidemic!

Year	New Cases	DEATHS/year	DEATHS/day
2013	1,660,290	580,350	1,590
2014	1,665,540	585,720	1,605
2015	1,658,370	589,430	1,615
2016	1,665,210	595,690	1,632
2017	1,688,780	600,920	1,646
2018	1,743,350	609,640	1,670
2019	1,762,450	606,880	1,663
2020	1,806,590	606,520	1,662
2021	1,898,160	608,570	1,667
2022	1,918,030	609,360	1,670
2023	1,958,310	609,820	1,671
2024	2,001,140	611,720	1,676
Increase	17.0%	5.1%	5.1%

Data from American cancer society

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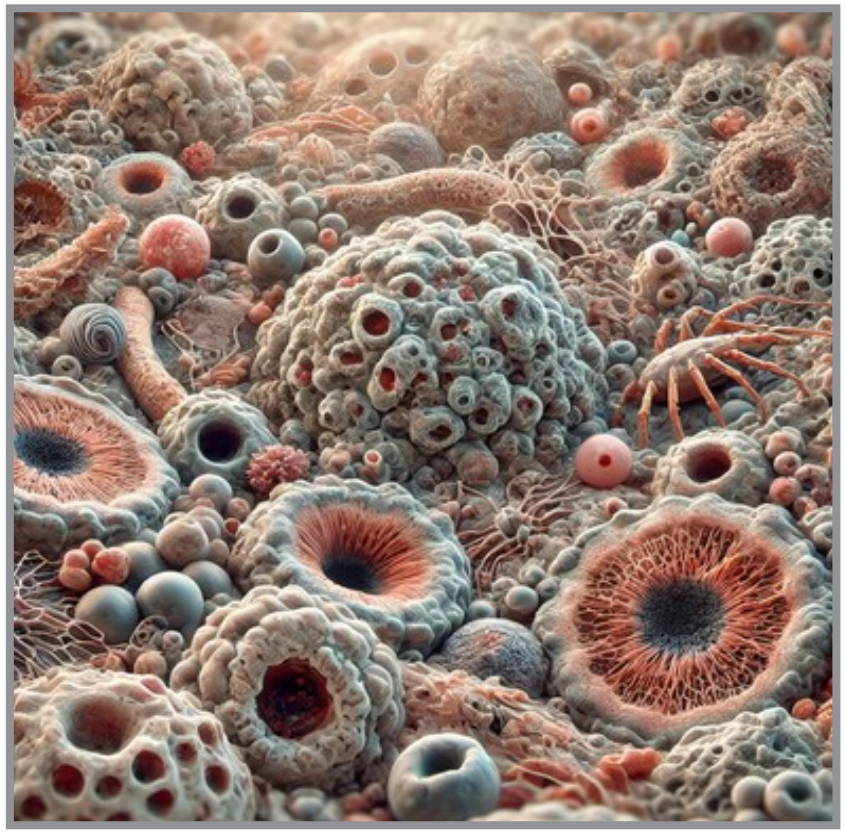
Somatic Mutation Theory?



WRONG!

Cancer is a heterogeneous mass of diverse cells with genetic and phenotypic diversity.

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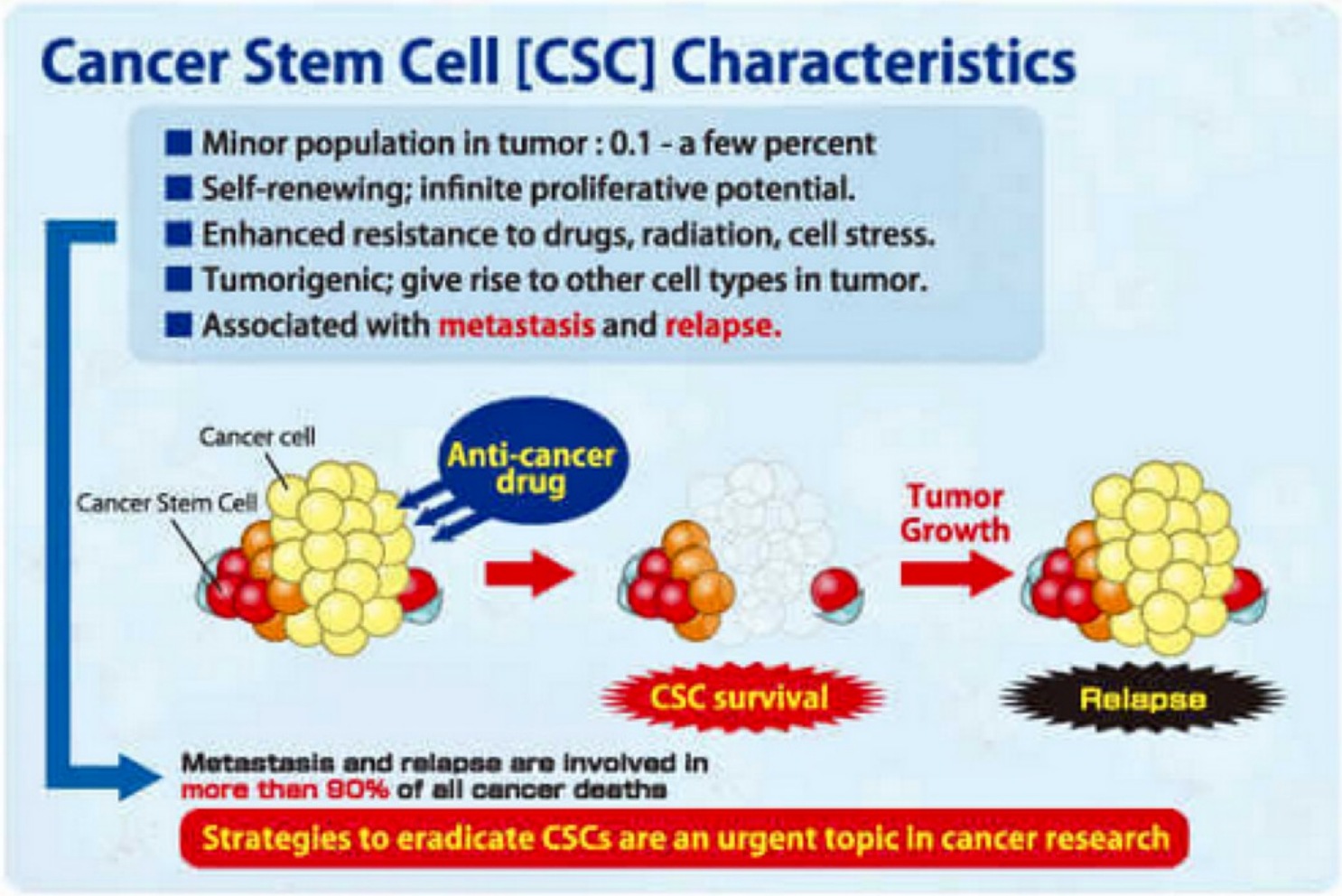
Cancer Stem Cells



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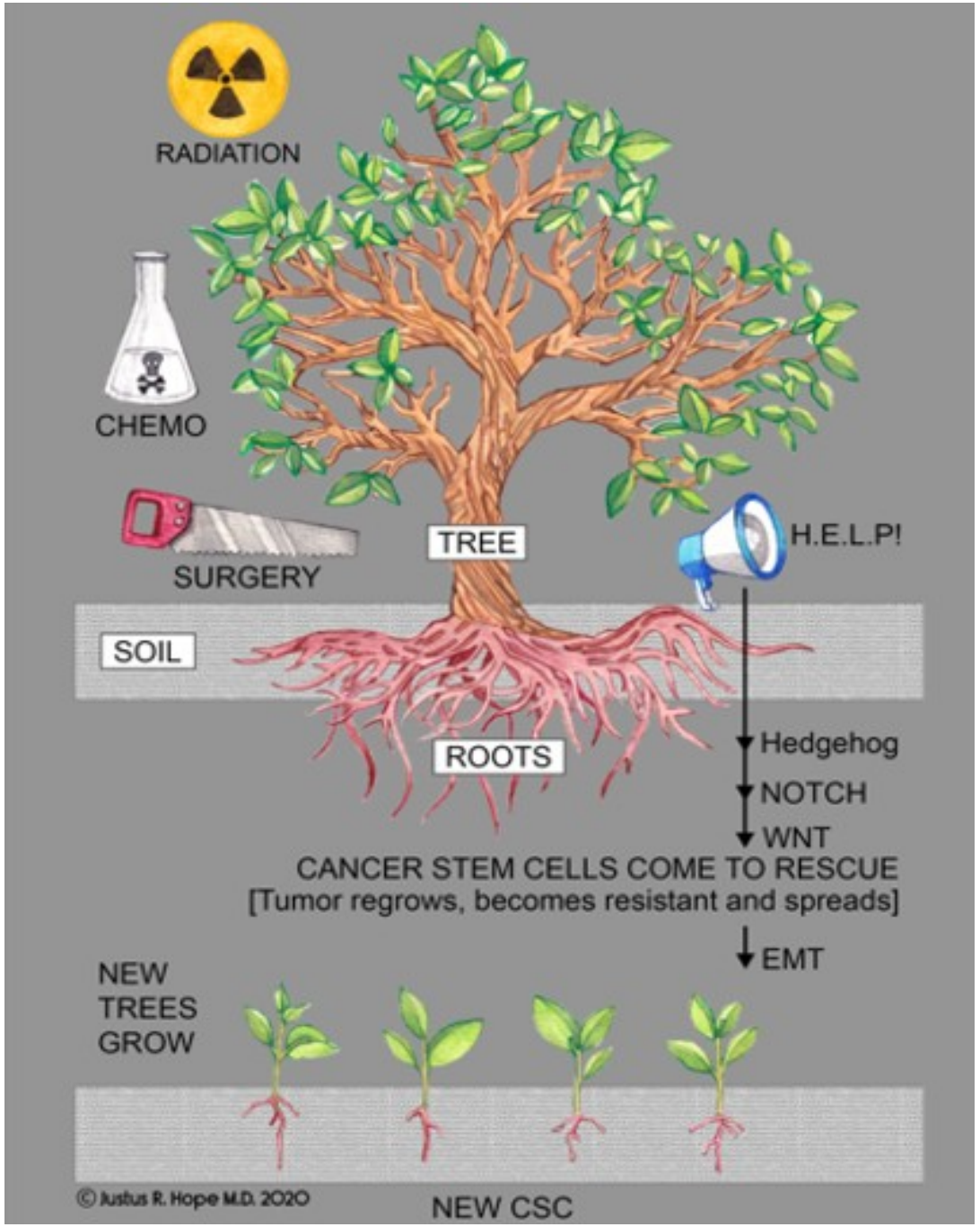
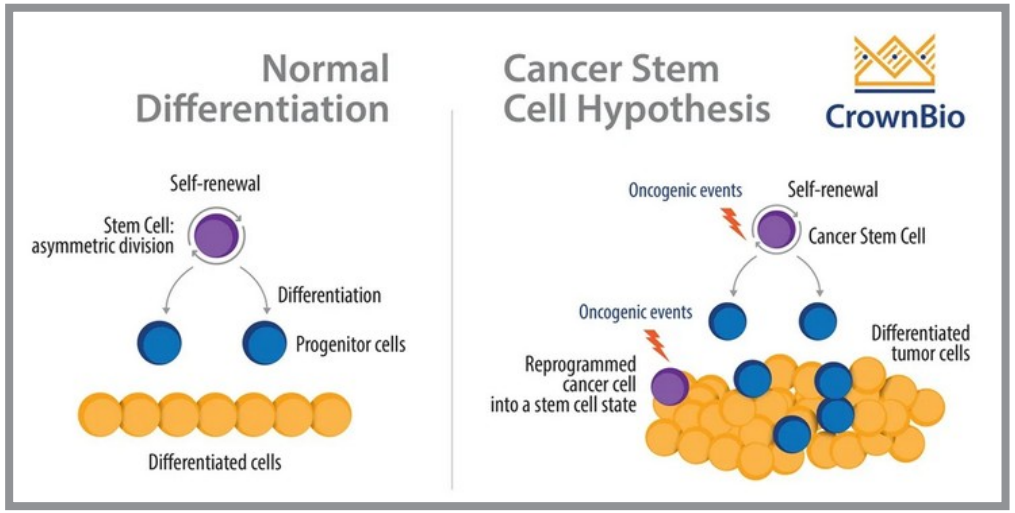


Cancer Stem Cells

Nat Rev Clin Oncol. 2015 August ; 12(8): 445–464. doi:10.1038/nrclinonc.2015.61.

Targeting Notch, Hedgehog, and Wnt pathways in cancer stem cells: clinical update

Numerous researchers hypothesize that treatments targeting the CSC population could be more effective than existing therapies, and could dramatically transform treatment outcomes in oncology



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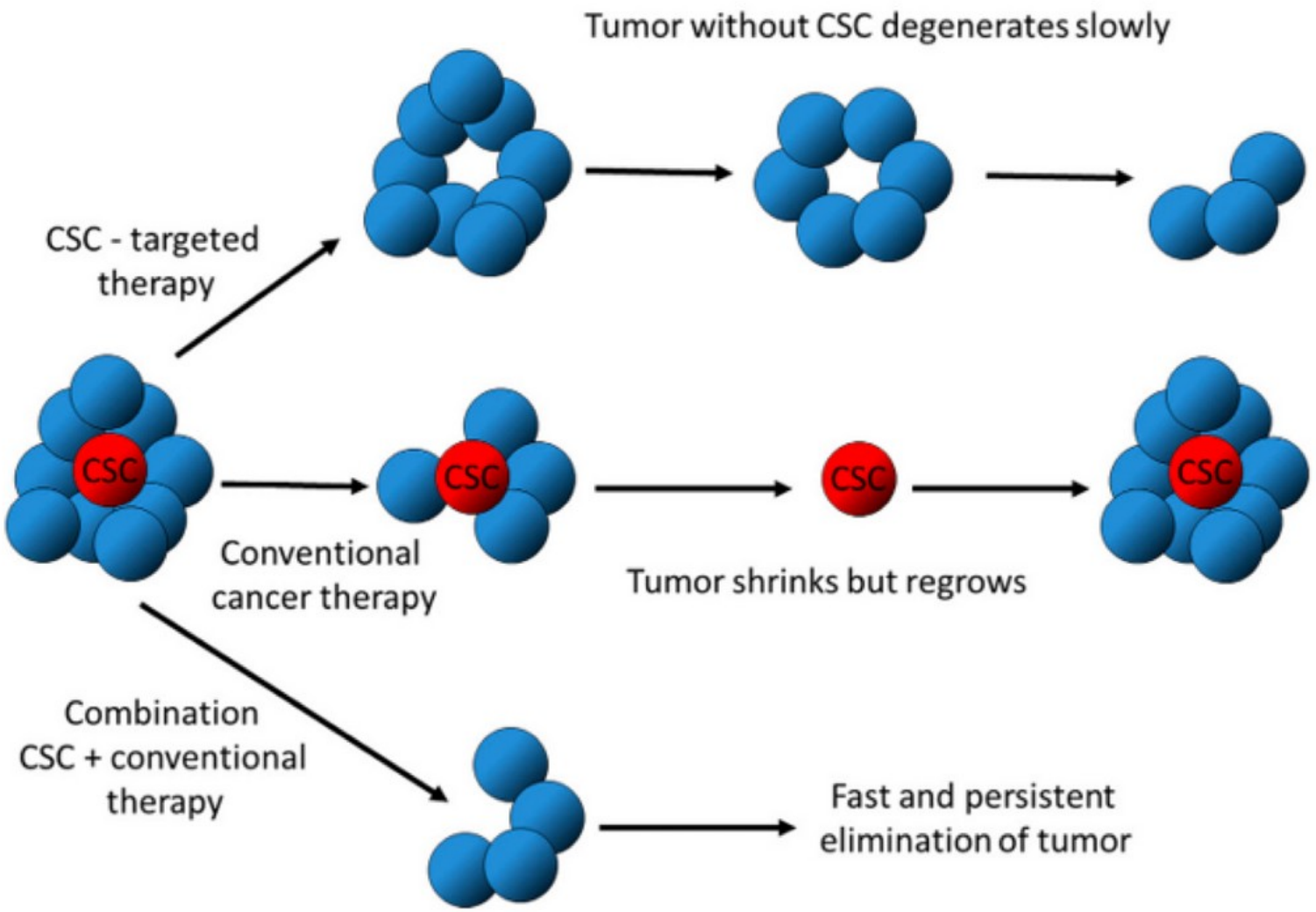
Cancer Stem Cells



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Top CSC Blocking Agents

Rank	Compound	Pathways Blocked (Strength of Evidence)	Safety
1	Ivermectin	Wnt, Hedgehog, Notch, NFκB, STAT3, P13K/Akt	Safe
2	Curcumin	Wnt, Hedgehog, Notch, NFκB, STAT3, TGF-beta	Safe
3	Sulforaphane	Wnt, Hedgehog, NFκB, STAT3	Safe
4	Doxycycline	Wnt, Hedgehog, Notch	Safe
5	EGCG	Wnt, STAT3, NFκB, Notch, P13K/Akt	Safe
6	Resveratrol	NFκB, STAT3, TGF-beta, P13K/Akt	Safe
7	Omega-3 (DHA)	STAT3, JAK-STAT, NFκB, Wnt	Extremely Safe
8	Mebendazole	Hedgehog	Safe
9	Metformin	P13K/Akt	Extremely Safe
10	Vitamin D	Notch, Hedgehog	Extremely Safe

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CSC Stimulation by Chemotherapy

Rank	Chemotherapeutic Agent	CSC Stimulation Level	Key Affected Pathways	Evidence Quality
1	5-Fluorouracil (5-FU)	Substantially stimulating	WNT/β-catenin, P13K/AKT, c-Yes/YAP	Strong
2	Paclitaxel	Moderately to substantially stimulating	Nrf2, EGFR, IL-6	Strong
3	Docetaxel	Moderately stimulating	Multiple pathways, similar to paclitaxel	Moderate
4	Oxaliplatin	Mildly to moderately stimulating	WNT, P13K/AKT (often with 5-FU)	Moderate
5	Gemcitabine	Mildly stimulating	Nrf2 pathway	Limited
6	Cisplatin	Mildly stimulating	Multiple pathways	Limited
7	Cabazitaxel	Mildly stimulating	Similar to other taxanes	Limited
8	Doxorubicin	Minimally to mildly stimulating	Multiple pathways	Limited

CSC Stimulation by Radiation Rx

Rank	Therapy	Full Name	CSC Stimulating Effect	Key Mechanisms
1	EBRT	External Beam Radiation Therapy	Highest	Induces EMT, promotes non-stem cancer cell conversion to CSCs, activates survival pathways
2	IMRT	Intensity-Modulated Radiation Therapy	High	Similar to EBRT but with more conformal dose distribution, still capable of inducing CSC phenotype
3	VMAT	Volumetric Modulated Arc Therapy	High	Arc-based version of IMRT with similar biological effects on CSC stimulation
4	APBI	Accelerated Partial Breast Irradiation	Moderate-High	Localized treatment with photon radiation that may still induce CSC phenotypes in treatment area
5	IGRT	Image-Guided Radiation Therapy	Moderate	Primarily improves targeting accuracy rather than altering biological effects
6	SBRT	Stereotactic Body Radiation Therapy	Moderate-Low	Higher ablative doses may reduce CSC stimulation compared to conventional fractionation
7	Proton Beam	Proton Beam Radiation Therapy	Low	Generate more ROS and DNA damage in CSCs, reduces CSC survival and self-renewal

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ONCOLOGY LETTERS 12: 3059-3065, 2016

Radiation induces the generation of cancer stem cells: A novel mechanism for cancer radioresistance (Review)

FENGSHENG LI[1*], KUNMING ZHOU[1*], LING GAO[2], BIN ZHANG[3], WEI LI[1], WEIJUAN YAN[1], XIUJUN SONG[1], HUIJIE YU[1], SINIAN WANG[1], NAN YU[1] and QISHENG JIANG[1]

[1]Central Laboratories, The Second Artillery General Hospital; [2]Key Laboratory of Radiological Protection and Nuclear Emergency, National Institute for Radiological Protection, China Center for Disease Control and Prevention; [3]Department of Colorectal Disease Surgery, The Second Artillery General Hospital, Beijing 100088, P.R. China

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All patients with cancer MUST be treated with a cancer stem cell agent

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