# PROSTATE CANCER

# TOPICS

# 10-14-2019

**October 14, 2019 Meeting**

**Larry Isely**

The Classic website → **www.prostatecancertopics.com**

Mobile website → **www.prostatecancertopics.com/m**

**info@prostatecancertopics.com** ← Email

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# PROSTATE CANCER TOPICS 10-14-2019

## Survival Optimization – Improving Your Odds

- When is it time to add to or change members of my medical team?
- How do I select the right tools for my case and select physicians who use these tools like craftsman?
- How do I choose among the many treatments available today?
- What do I need to know in order to improve the likelihood of achieving a durable remission?
- Do I need to read research papers to gain better insight into my conversations with my medical team?
- Exactly how does prostate cancer grow and why do I need to know some basics of cellular biology ?

"Significant" Tumor Growth Suppression

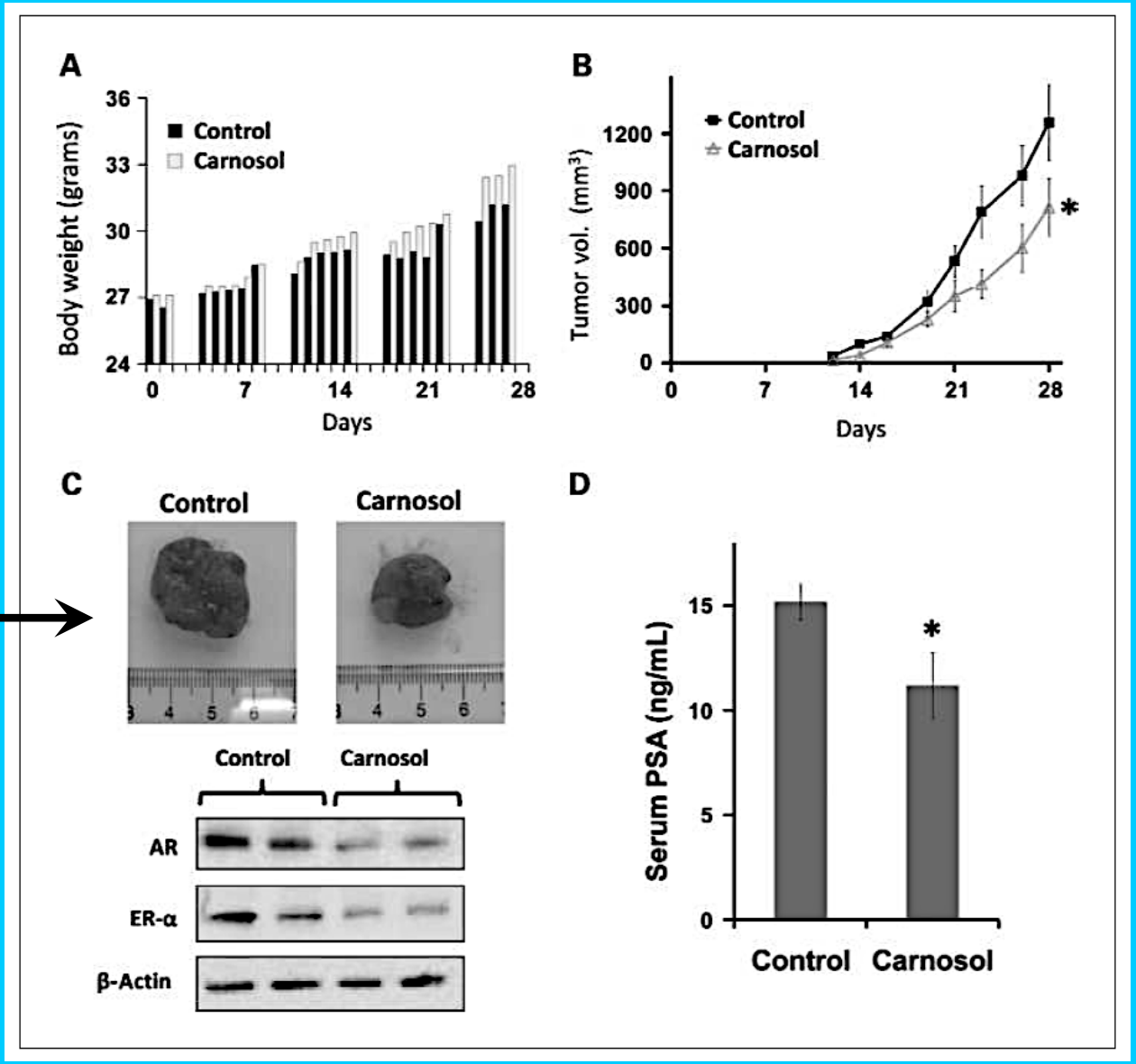
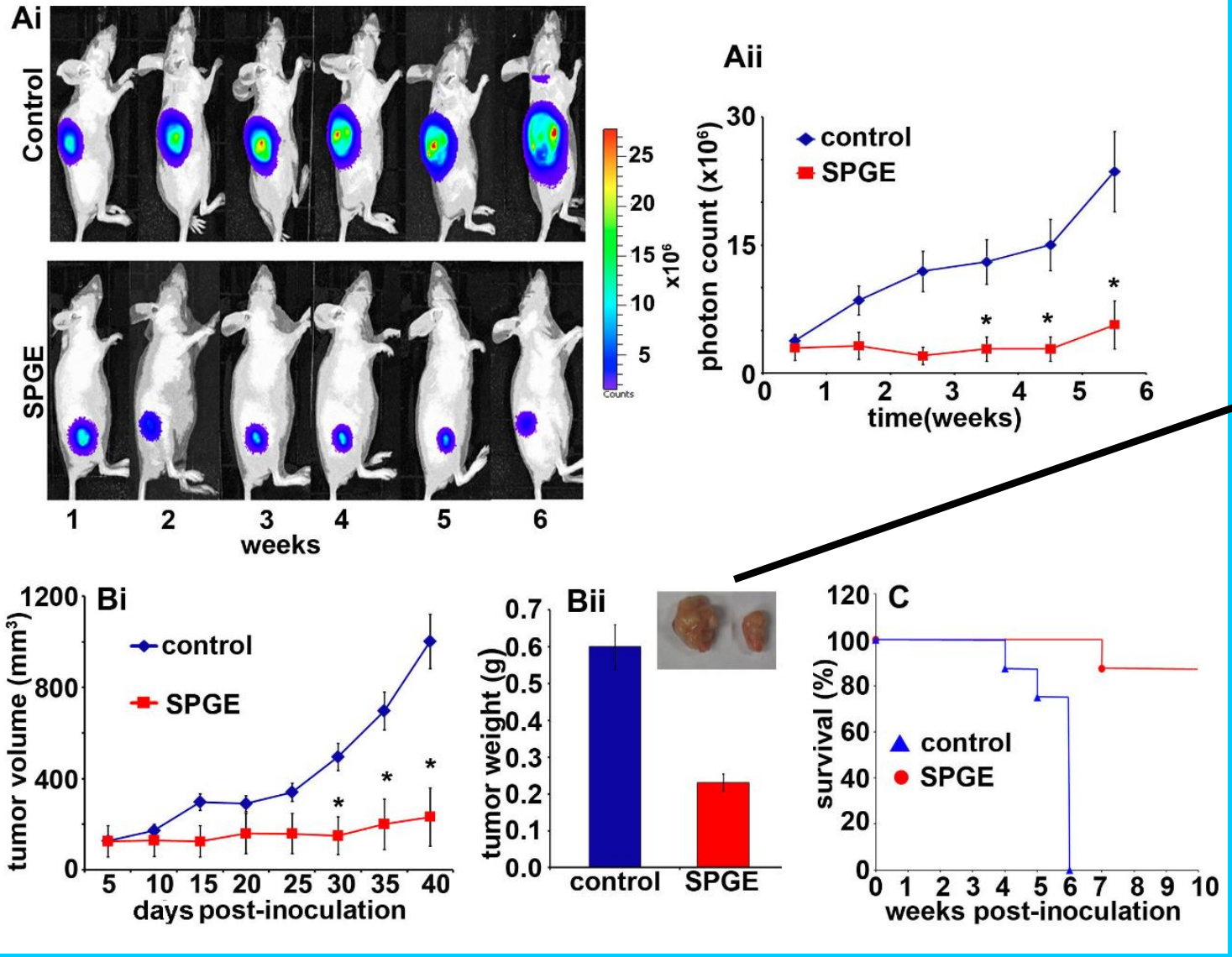


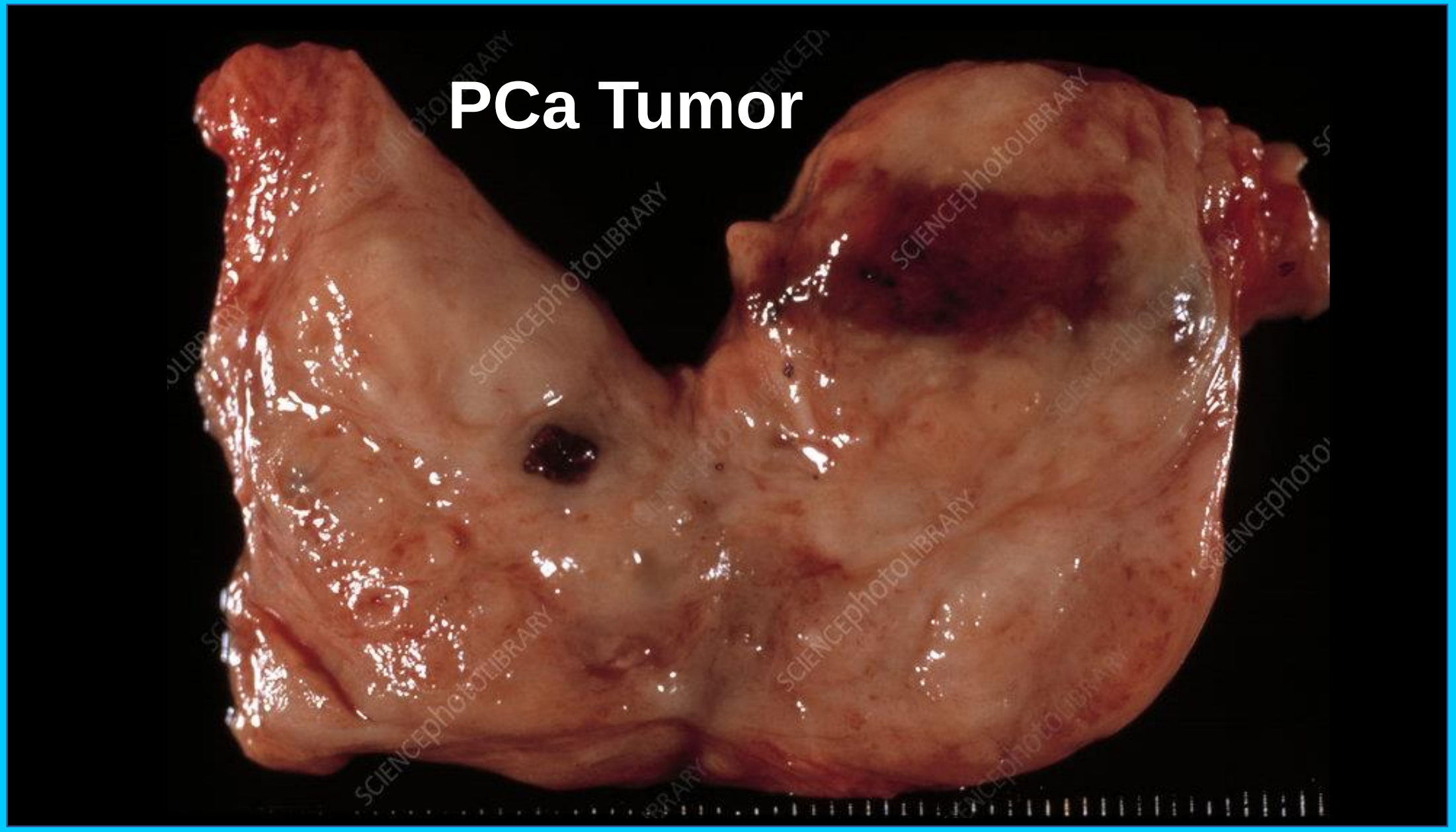
Figure 5 (Karna et al.)



"Highly Significant" Tumor Growth Suppression

**Carcinogenesis** Ritu Aneja **September 26, 2011**

# PCa Tumor



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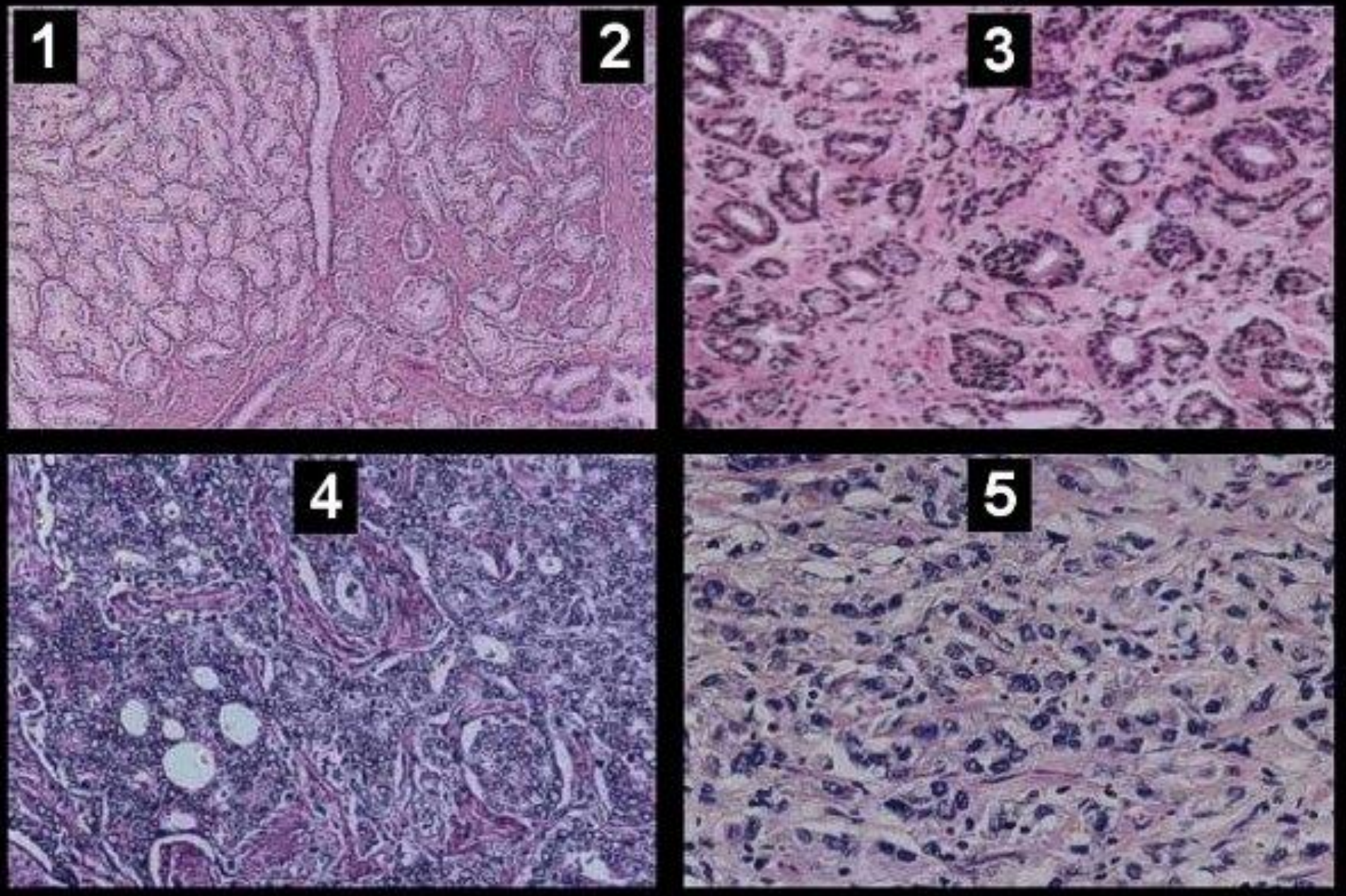
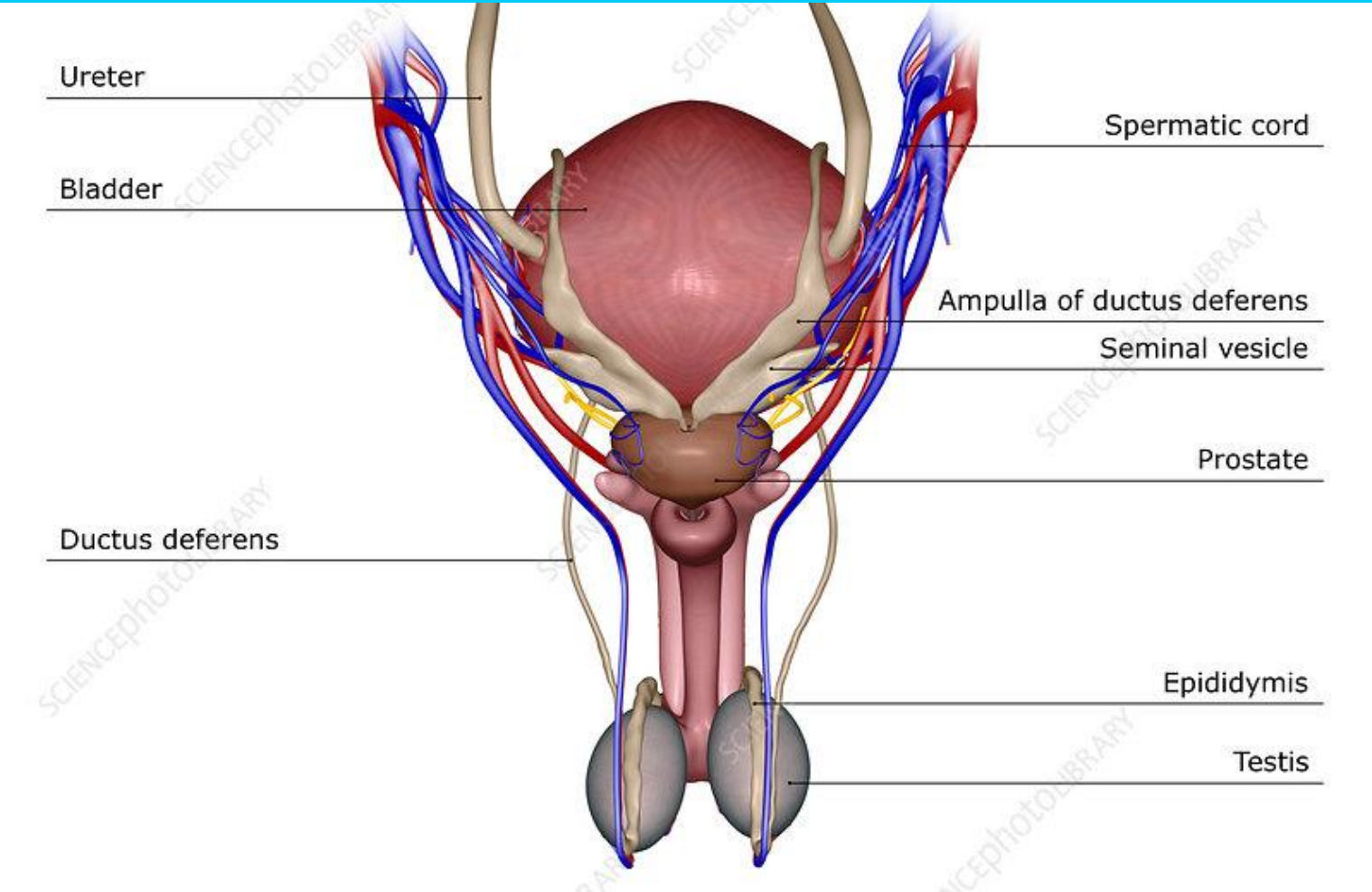
# Gleason Grades 1 through 5



# Some Basic Cellular Biology

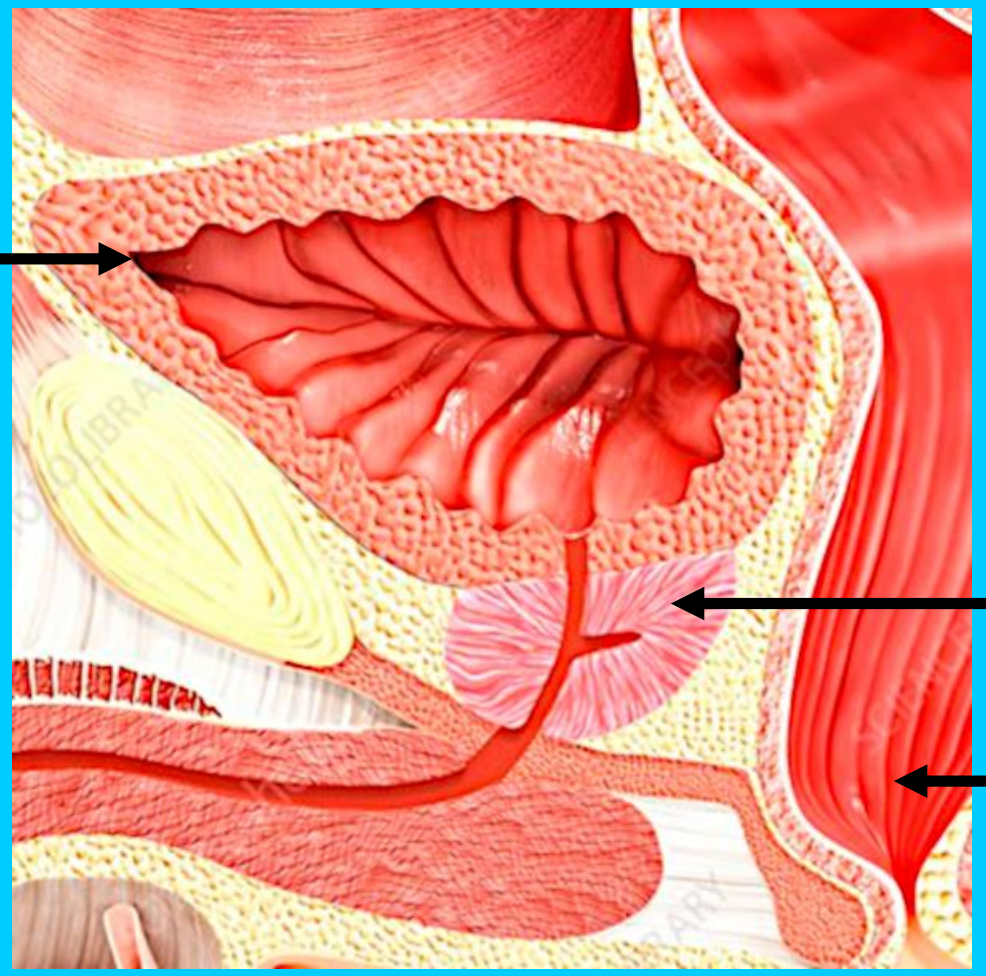
- Where are the Prostate Gland, the Seminal Vesicles and the Bladder?




Credits: SciencePhotoLibrary

# Some Basic Cellular Biology

- Where are the Prostate Gland, the Bladder and the Rectum?



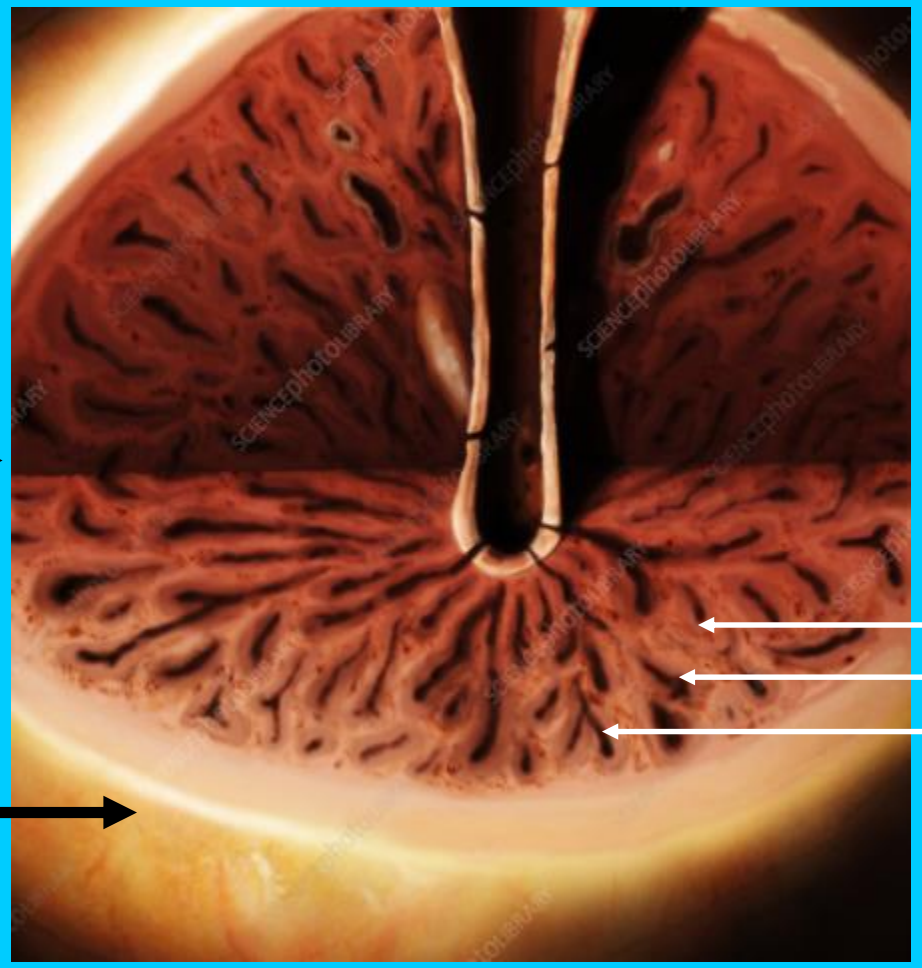

Credits:
SciencePhotoLibrary

# Some Basic Cellular Biology

- What is the Prostate Gland and what are prostate glands?

**Prostate Gland**

**“capsule”**



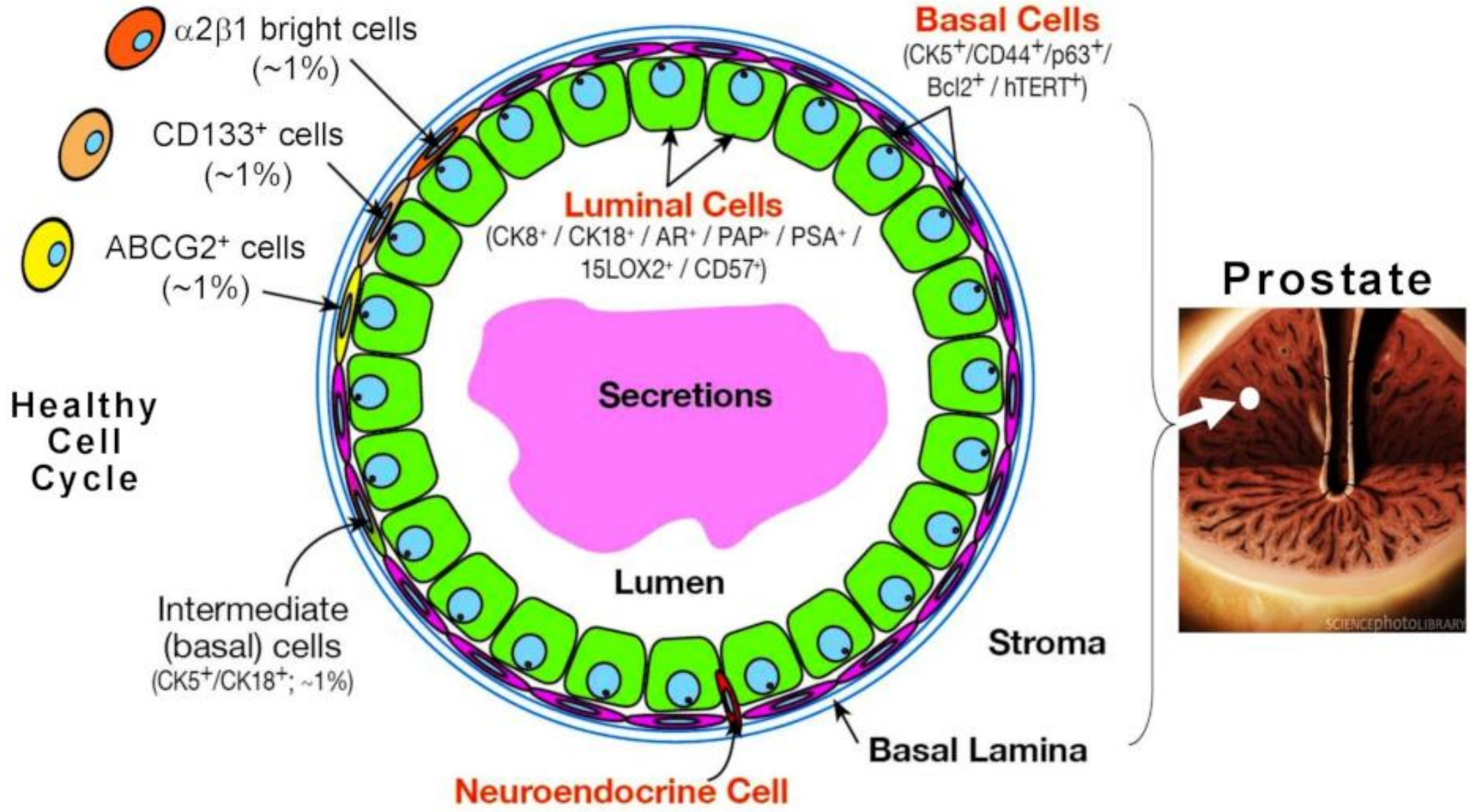
Two-thirds of the prostate is glandular while the remaining third is fibromuscular.

Prostatic secretions help prevent infection in the urethra, energize sperm and keep the urethral lining moist.

**prostate glands**

Credits: SciencePhotoLibrary

Honorio et al., Figure 1 - Cartoon showing the general structure of a human prostatic gland.



# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

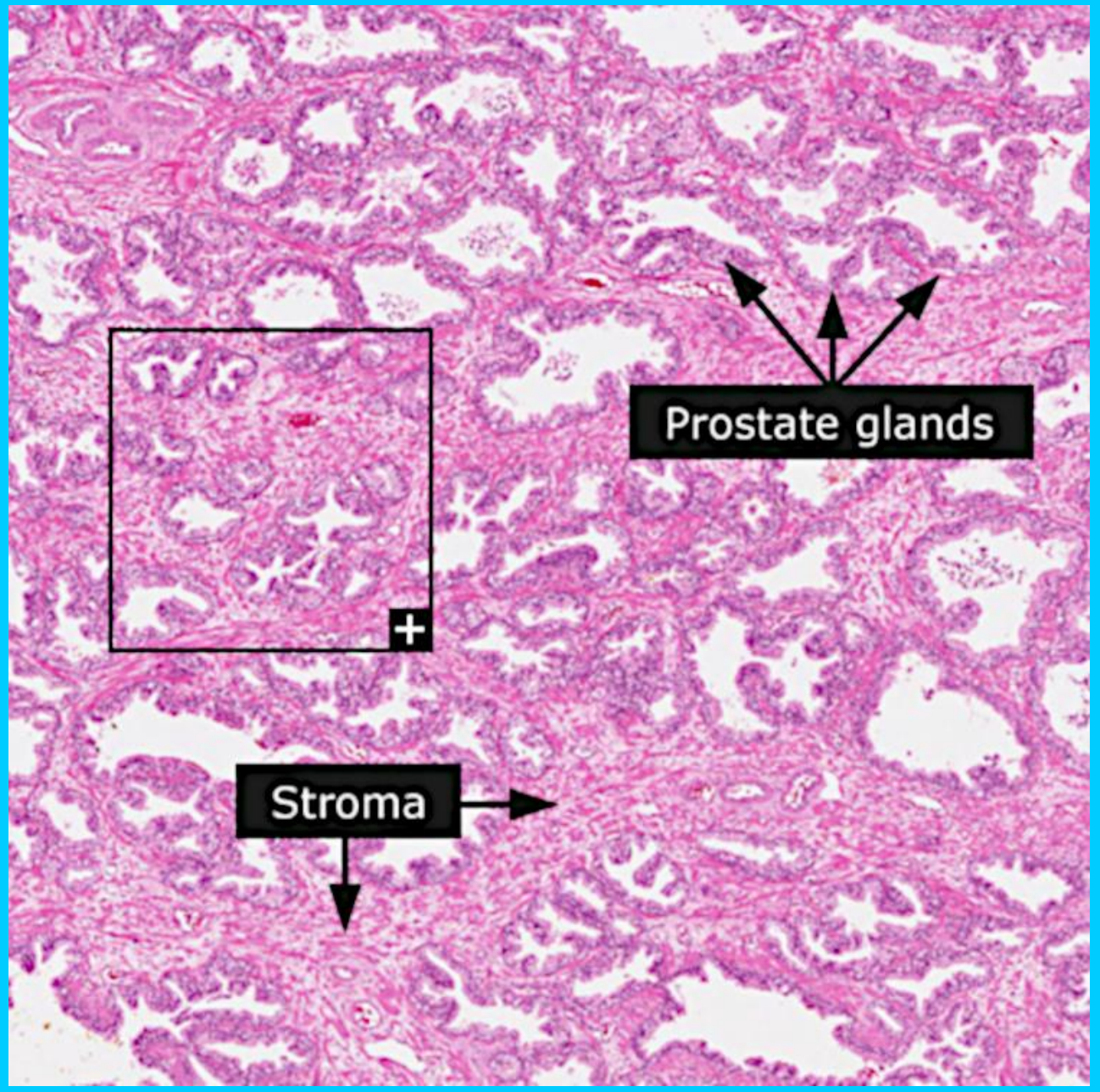
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Normal Prostate Tissue**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

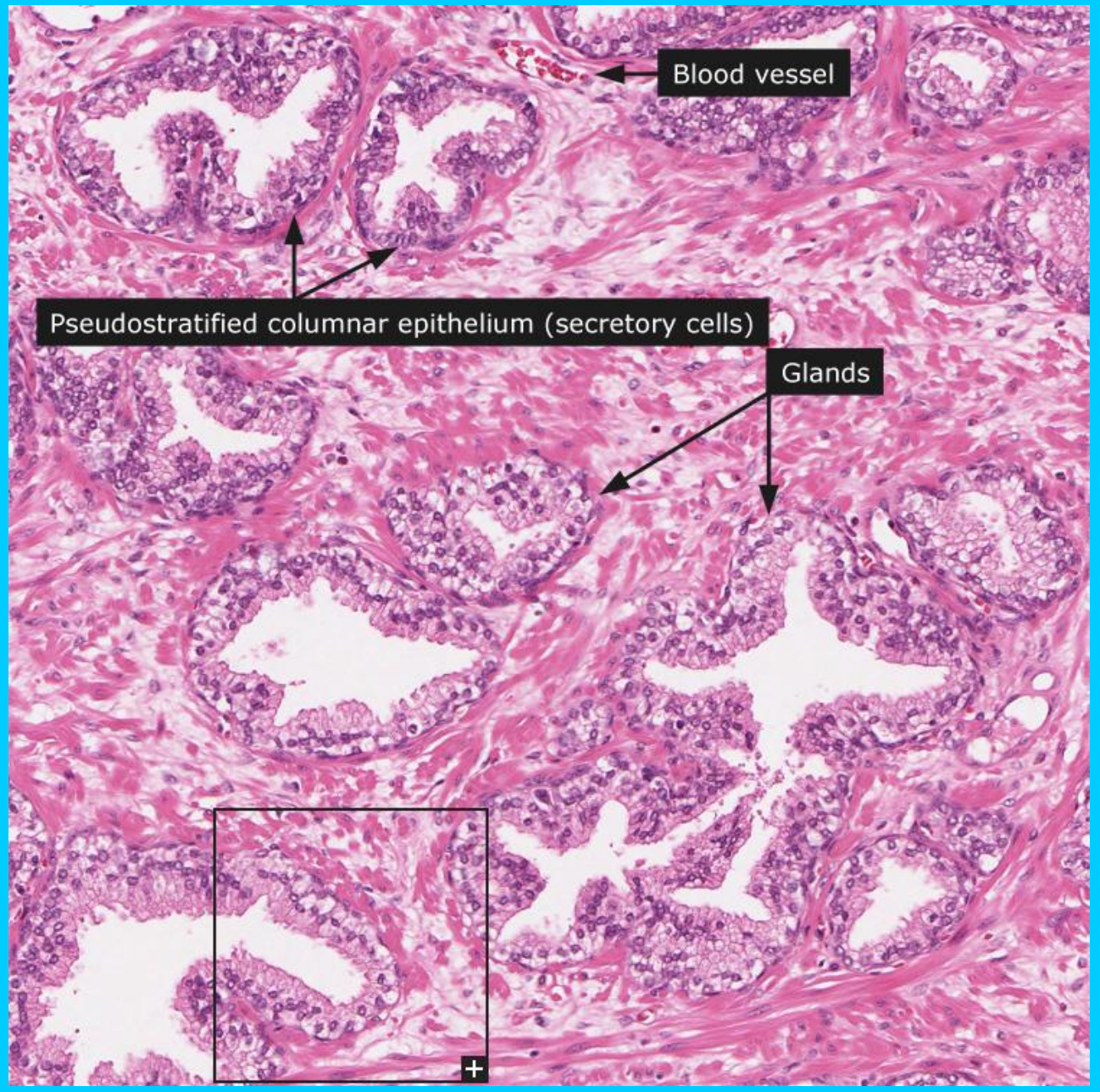
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Normal Prostate Tissue**

**Enlarged**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

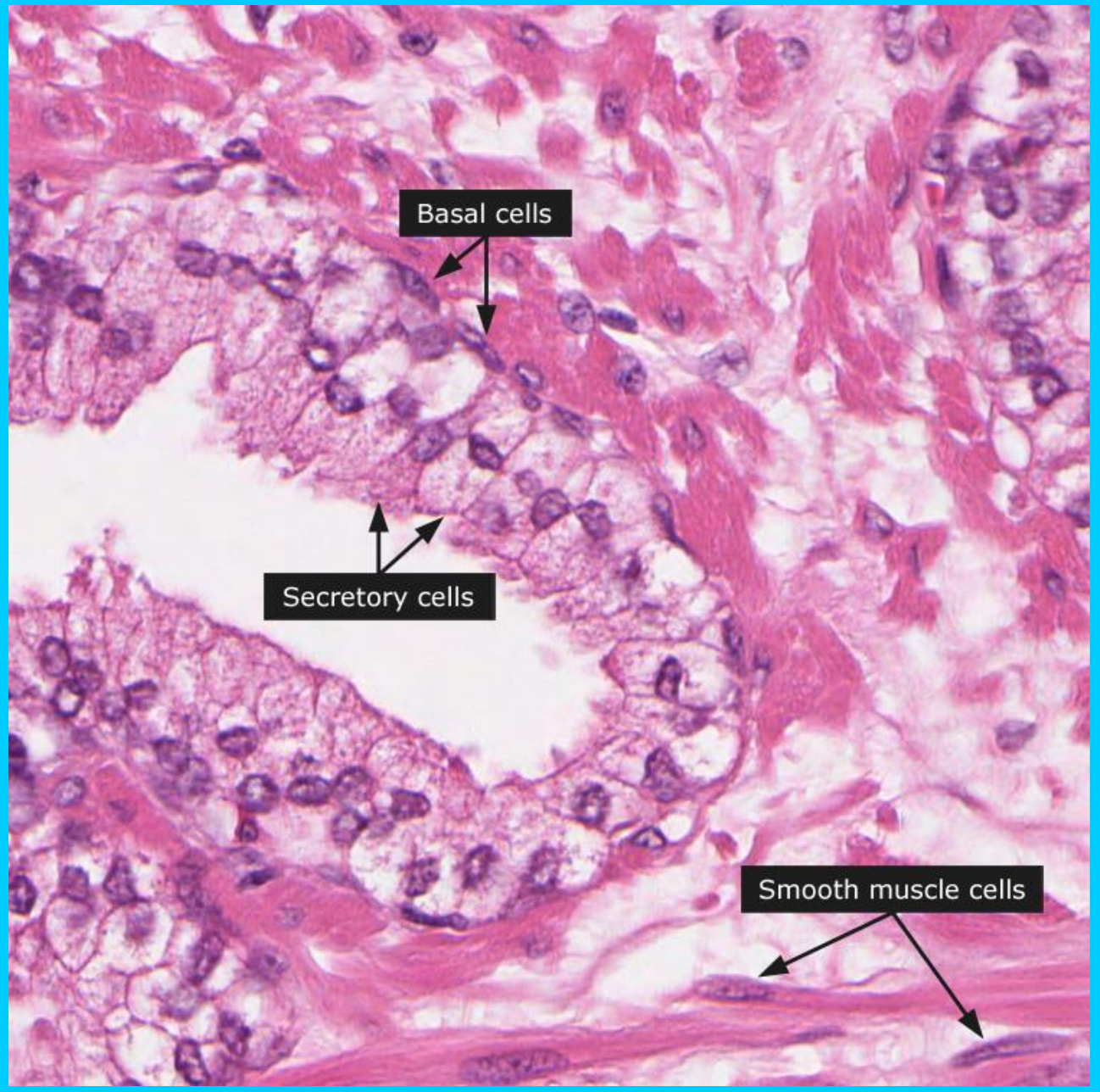
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Normal Prostate Tissue**

←

**Enlarged Maximum**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Scanning

Electron

Micrograph (SEM)

Glandular Wall

Normal Prostate

Secretory Cells

(PSA Producers)

**Normal Prostate Tissue**

**Enlarged X 3600**

Credits: SciencePhotoLibrary

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

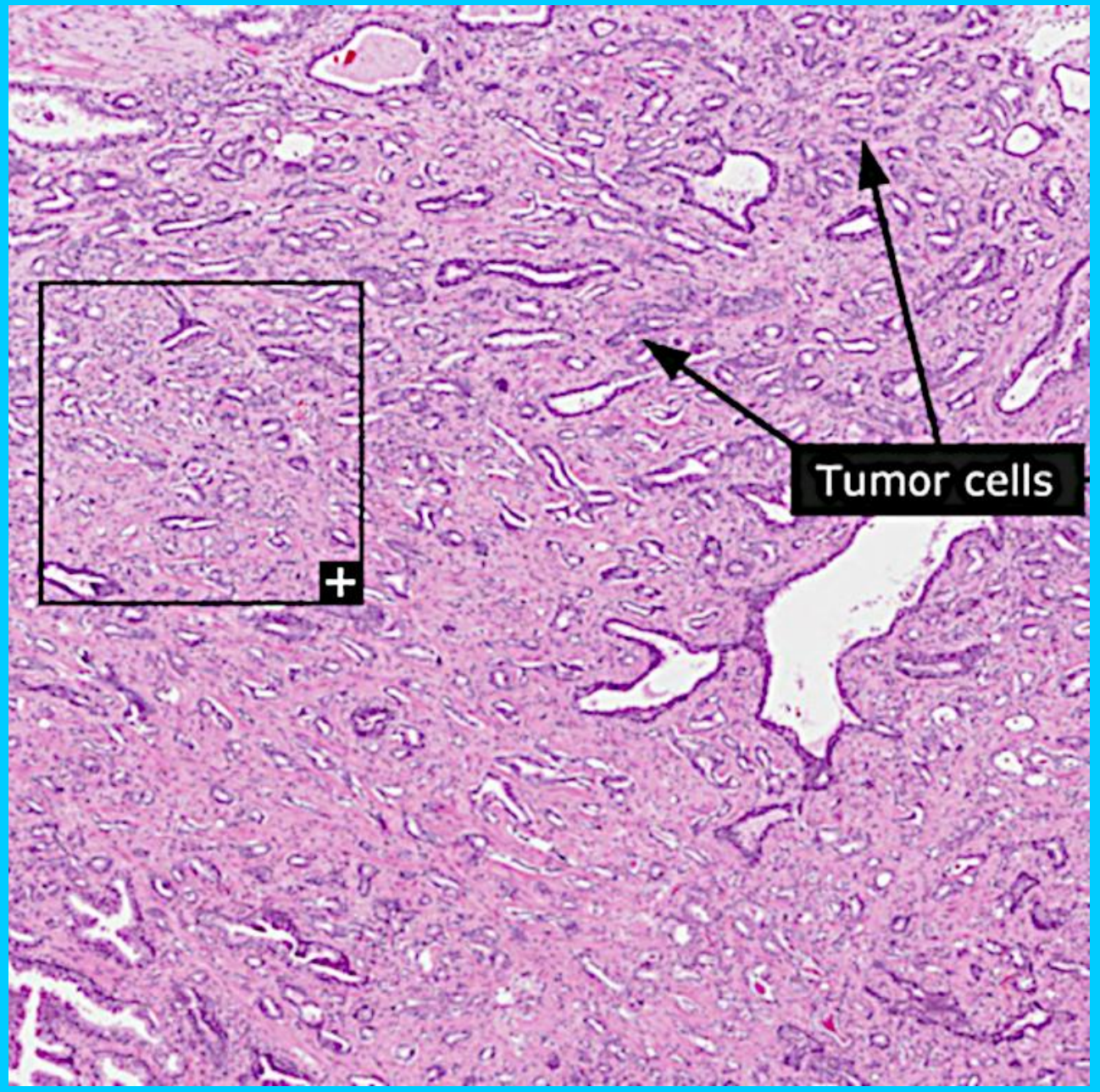
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 6 Prostate Cancer Tissue**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

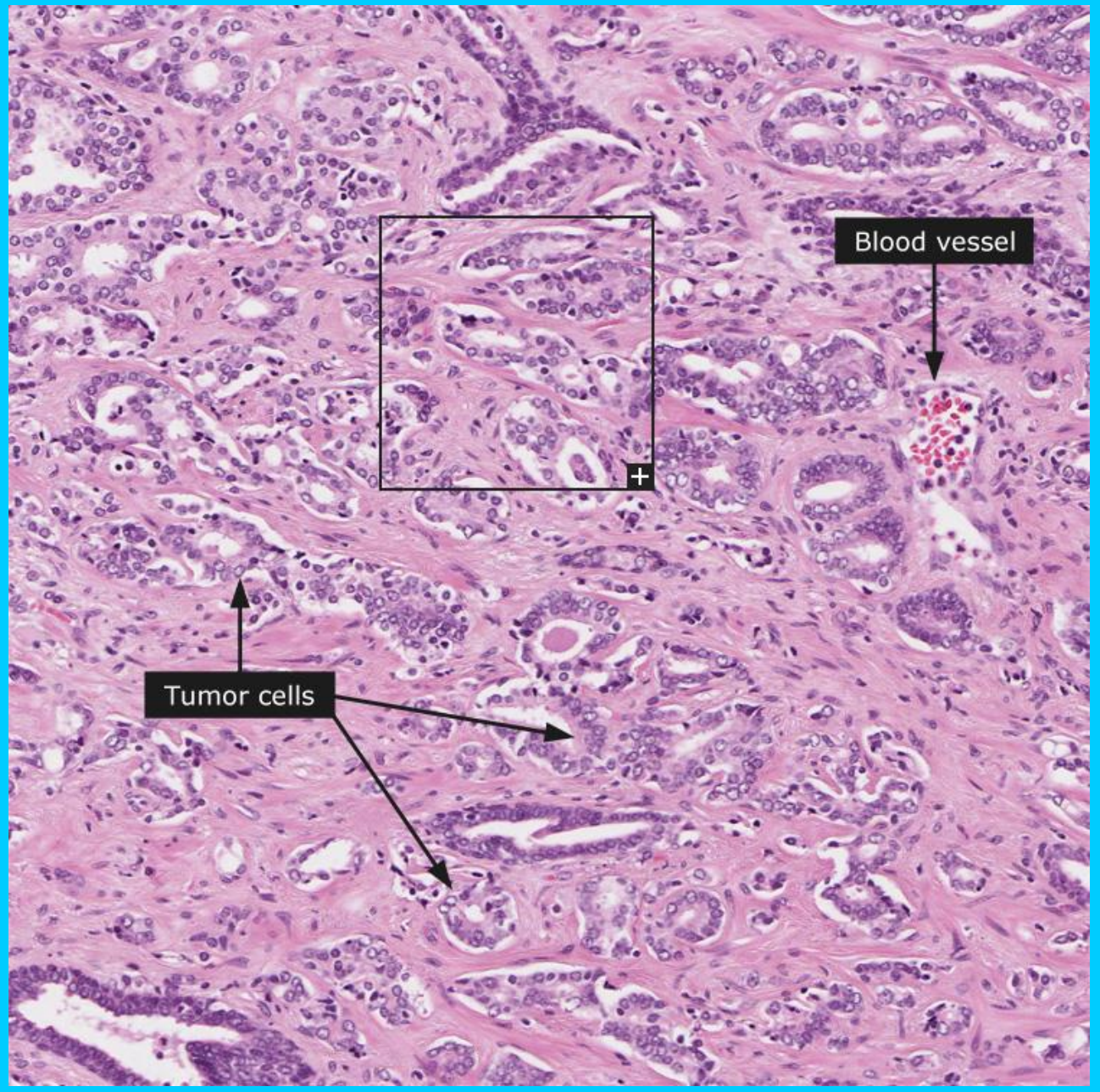
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 6 Prostate Cancer Tissue**

**Enlarged**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

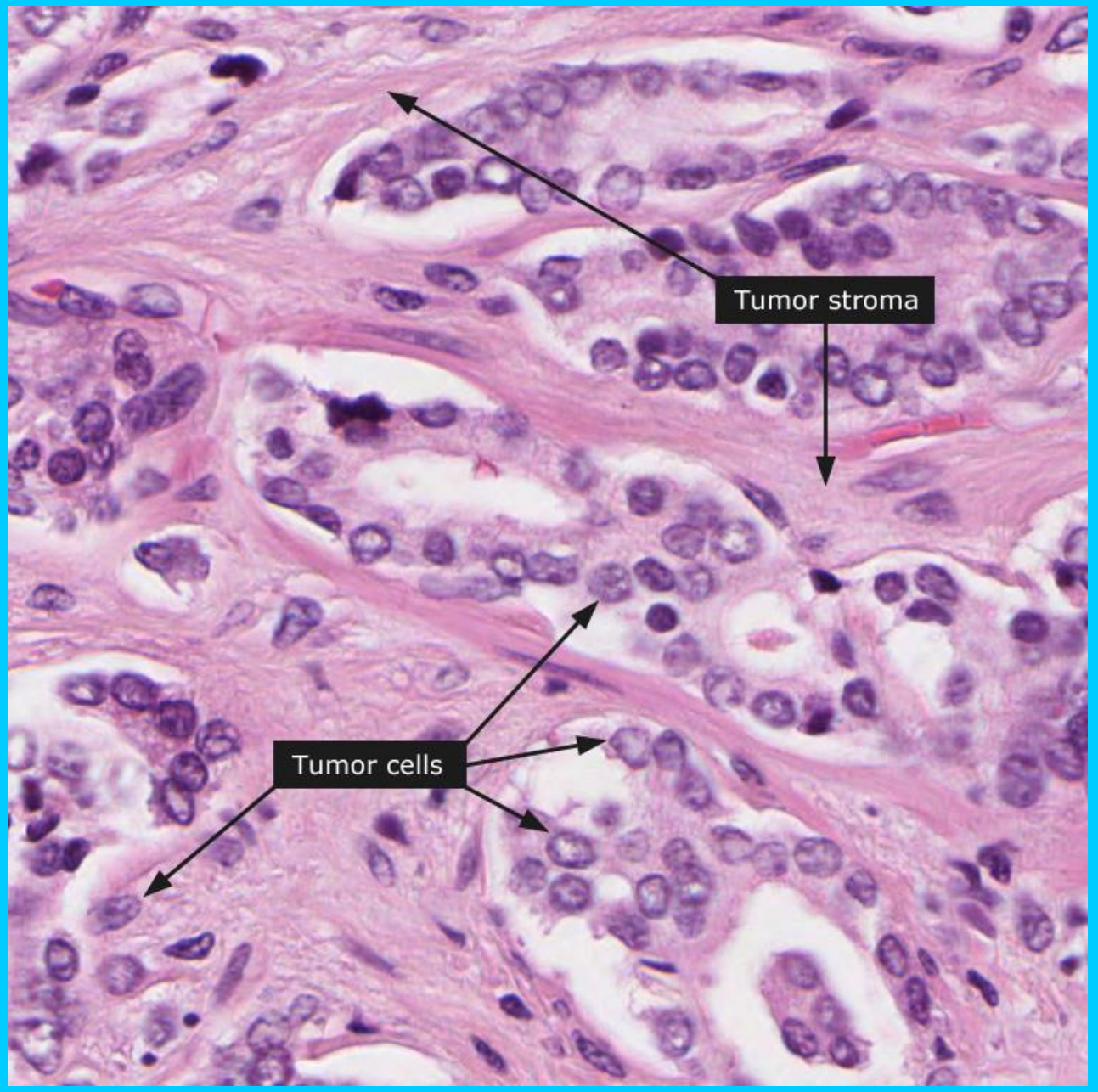
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 6 Prostate Cancer Tissue**

**Enlarged Maximum**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

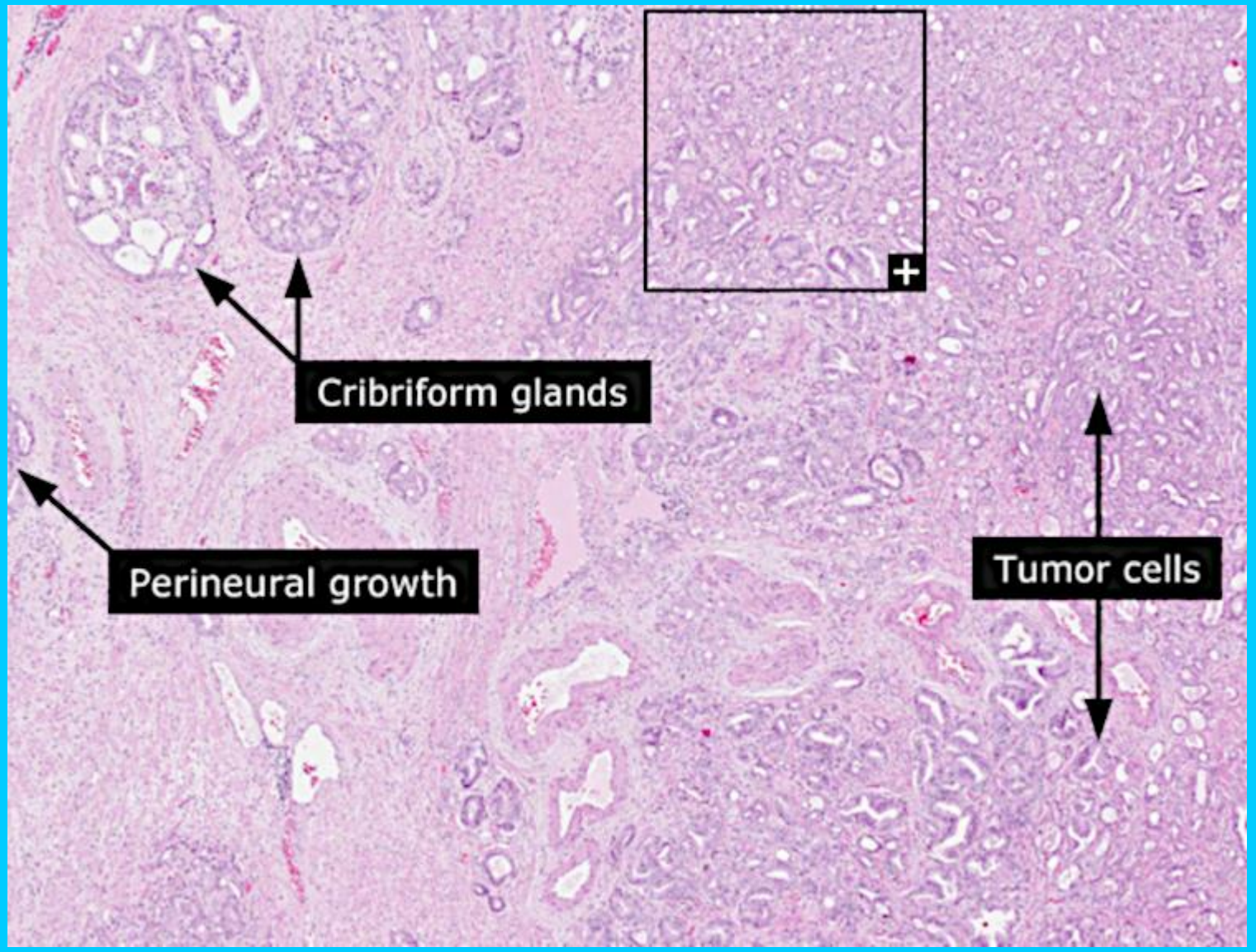
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 7 Prostate Cancer Tissue**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

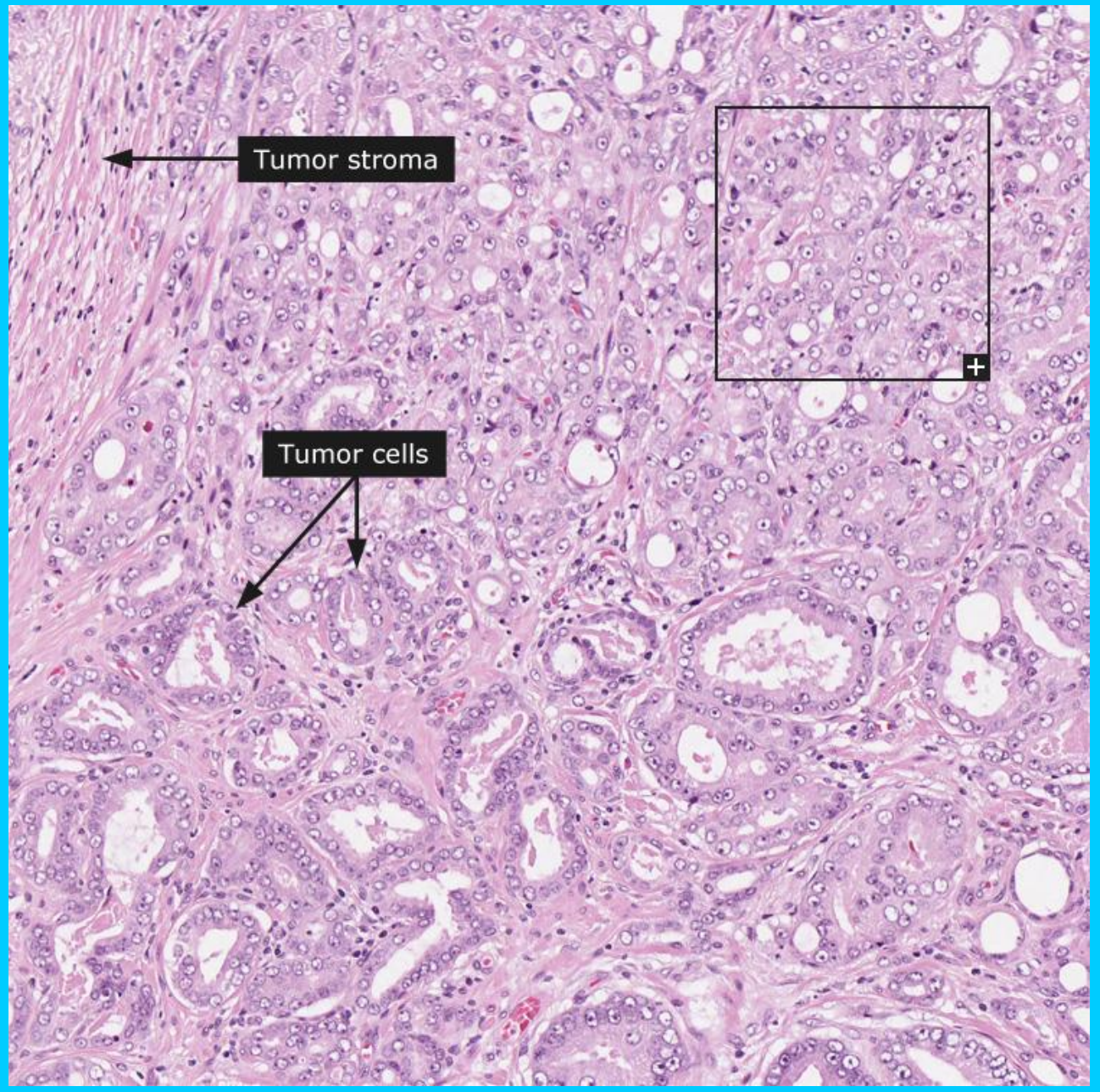
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 7 Prostate Cancer Tissue**

**Enlarged**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

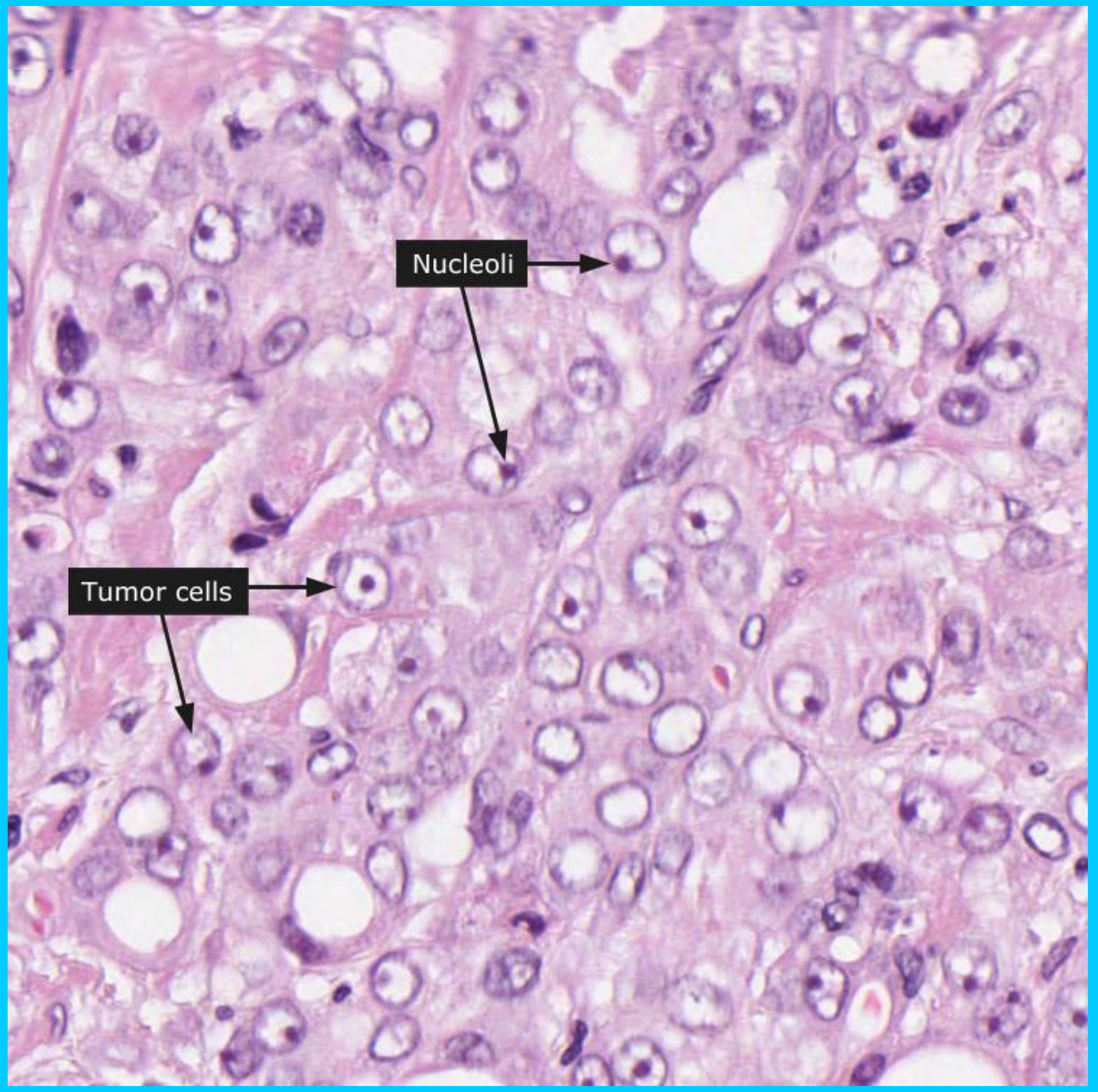
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 7 Prostate Cancer Tissue**

**Enlarged Maximum**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

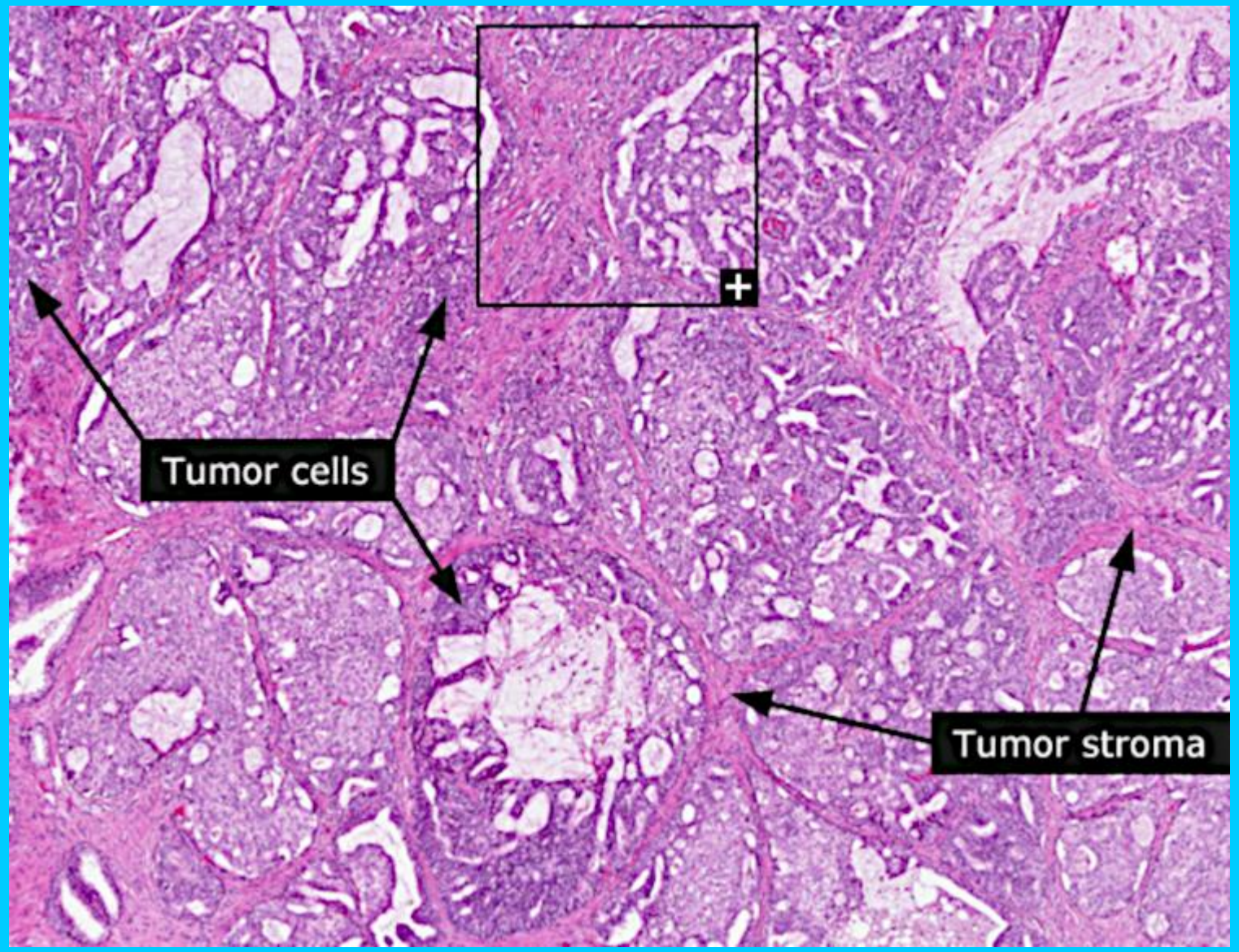
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 8 Prostate Cancer Tissue**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

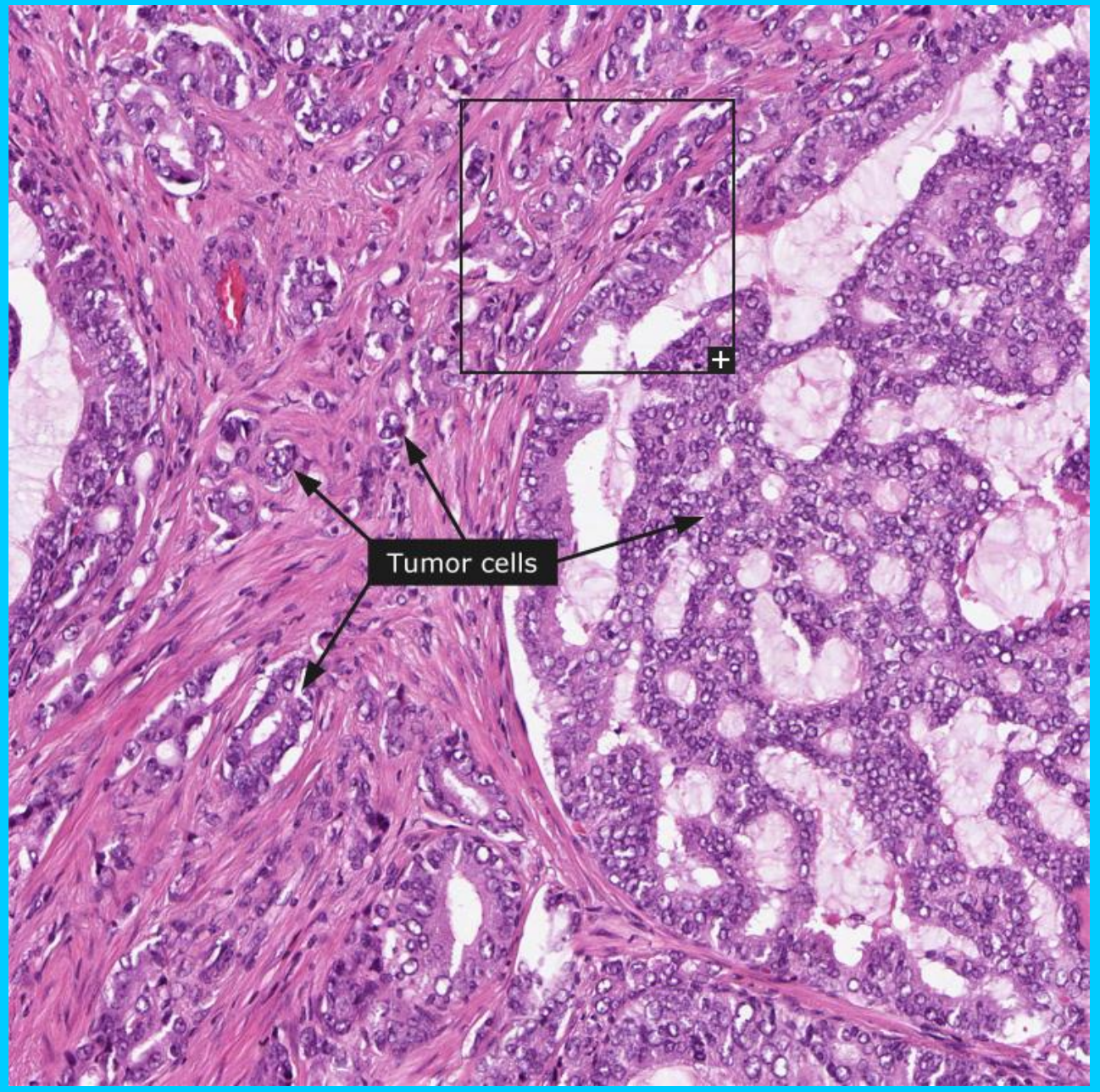
assign PCa

Gleason Scores

by looking at

prostate tissue with

Light Microscopes




**Gleason 8 Prostate Cancer Tissue**

**Enlarged**

Credits:
Human Protein Atlas

# PROSTATE CANCER TOPICS 10-14-2019

Pathologists

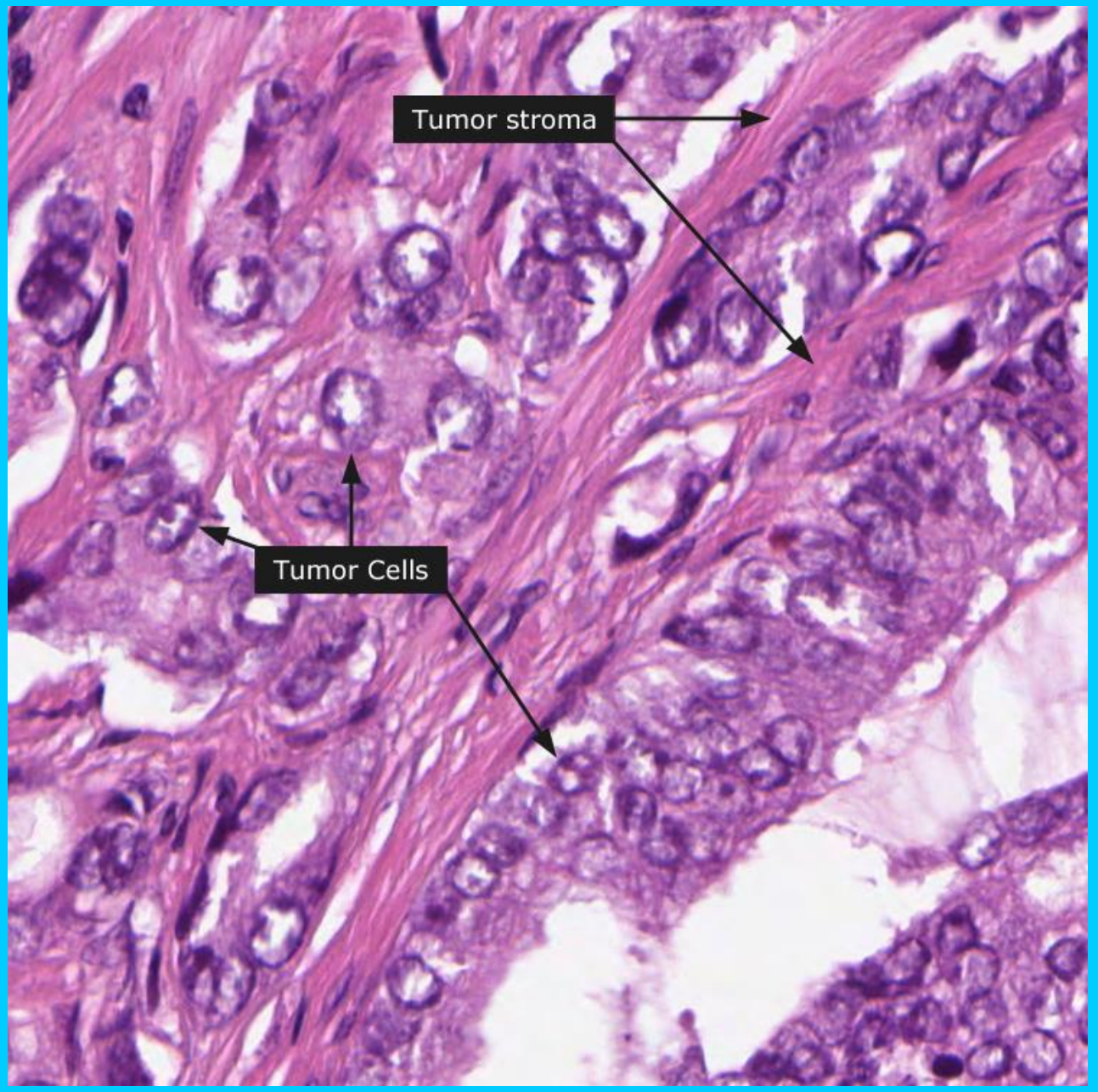
assign PCa

Gleason Scores

by looking at

prostate tissue with

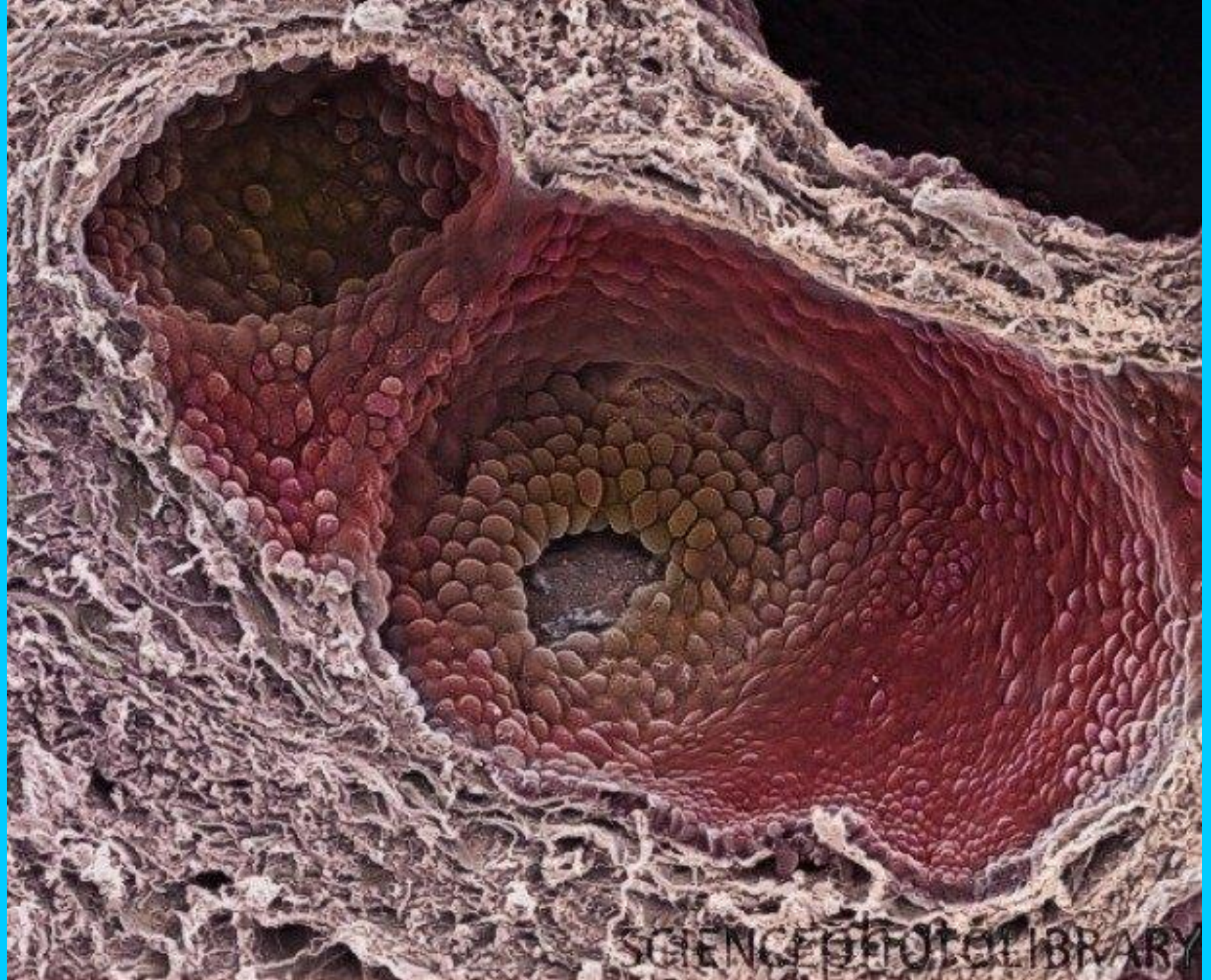
Light Microscopes




**Gleason 8 Prostate Cancer Tissue**

**Enlarged Maximum**

Credits:
Human Protein Atlas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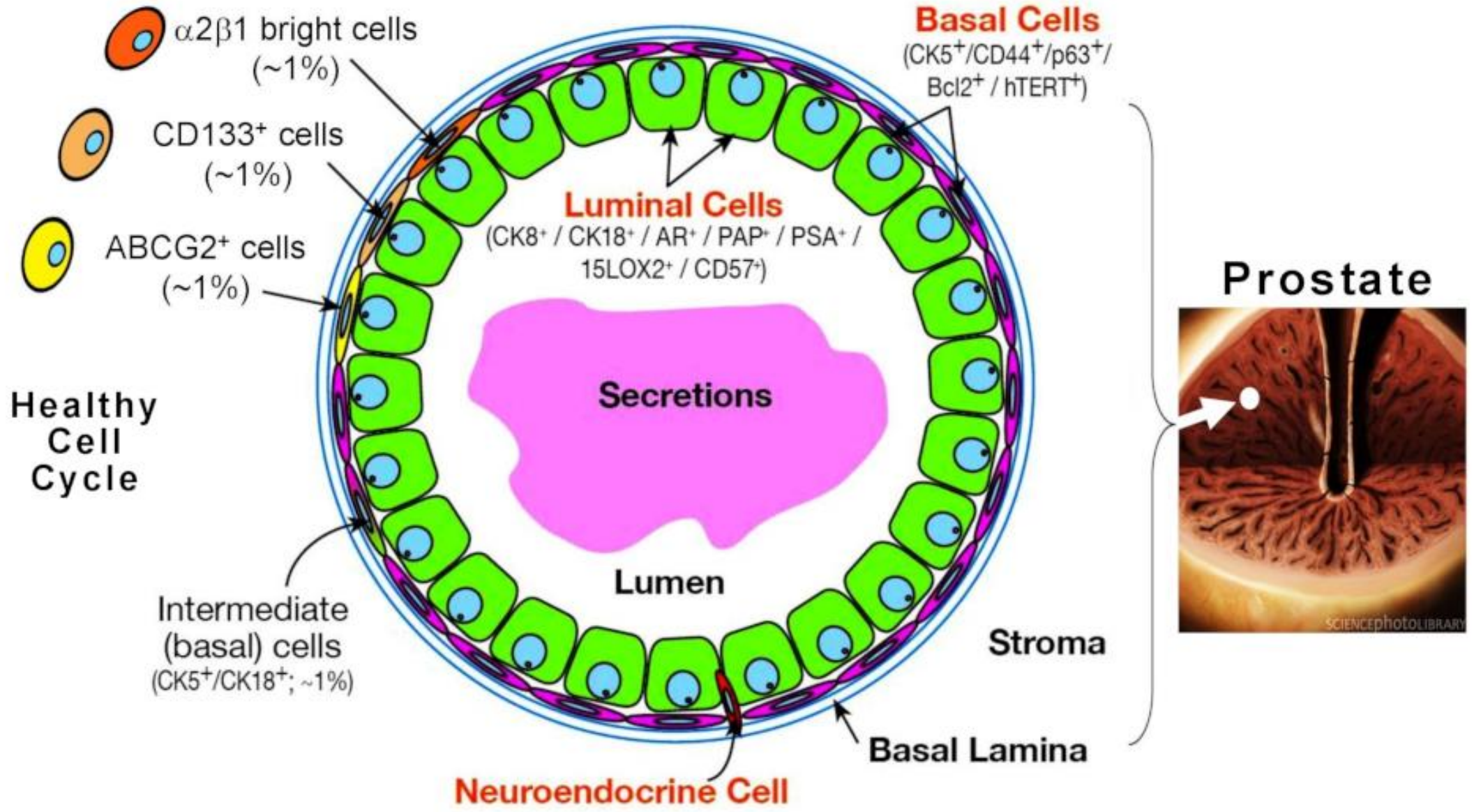
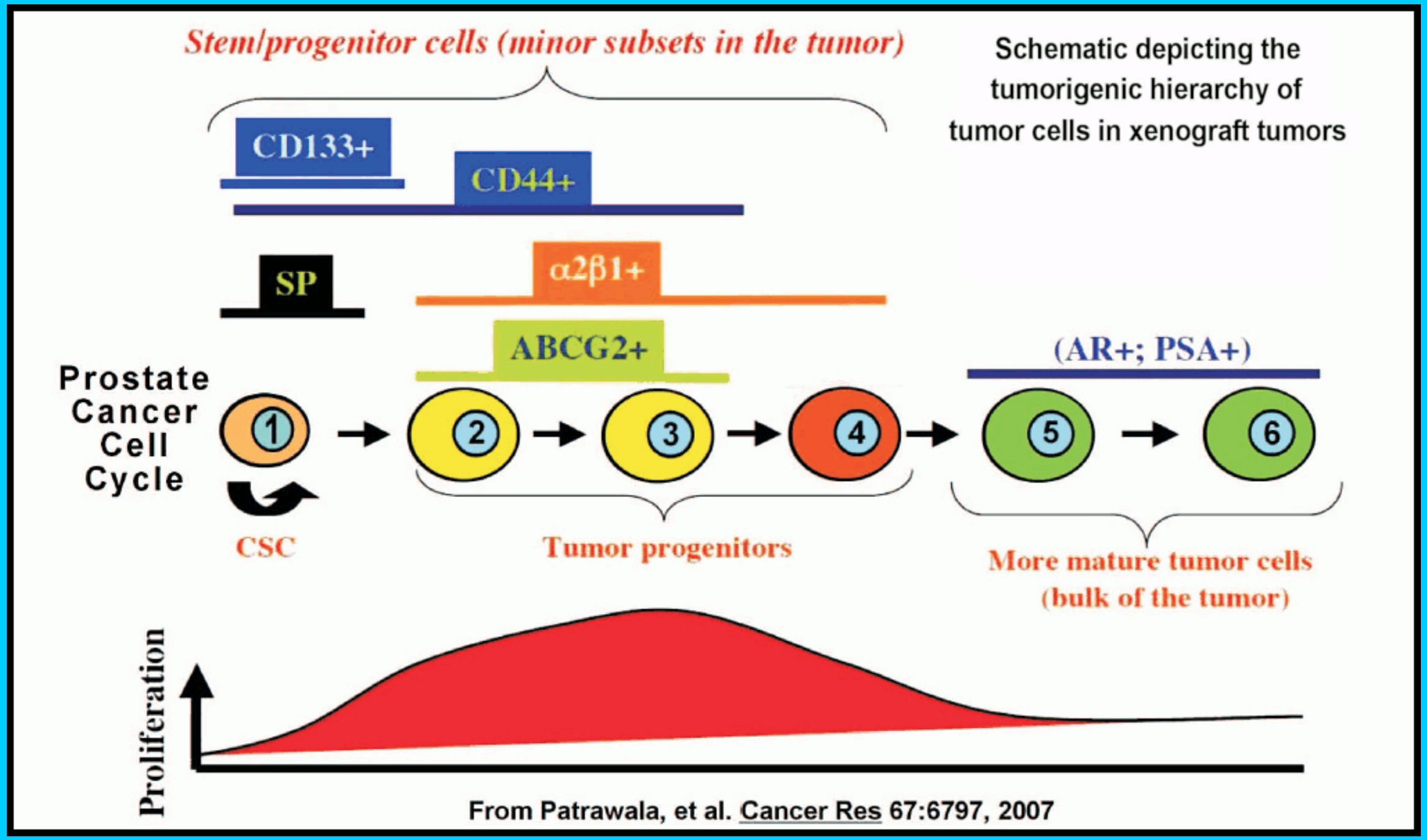
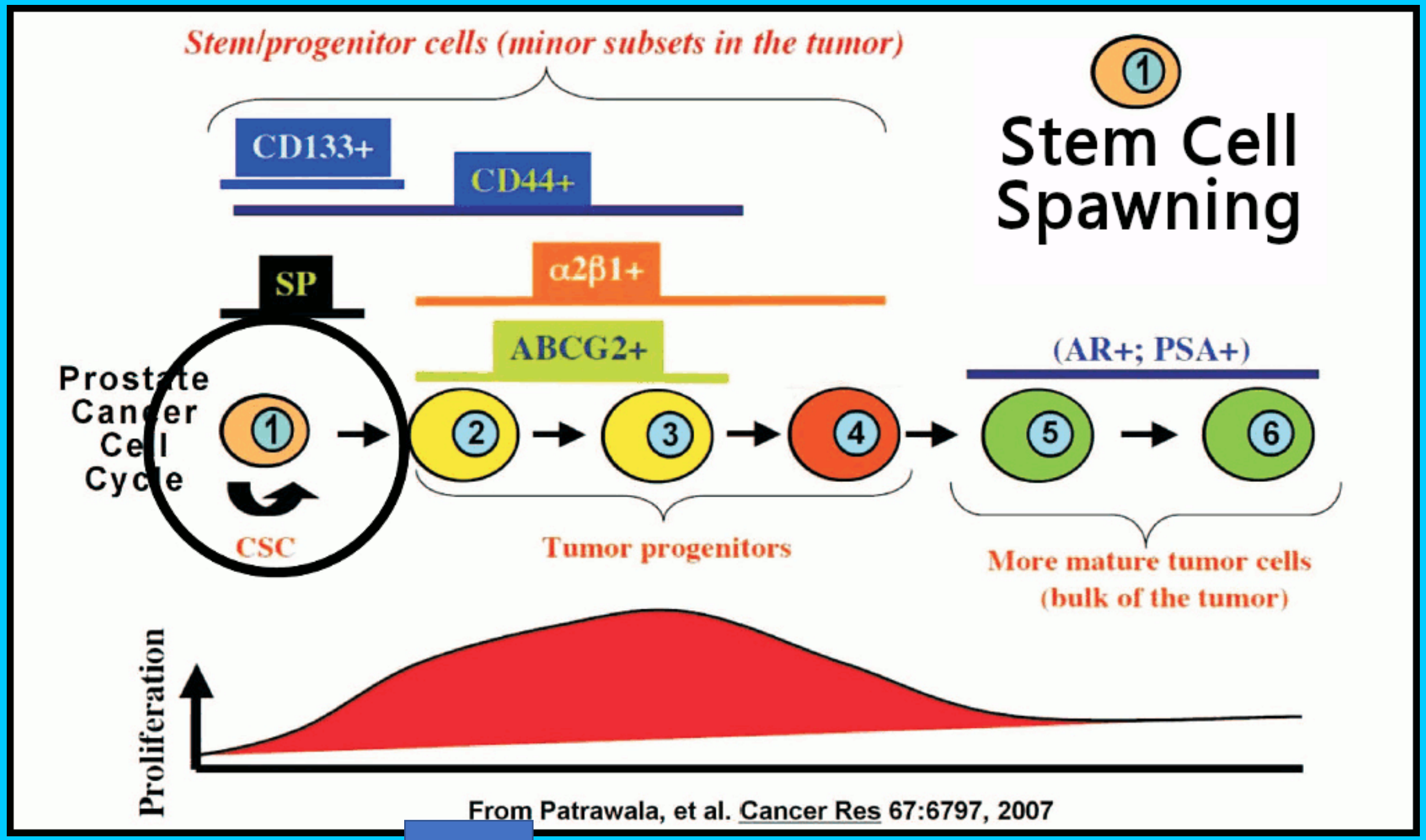
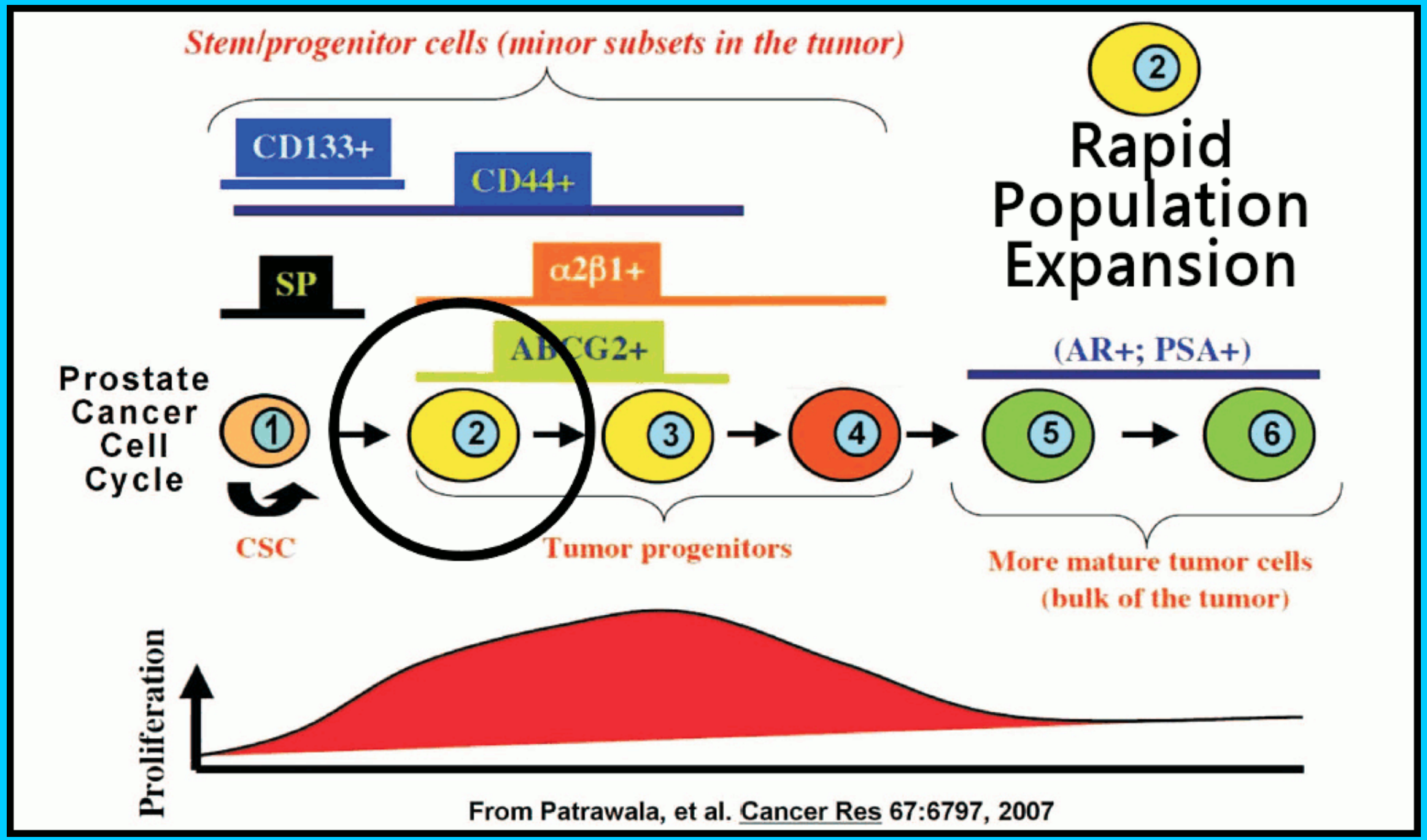
Honorio et al., Figure 1 - Cartoon showing the general structure of a human prostatic gland.

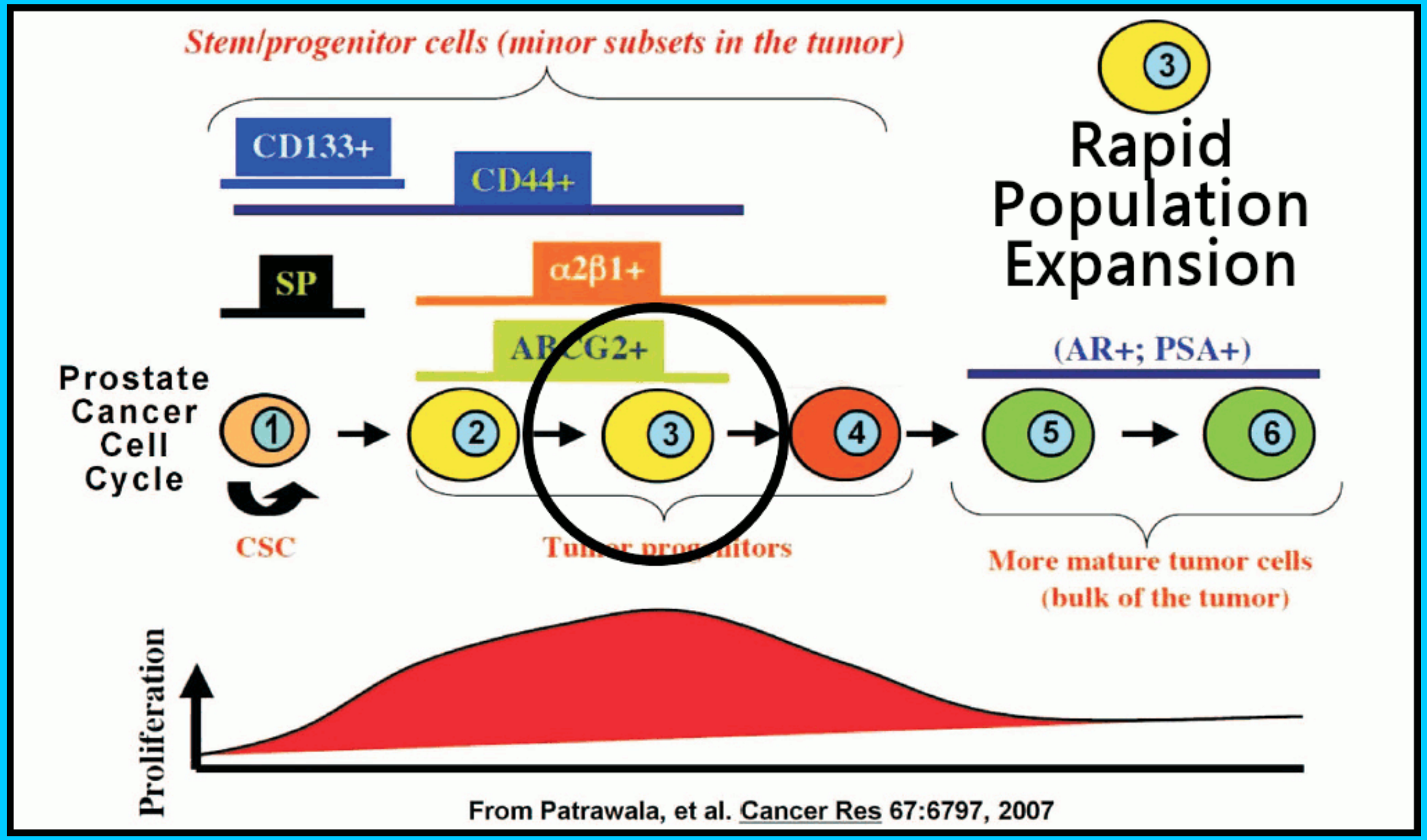


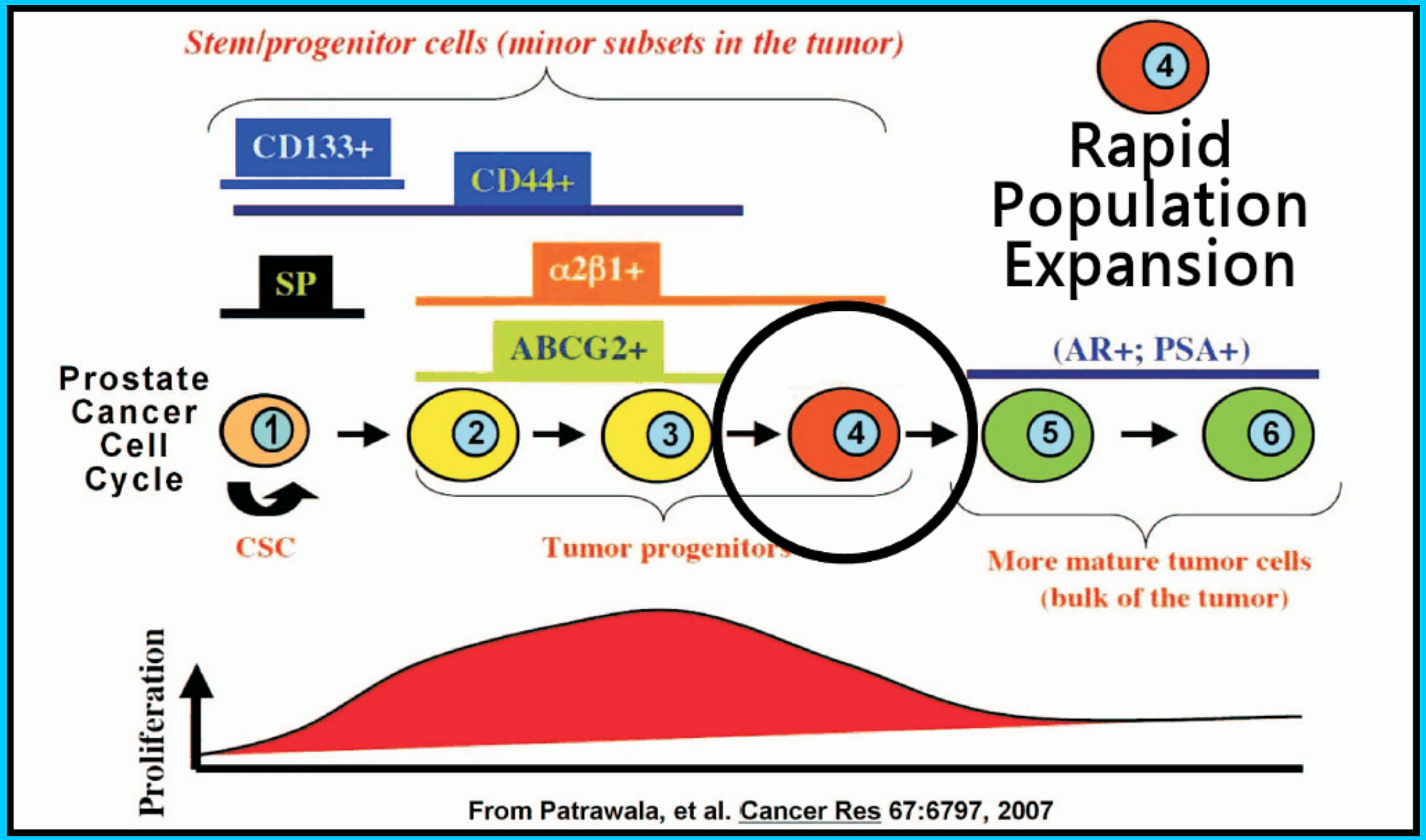

Stem/progenitor cells (minor subsets in the tumor)
Schematic depicting the tumorigenic hierarchy of tumor cells in xenograft tumors
CD133+
CD44+
SP
α2β1+
ABCG2+
(AR+; PSA+)
Prostate Cancer Cell Cycle
1
2
3
4
5
6
CSC
Tumor progenitors
More mature tumor cells (bulk of the tumor)
Proliferation
From Patrawala, et al. Cancer Res 67:6797, 2007


Stem/progenitor cells (minor subsets in the tumor)
CD133+
CD44+
SP
α2β1+
ABCG2+
(AR+; PSA+)
Prostate Cancer Cell Cycle
1
2
3
4
5
6
CSC
Tumor progenitors
More mature tumor cells
(bulk of the tumor)
Stem Cell Spawning
Proliferation
From Patrawala, et al. Cancer Res 67:6797, 2007

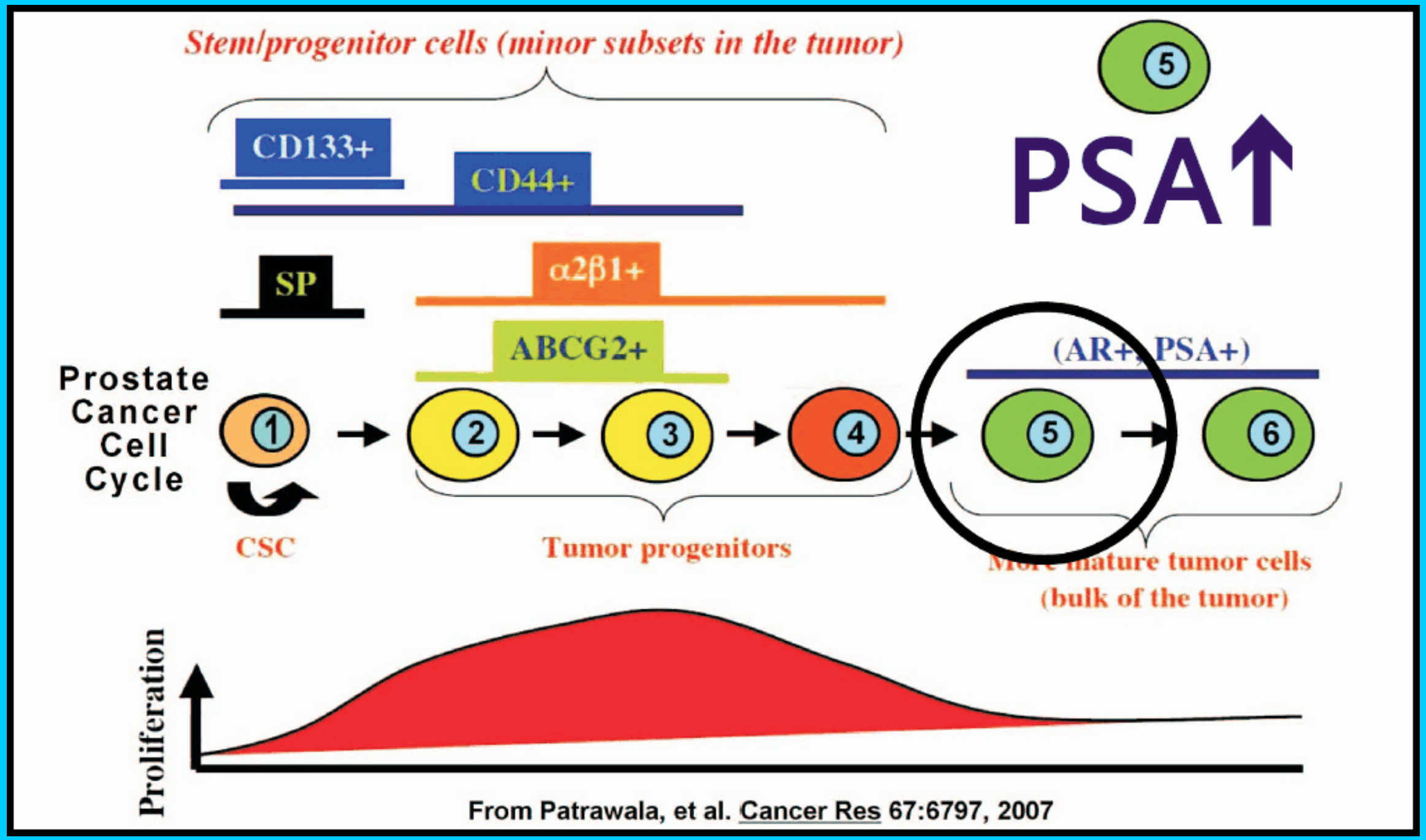


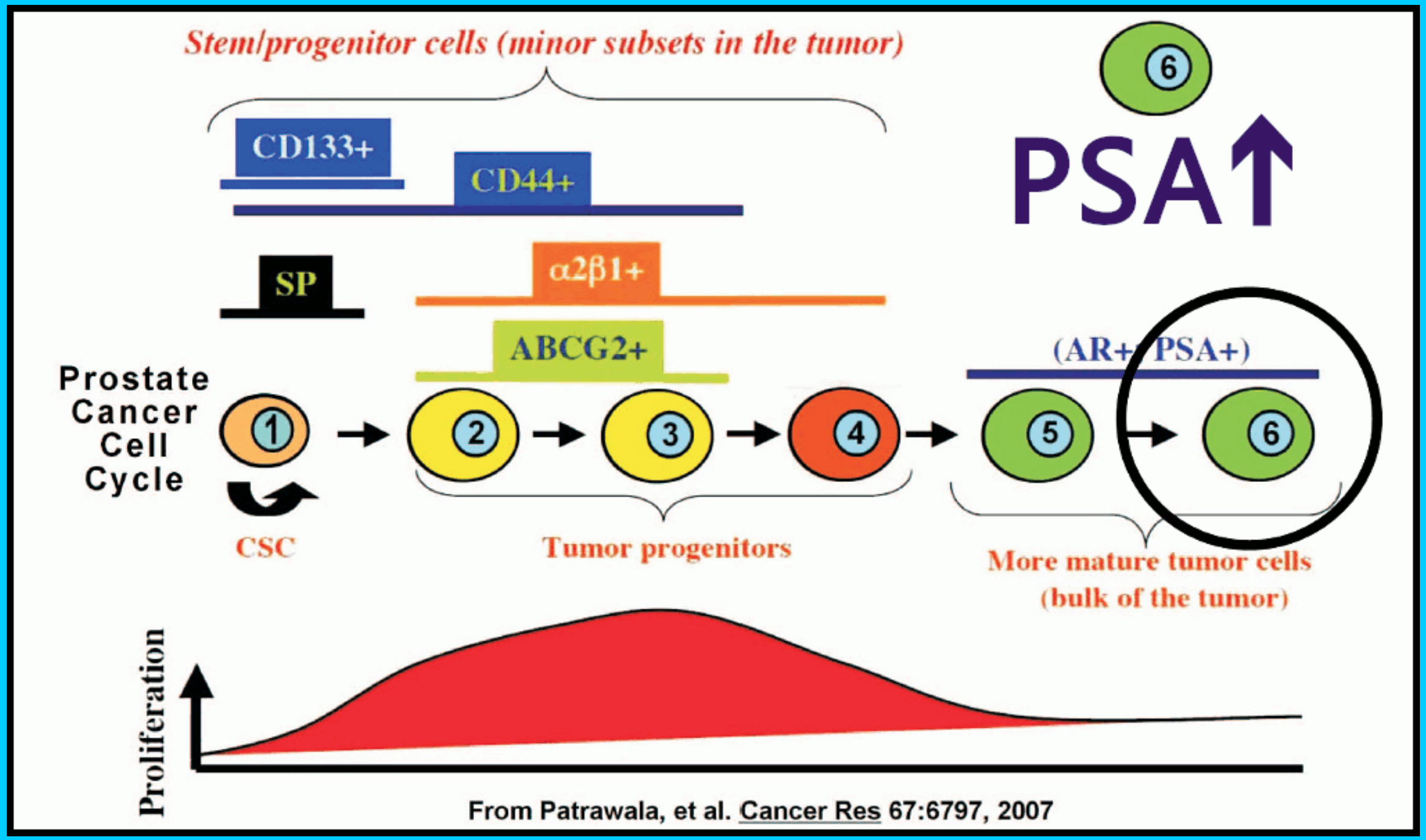

From Patrawala, et al. Cancer Res 67:6797, 2007


Stem/progenitor cells (minor subsets in the tumor)
CD133+
CD44+
SP
α2β1+
ABCG2+
Prostate Cancer Cell Cycle
1
2
3
4
5
6
CSC
Tumor progenitors
(AR+; PSA+)
More mature tumor cells
(bulk of the tumor)
3
Rapid Population Expansion
Proliferation
From Patrawala, et al. Cancer Res 67:6797, 2007




From Patrawala, et al. Cancer Res 67:6797, 2007


Stem/progenitor cells (minor subsets in the tumor)
CD133+
CD44+
SP
α2β1+
ABCG2+
PSA↑
Prostate Cancer Cell Cycle
1
2
3
4
5
6
(AR+, PSA+)
CSC
Tumor progenitors
More mature tumor cells
(bulk of the tumor)
Proliferation
From Patrawala, et al. Cancer Res 67:6797, 2007


Stem/progenitor cells (minor subsets in the tumor)
CD133+
CD44+
SP
α2β1+
ABCG2+
6
PSA↑
(AR+ PSA+)
Prostate Cancer Cell Cycle
1
2
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CSC
Tumor progenitors
More mature tumor cells (bulk of the tumor)
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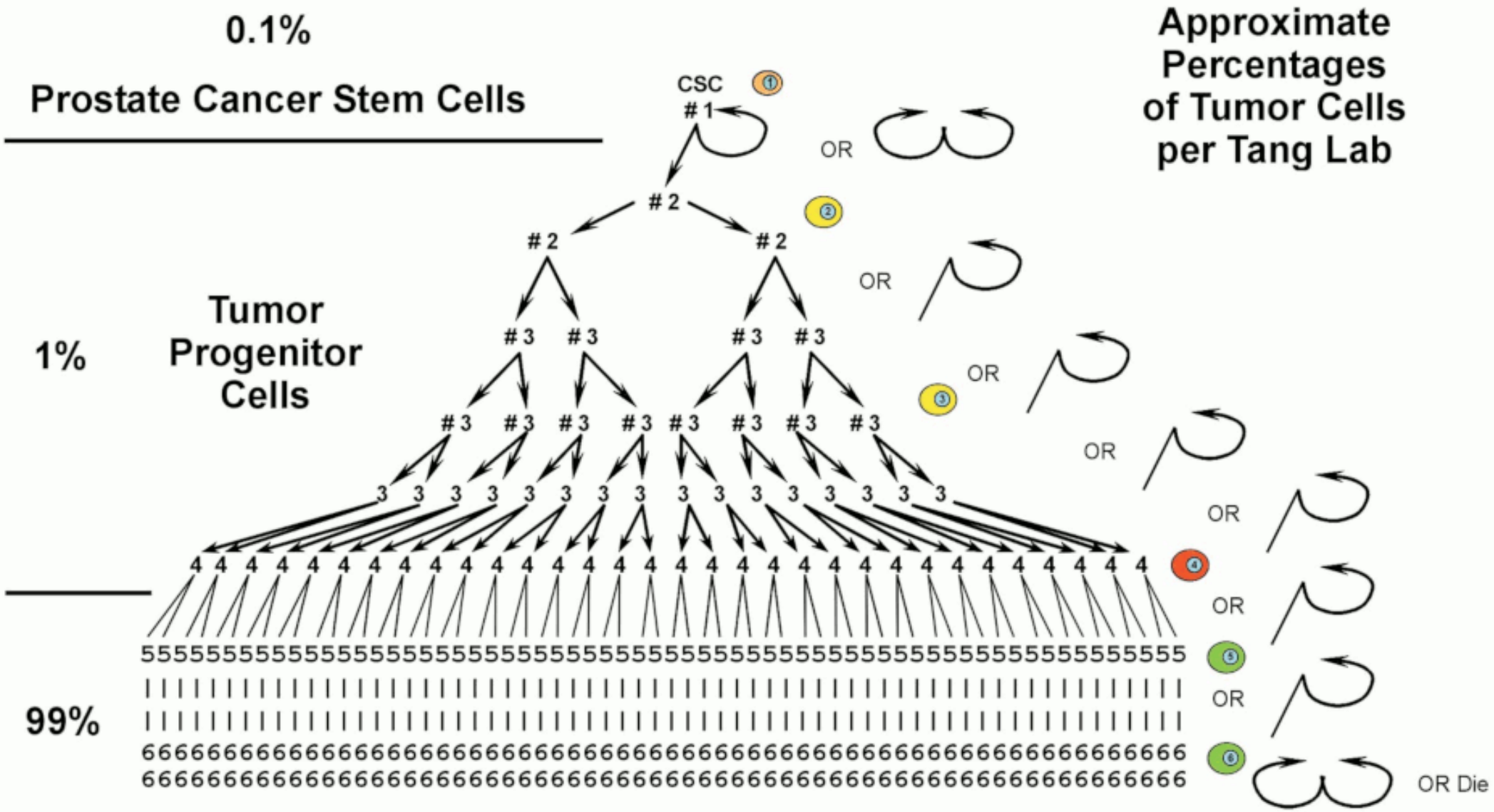
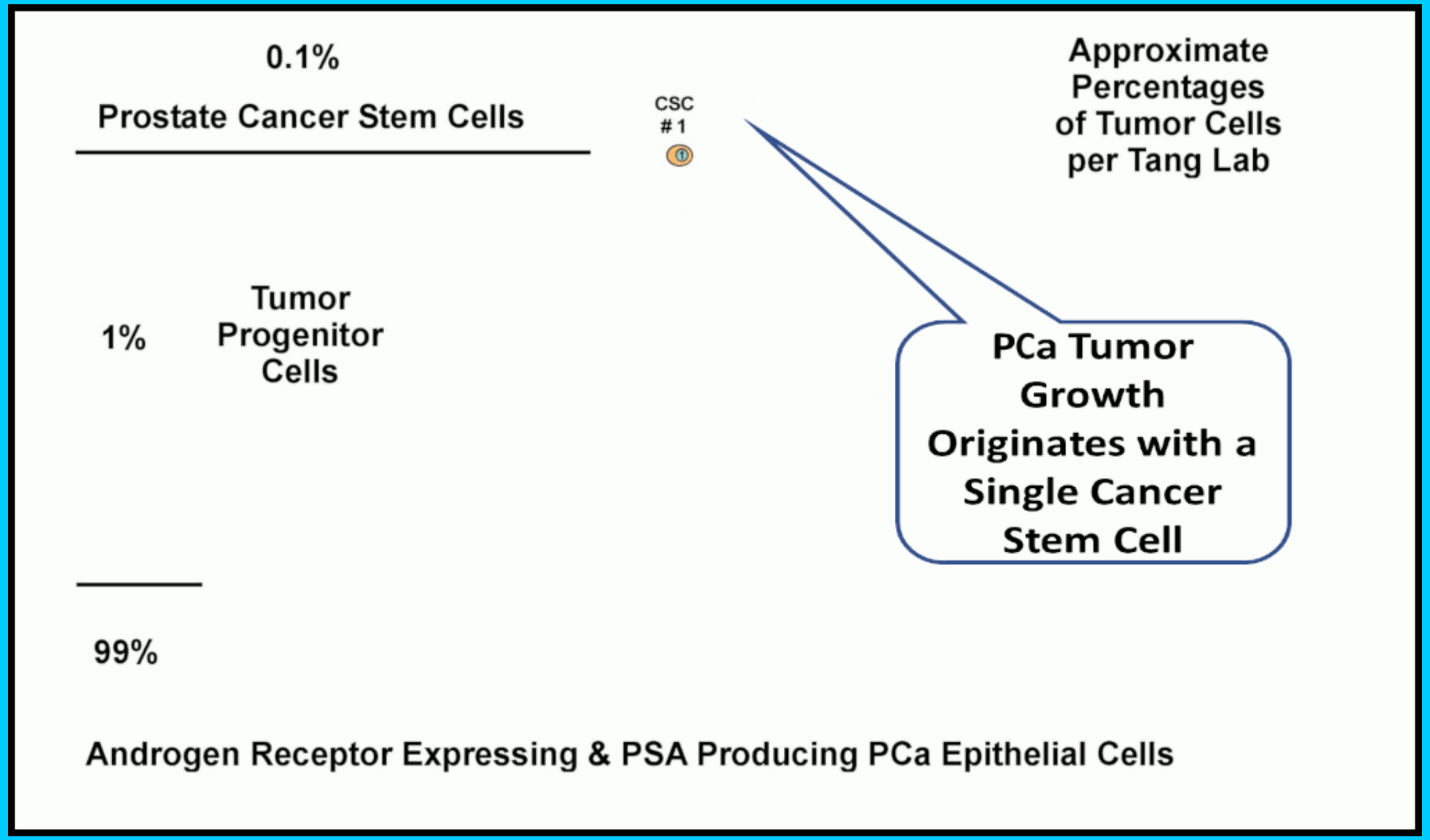
From Patrawala, et al. Cancer Res 67:6797, 2007

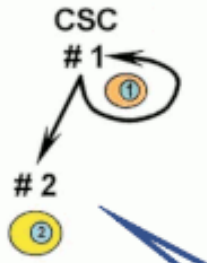

0.1%
Prostate Cancer Stem Cells
Approximate Percentages of Tumor Cells per Tang Lab
CSC
#1
OR
#2
#2
#2
OR
1%
Tumor Progenitor Cells
#3
OR
OR
OR
OR
OR
OR
OR Die
99%
Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells


0.1%
Prostate Cancer Stem Cells
CSC
# 1
1
Approximate
Percentages
of Tumor Cells
per Tang Lab
1%
Tumor
Progenitor
Cells
PCa Tumor
Growth
Originates with a
Single Cancer
Stem Cell
99%
Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

Prostate Cancer Stem Cells

Approximate Percentages of Tumor Cells per Tang Lab




1%

Tumor Progenitor Cells

The PCa Cancer Stem Cell divides spawning an IDENTICAL Stem Cell plus one Type #2 PCa Progenitor cell

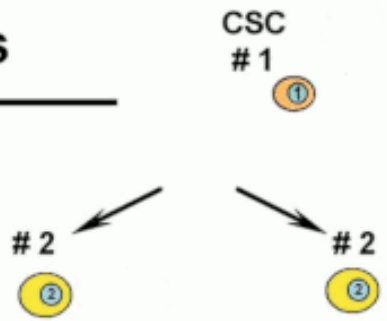
99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

Prostate Cancer Stem Cells

Approximate Percentages of Tumor Cells per Tang Lab




1%

Tumor Progenitor Cells

Type #2 PCa Progenitor cell divides spawning Two IDENTICAL Type #2 PCa Progenitor cells

99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

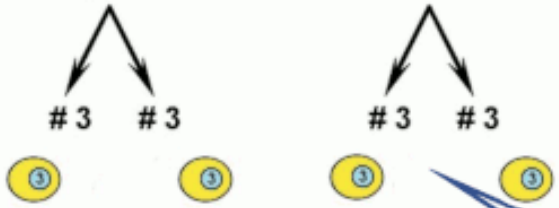
0.1%

Prostate Cancer Stem Cells

Approximate Percentages of Tumor Cells per Tang Lab

1%

Tumor Progenitor Cells




Both #2 PCa Progenitor cells divide spawning Four Type #3 PCa Progenitor cells

99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

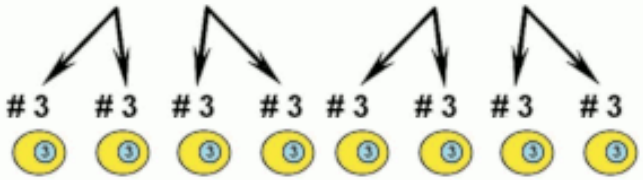
Prostate Cancer Stem Cells

CSC
#1

Approximate Percentages of Tumor Cells per Tang Lab

1%

Tumor Progenitor Cells




Four #3 PCa Progenitor cells divide spawning Eight Type #3 PCa Progenitor cells

99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

Prostate Cancer Stem Cells

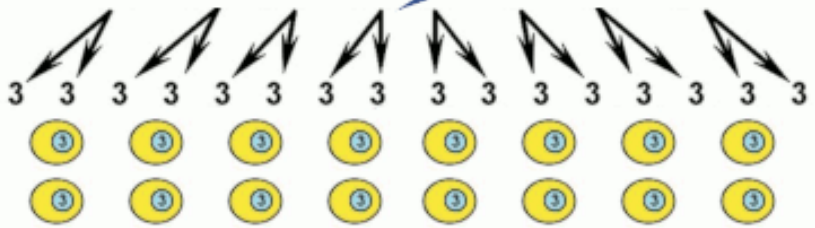
CSC
# 1

Approximate Percentages of Tumor Cells per Tang Lab

Eight #3 PCa Progenitor cells divide spawning Sixteen Type #3 Pca Progenitor cells

1%

Tumor Progenitor Cells



99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

Prostate Cancer Stem Cells

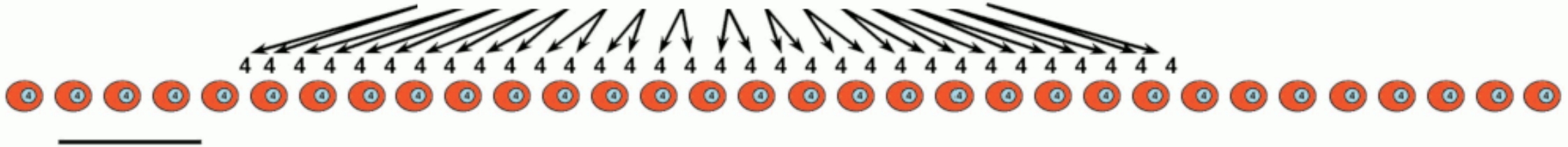
CSC
# 1

Approximate
Percentages
of Tumor Cells
per Tang Lab

Sixteen #3 PCa Progenitor cells
divide spawning Thirty-Two
Type #4 PCa Progenitor cells

1%

Tumor
Progenitor
Cells



99%

Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

0.1%

Prostate Cancer Stem Cells

CSC
# 1

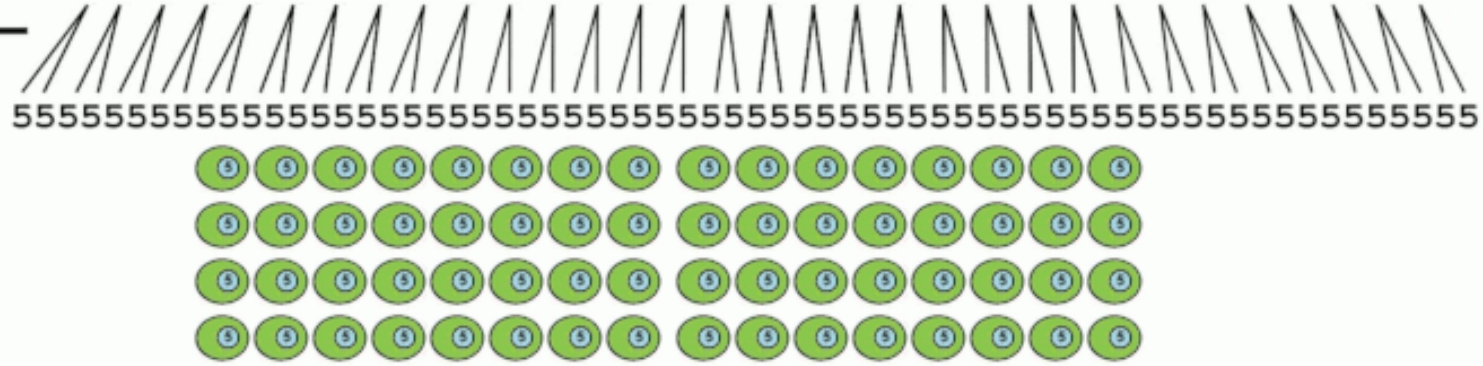
Approximate Percentages of Tumor Cells per Tang Lab

1%

Tumor Progenitor Cells

Thirty-two #4 PCa Progenitor cells divide spawning Sixty-four Type #5 PSA+ AR+ PCa cells

99%



0.1%

Prostate Cancer Stem Cells

CSC
# 1

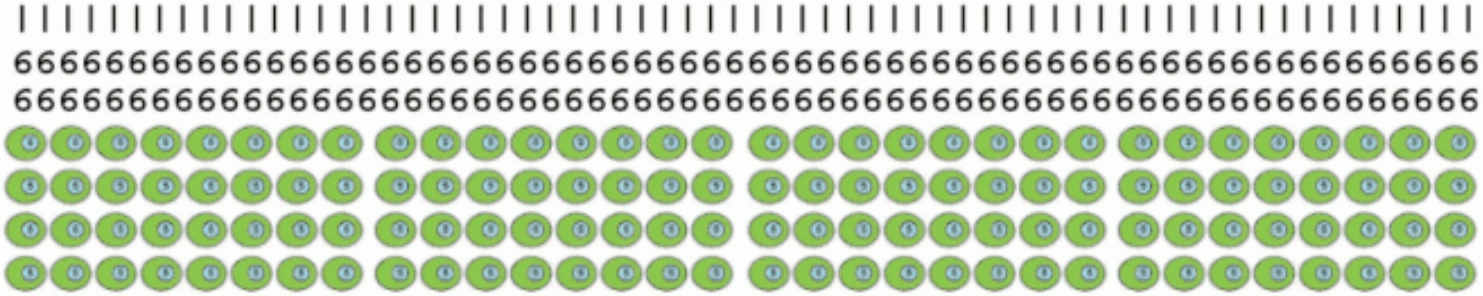
Approximate Percentages of Tumor Cells per Tang Lab

1%

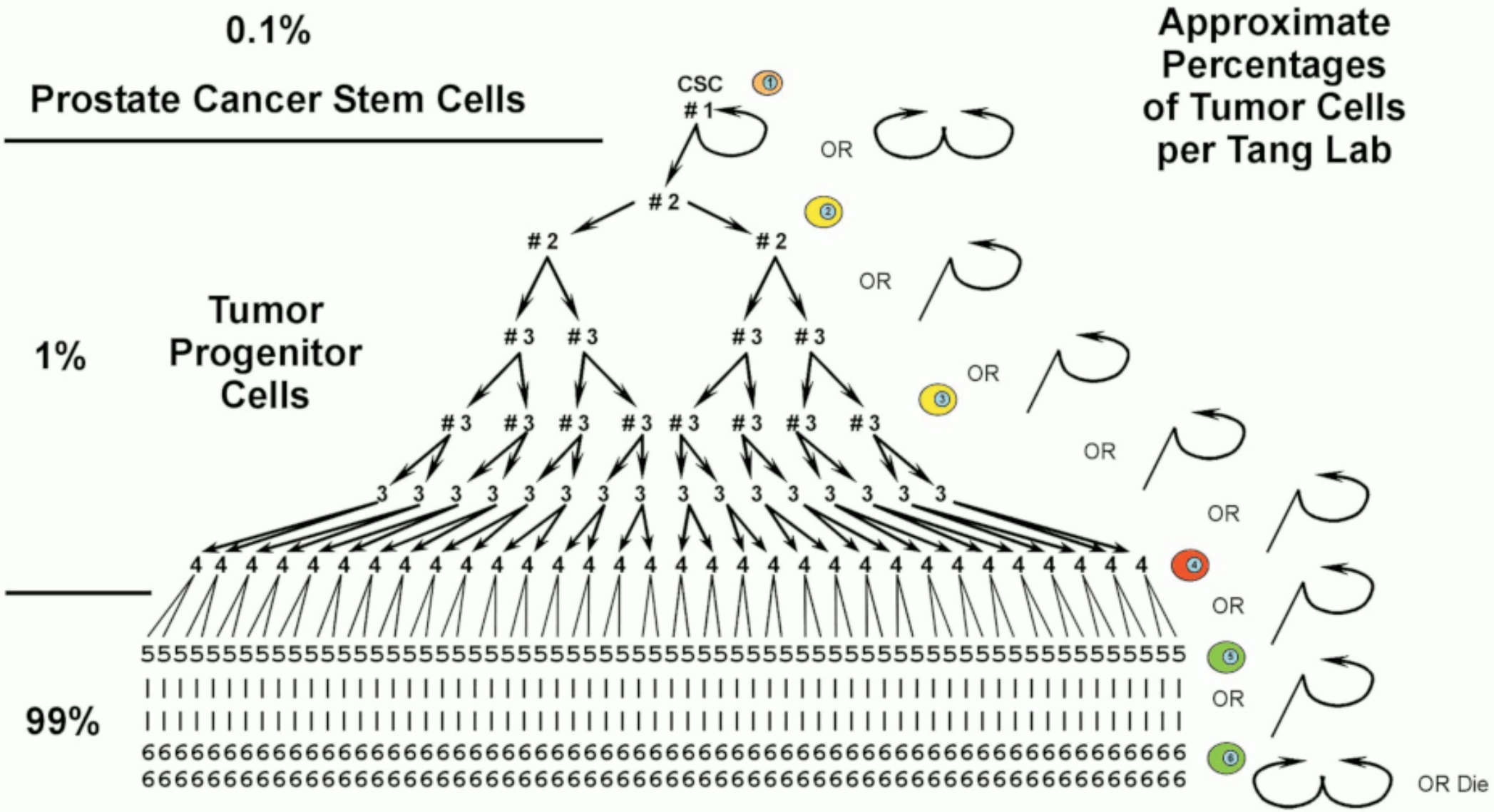
Tumor Progenitor Cells

Sixty-four #5 PCa PSA+ cells divide spawning 128 Type #6 AR+ PSA+ PCa cells

99%



Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells


0.1%
Prostate Cancer Stem Cells
Approximate Percentages of Tumor Cells per Tang Lab
CSC
#1
OR
#2
#2
#2
OR
1%
Tumor Progenitor Cells
#3
OR
OR
OR
OR
OR
OR
OR Die
99%
Androgen Receptor Expressing & PSA Producing PCa Epithelial Cells

Honorio et al., Figure 1 - Cartoon showing the general structure of a human prostatic gland.

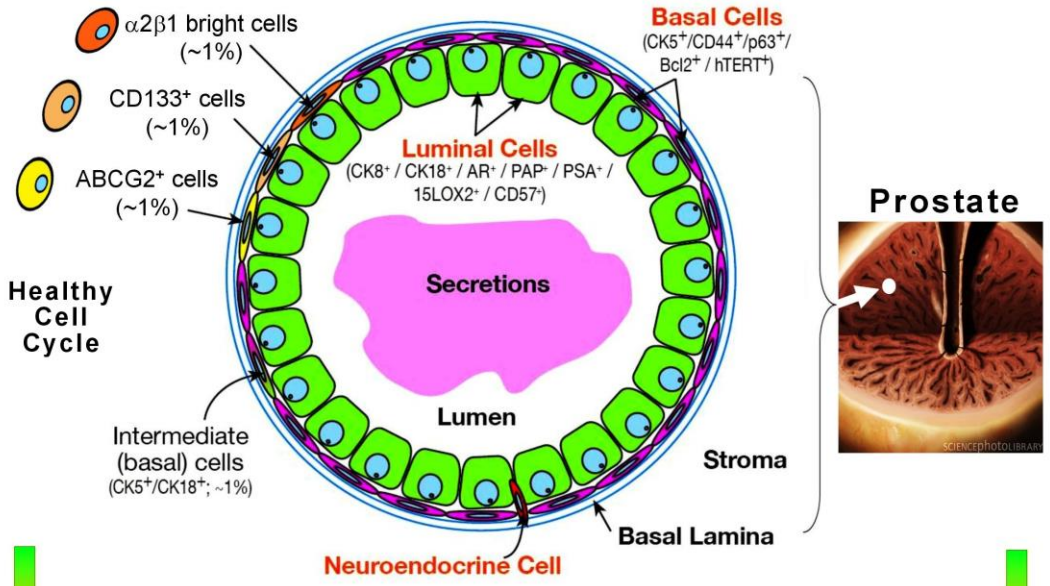
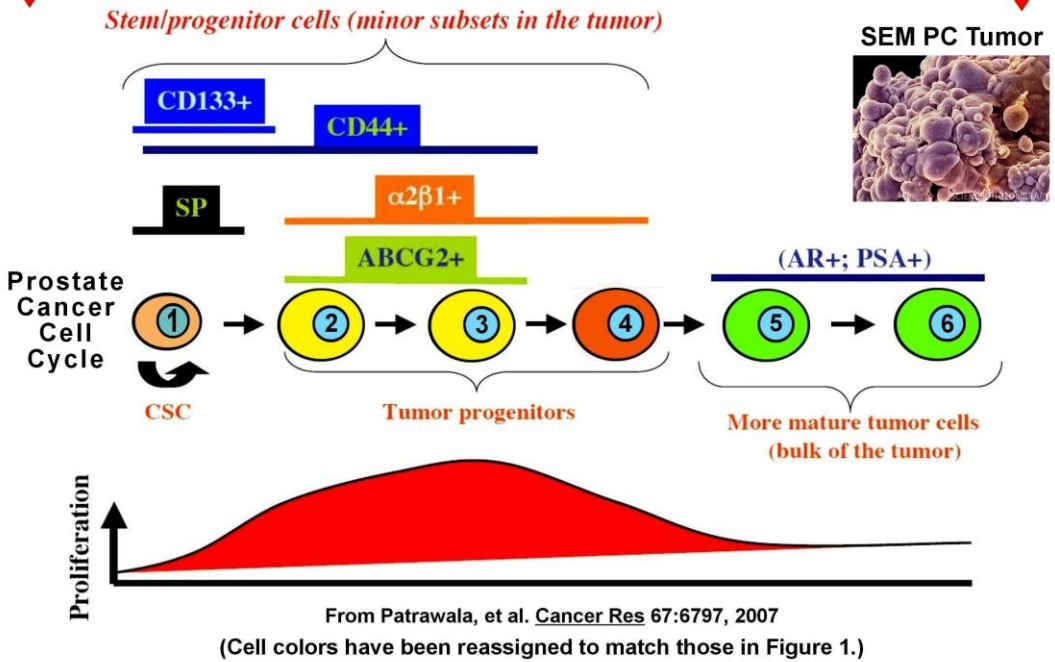



Figure 2. Schematic depicting the tumorigenic hierarchy of tumor cells in xenograft tumors.




From Patrawala, et al. Cancer Res 67:6797, 2007

(Cell colors have been reassigned to match those in Figure 1.)

# Appendix

# SO WHICH IS IT ?

| Objective Fact | Theory and/or Hypothesis | Opinion |
|---|---|---|
| **305 distinct cells and countable on a slide looking at 100x** | **Chemical Z @ 30 mg/kg of body weight should slow PCa growth rate** | **Patients should be treated with chemical Z (medical opinion)** |
| **The patient missed their morning dose of drug Z** | **Missing one dose should not matter due to fat storage of chemical Z** | **Do not double the next dose for safety (medical opinion)** |
| **PSADT was 4.2 months using exponential curve fitting over last 12 months of PSA test data** | **After missing one dose, it is critical to double the next dose of chemical Z** | **Double the next dose to maintain treatment (medical opinion)** |
| **PSA was undetectable @ < 0.01 ng/ml for the tenth month in a row** | **Z taken with Y can increase response by 4 x vs. Z alone** | **30 mg/kg is a safe and effective dose for Z (FDA opinion)** |

# PROSTATE CANCER TOPICS 10-14-2019