

IMS Aloquium · Keynote Address · Dr. Angel Alvarez

1998

2023





Dr. Angel Alvarez, PhD

- Director of Northwestern Stem Cell Core
 - PhD, Biomedical Sciences, University of Central Florida
 - Certificate in Life Science Entrepreneurship, University of Alabama at Birmingham
 - BS, Biological Sciences, University of Illinois at Chicago
- IMSA Class of 1998
- Unique role, perspective on academia
- Overcame setbacks early on in career



Clouds and Rainbows



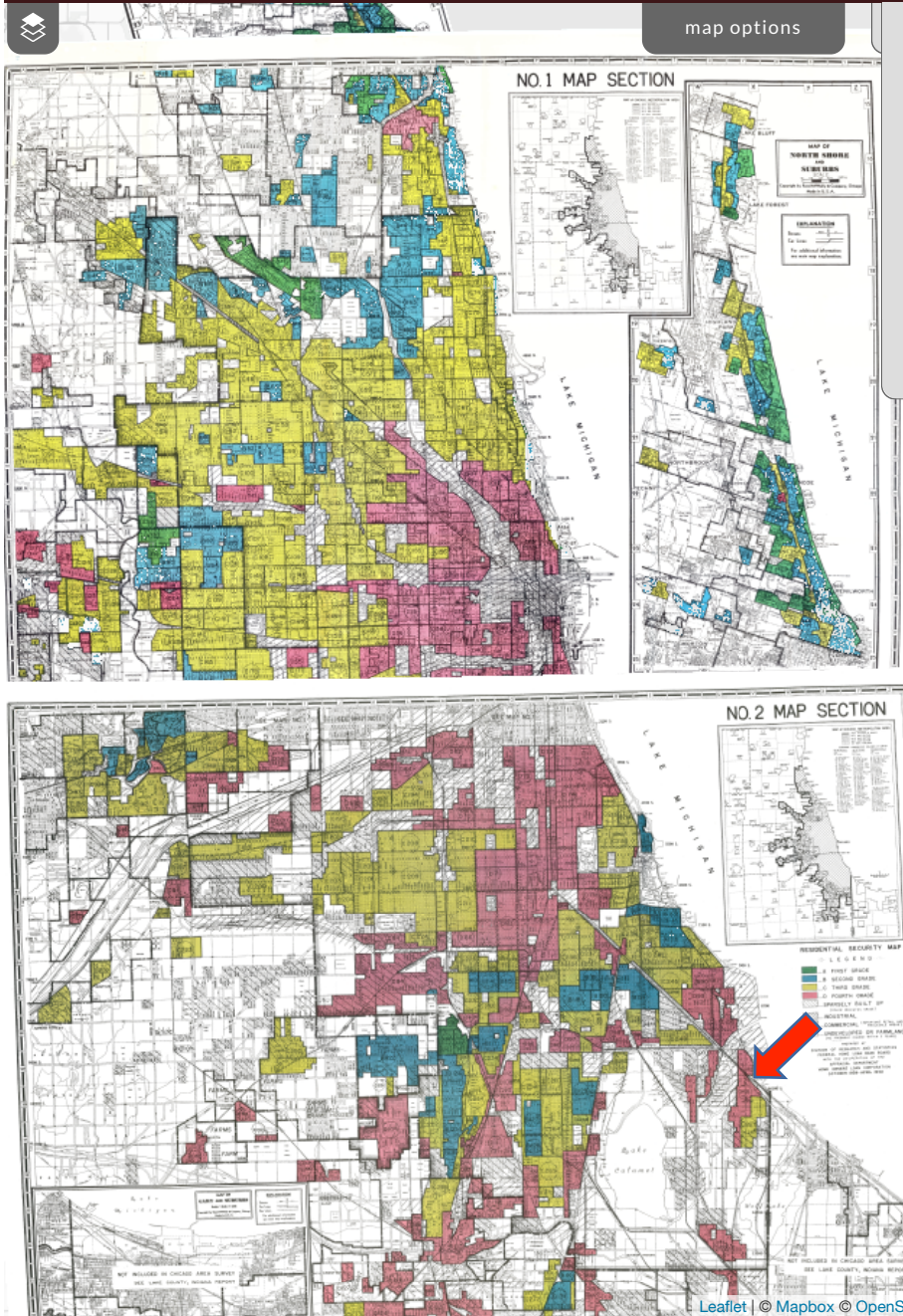


Rainbows are beautiful



Developmental Potential





Developmental Potential

What are meant to do with our lives?
Who decides?

What does it mean to be undesirable,
dangerous, hazardous?

A new beginning at IMSA

What did IMSA mean to me?

What were the costs?

What opportunities I was given?



SIR

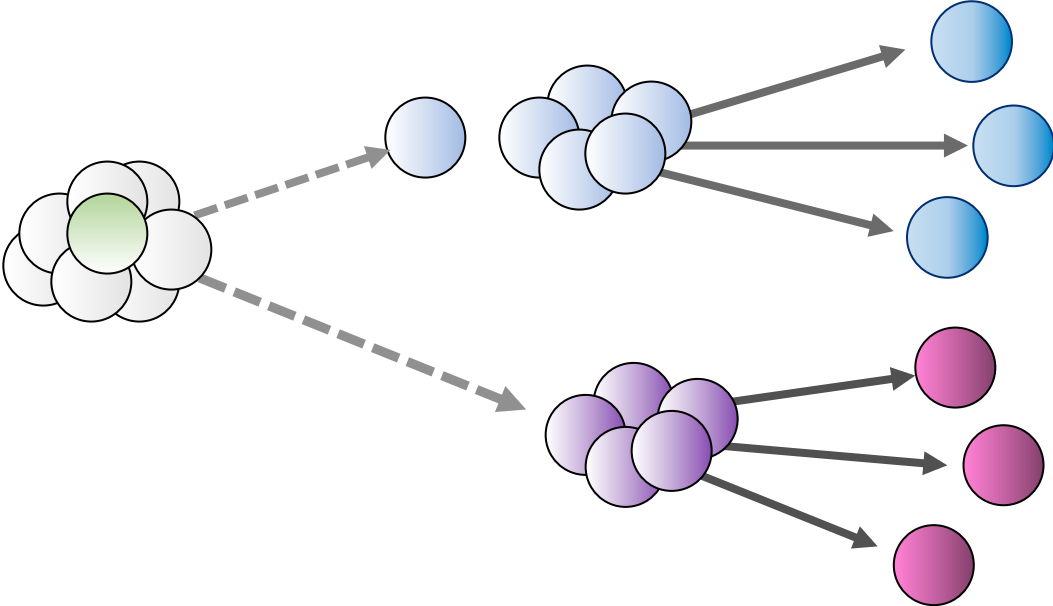
Dr. Ilangoan

Cook County and a place
to stay

The ability to apply
knowledge



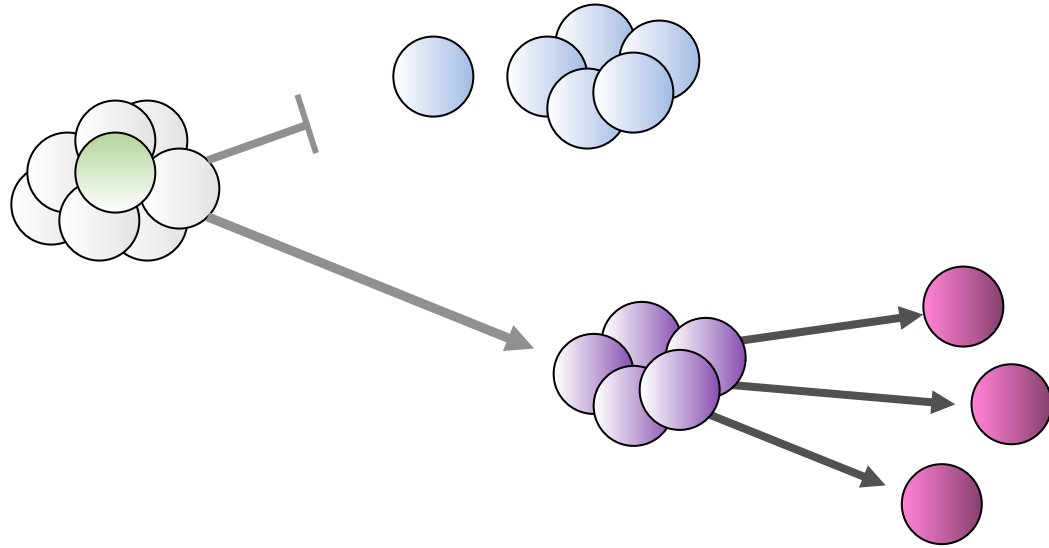
Developmental Potential



Stem Cells:

- Perpetual self-renewal
- Pluripotency

Developmental Potential



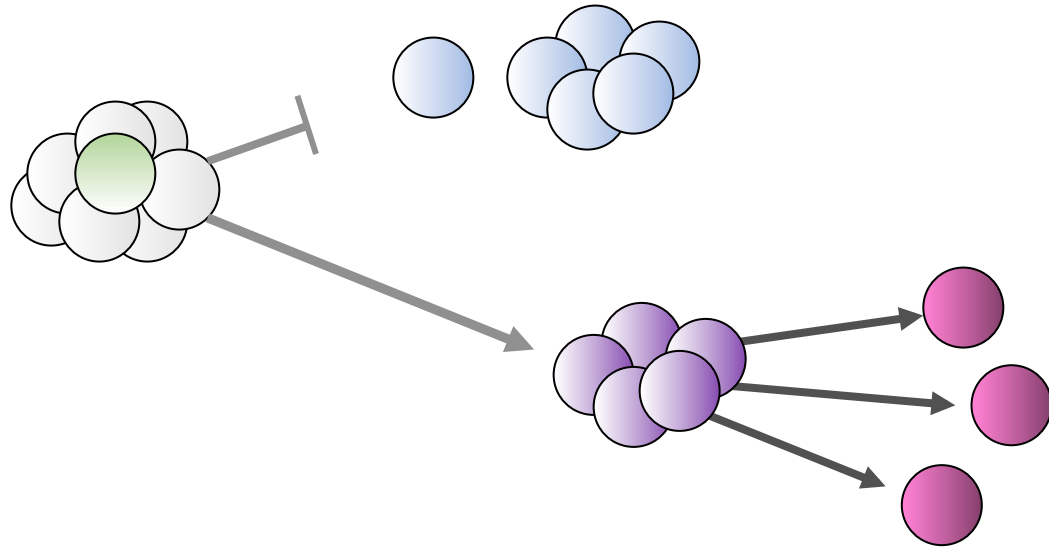
Stem Cells:

- Perpetual self-renewal
- Pluripotency

Differentiation:

- Development toward a specialized cell fate
- Results in the loss of “stemness”

Developmental Potential



Stem Cells:

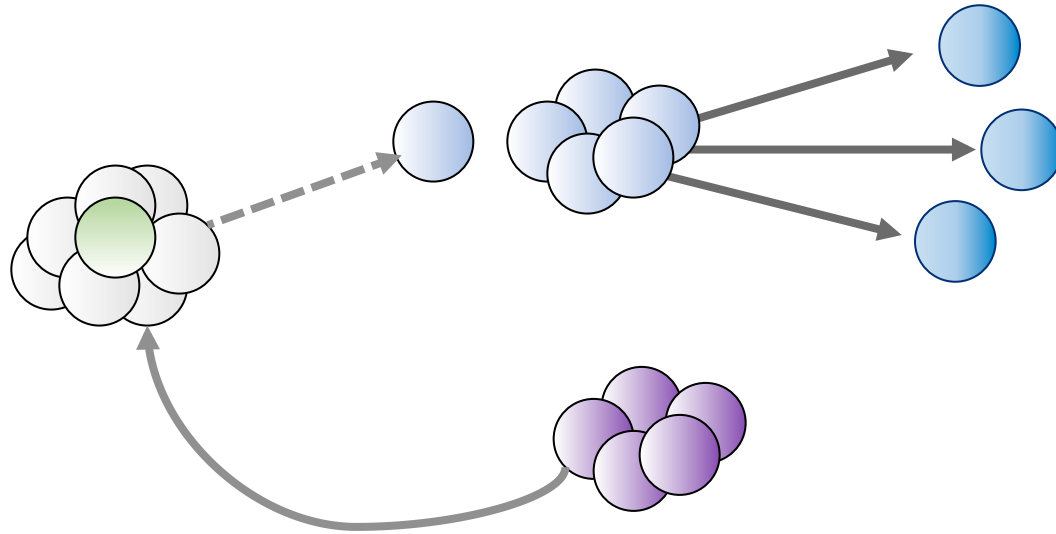
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Differentiation:

- Development toward a specialized cell fate
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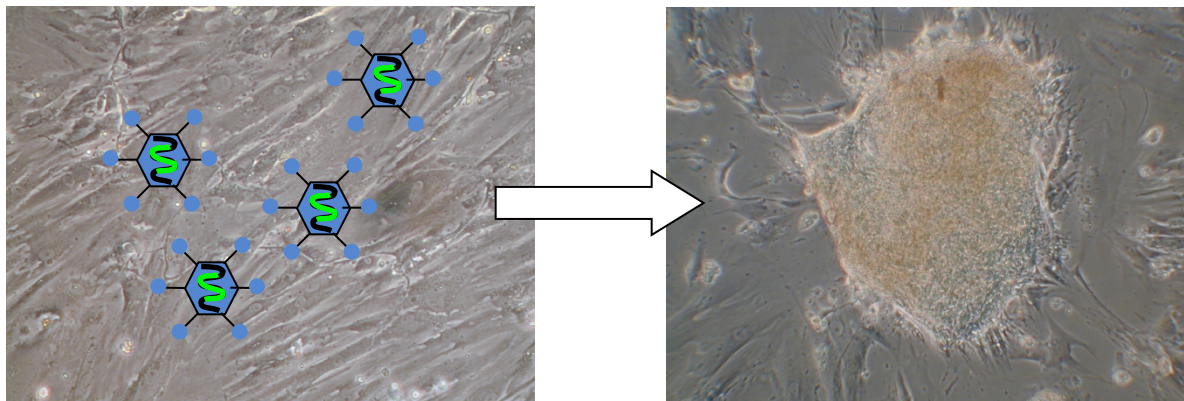
Specialization comes at the expense of developmental potential.

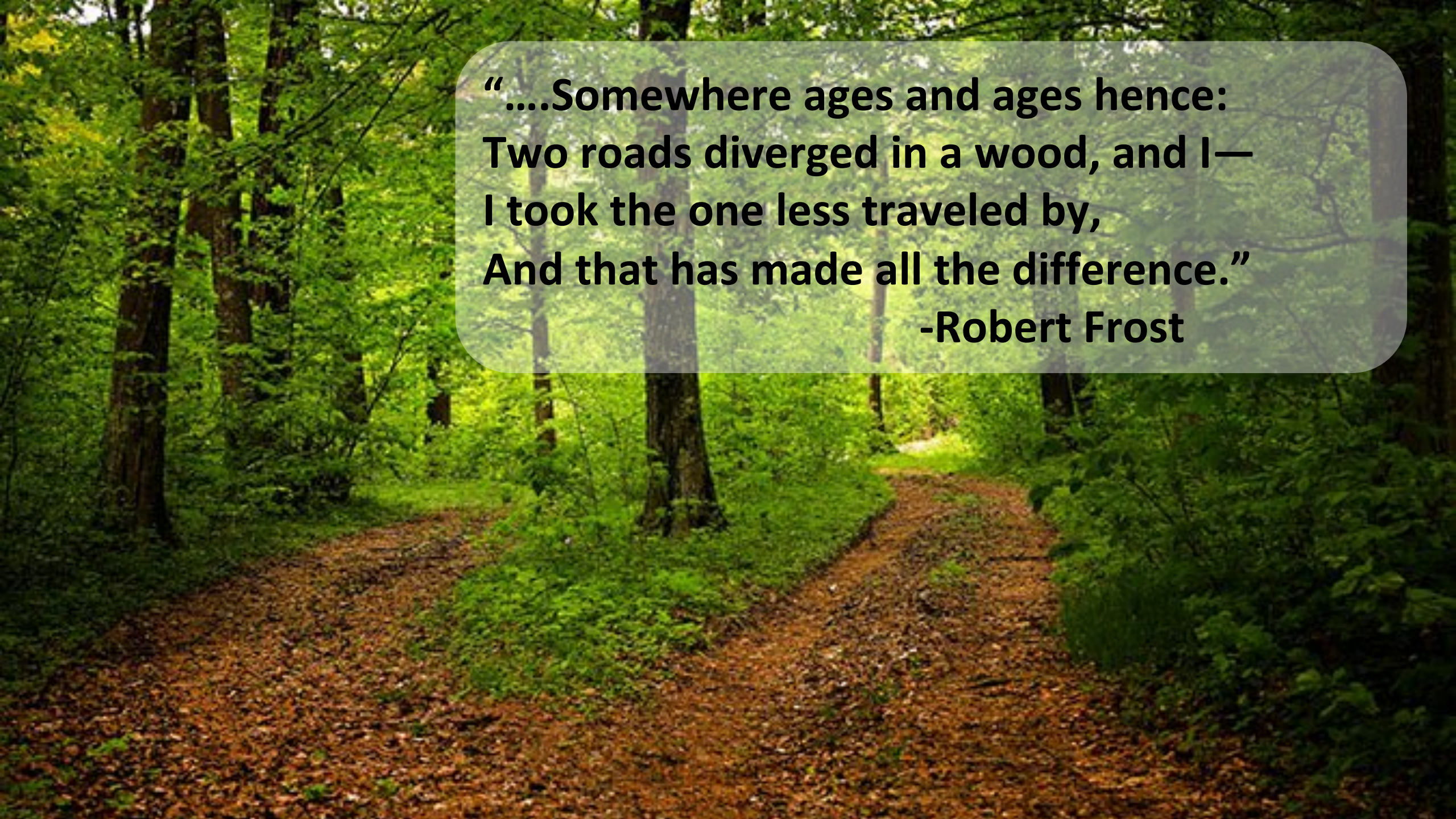
Developmental Potential



Can we alter cell fate by inducing pluripotency?

- 2003 the gene **nanog** is identified
- We believed we could expand the pluripotency of cells by **reactivating stem cell pathways**
- Promising early results
- Switched from medical school to graduate school in 2004

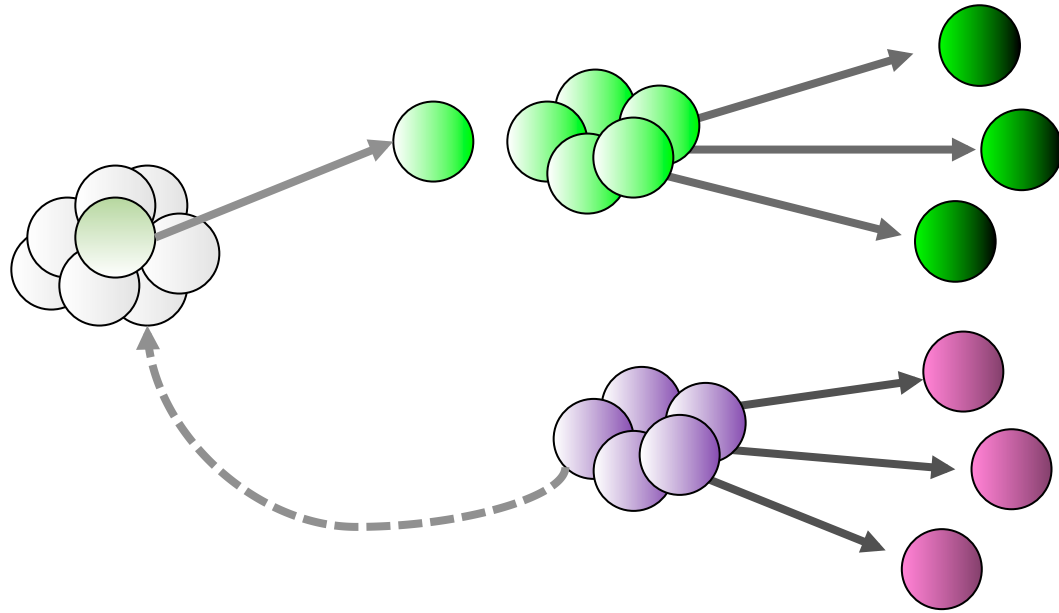


A photograph of a forest path. The path is covered in fallen brown leaves and splits into two directions. The trees are lush green, and the scene is brightly lit, suggesting a sunny day. The text is overlaid on a semi-transparent grey box in the upper right quadrant.

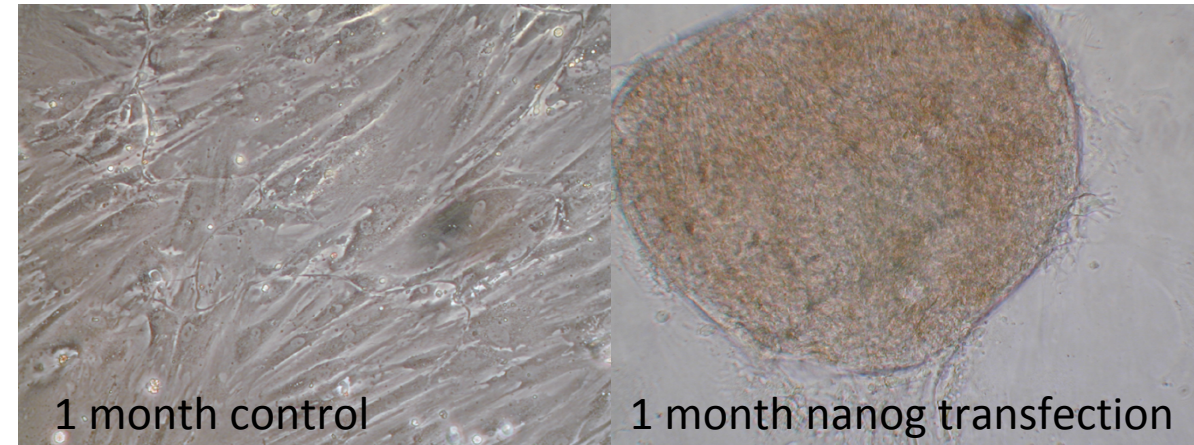
**“....Somewhere ages and ages hence:
Two roads diverged in a wood, and I—
I took the one less traveled by,
And that has made all the difference.”**

-Robert Frost

Developmental Potential

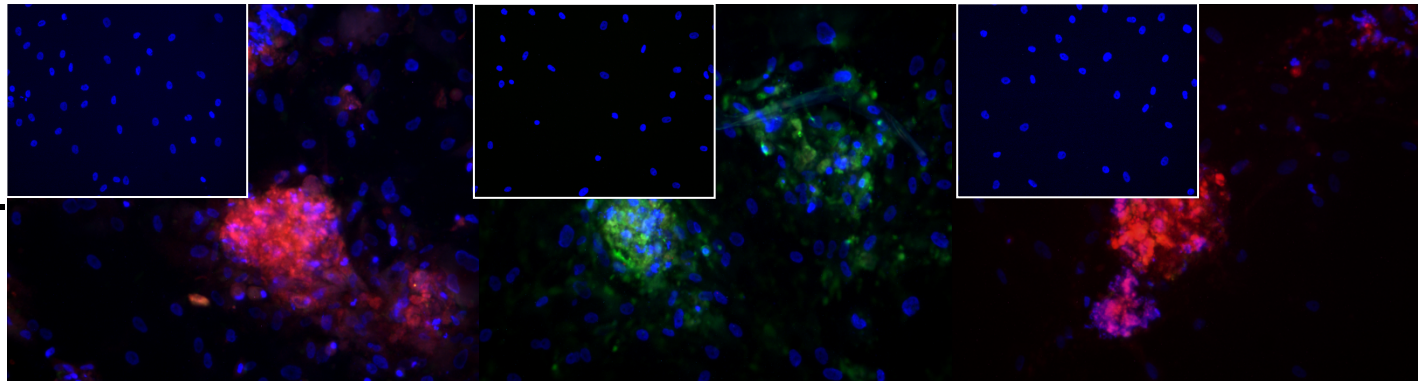


Nanog *Expression* ESC-like phenotype

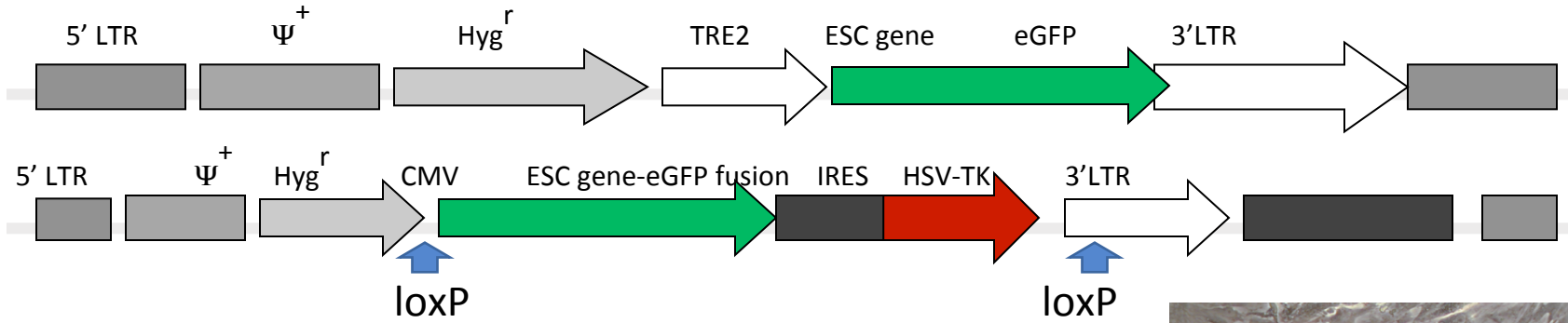


Induced expression of Nanog:

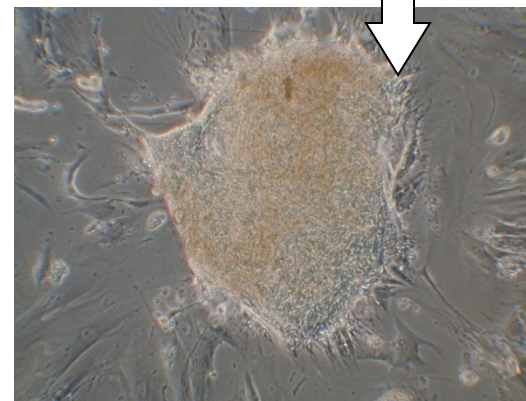
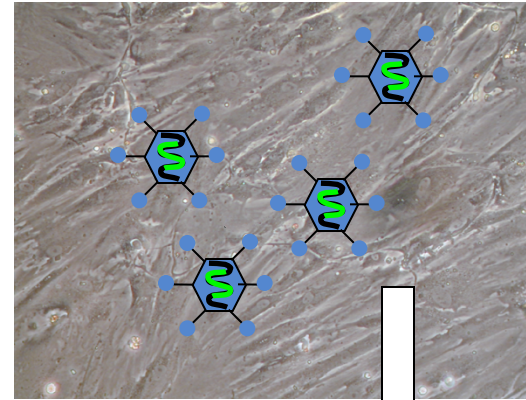
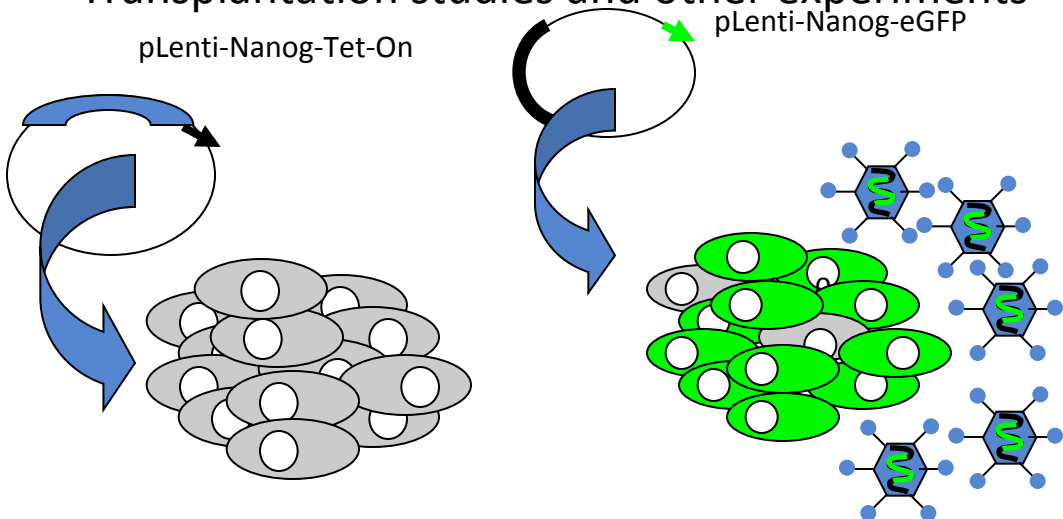
- Cells more readily expand
- Cells express OCT4, SSEA4, SOX2, etc.
- Selection and expansion a challenge



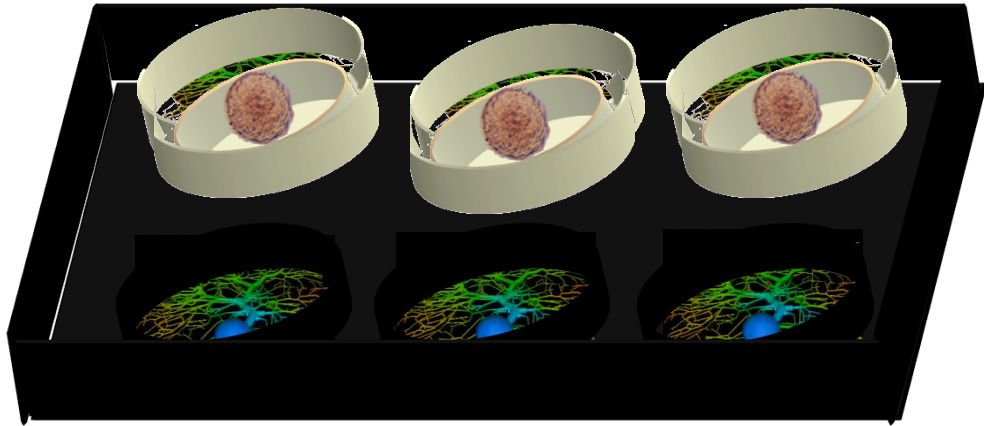
Lentiviral Vectors



- Select out Nanog/other ESC genes-eGFP+ cells
- Examine dose-dependent effects of Nanog
- Examine changes in cell cycle dynamics
- Remove gene with Cre-recombinase
- Transplantation studies and other experiments



Neural Commitment Process



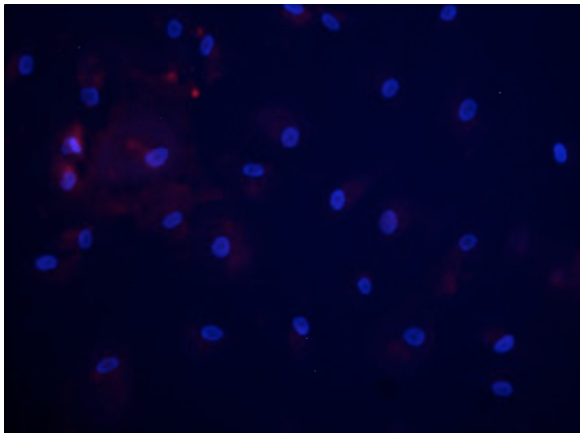
Pluripotent cells placed atop semi-permeable membrane

- Exchange of factors
- Prevents direct contact

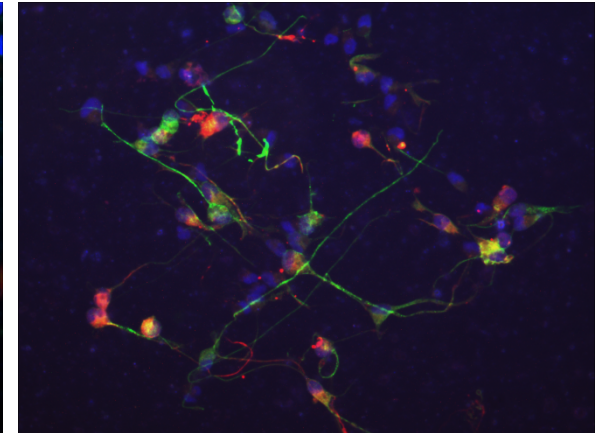
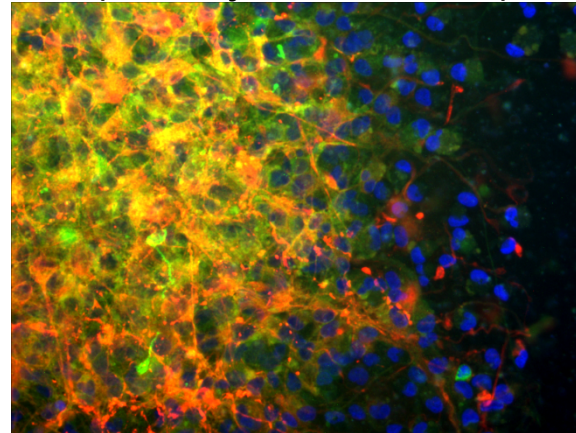
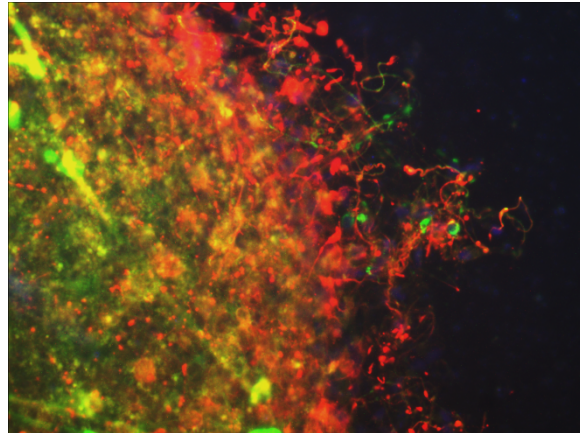
Feeder layer of differentiated neurons and astrocytes



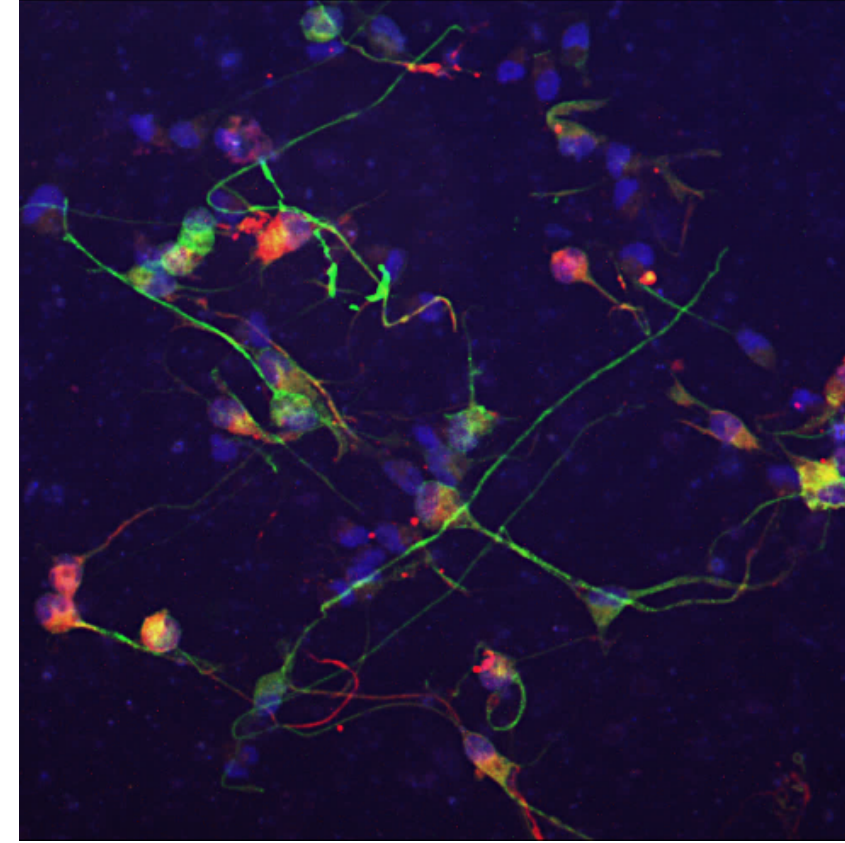
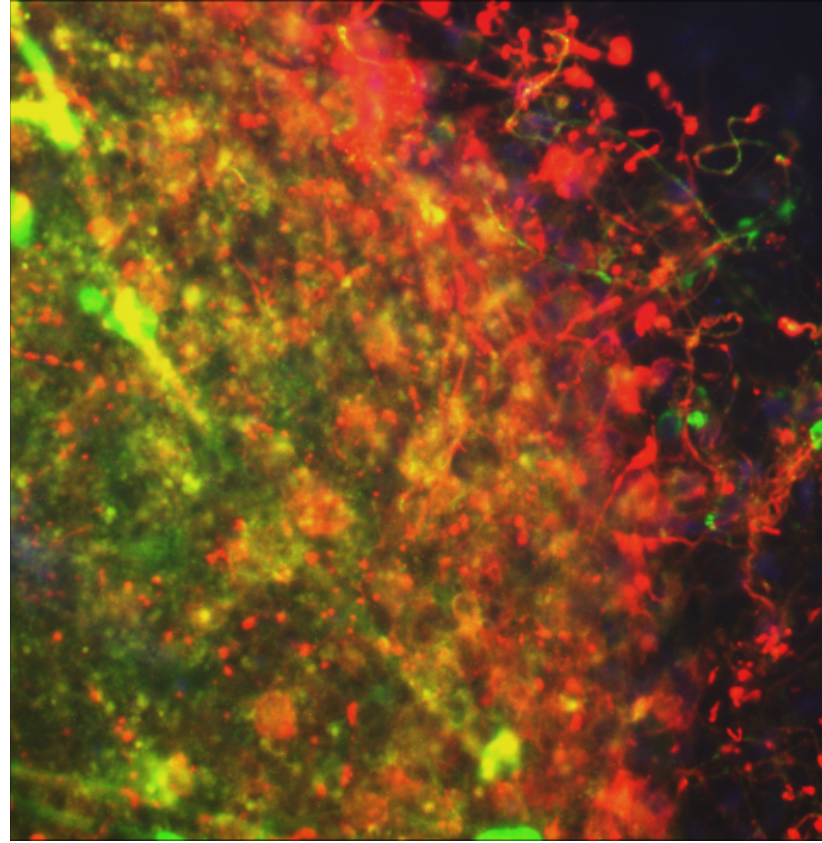
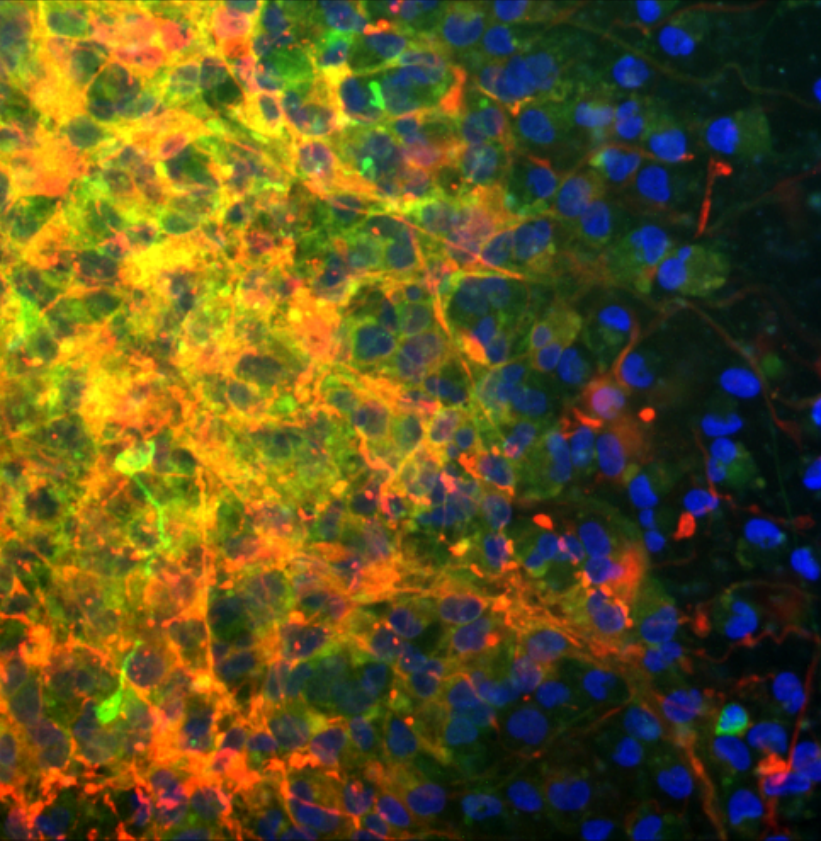
Control



Differentiated stem cells (10 days co-culture)



Red: GFAP (astrocytes), Green: β III-tubulin (neurons)



Neural Commitment Process

Red: GFAP (astrocytes), Green: β III-tubulin (neurons)

New Research Focus in late 2007....



Yamanaka lab, 2007: Based on their work creating mouse iPS cells, the Yamanaka lab was able to create human iPS cells for the first time using retroviral transduction of 4 key factors:
Oct3/4, Sox2, Klf4, and c-Myc.

Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,¹ Koji Tanabe,¹ Mari Ohnuki,¹ Megumi Narita,^{1,2} Tomoko Ichisaka,^{1,2} Kiichiro Tomoda,³ and Shinya Yamanaka^{1,2,3,4,*}

Cell 131(5): 861-872, 2007.

Awarded the Nobel Prize in Physiology / Medicine, 2012



Almost simultaneously, the Thomson lab (Madison WI) based their work on Yamanaka's successful mouse iPS creation, and were able to create human iPS cells using lentiviral transfection of 4 factors: **Oct3/4, Sox2, Nanog, and Lin28.**

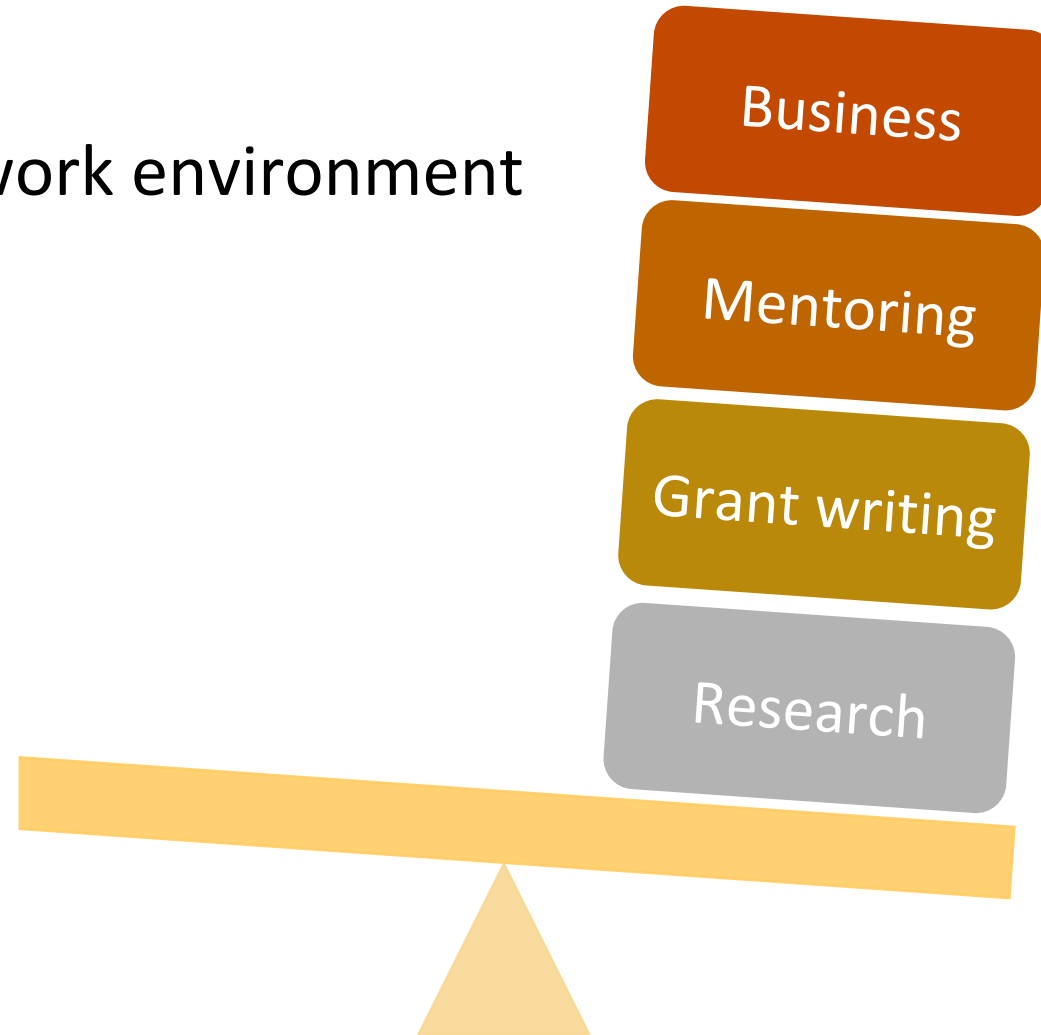
Induced Pluripotent Stem Cell Lines Derived from Human Somatic Cells

Junying Yu,^{1,2*} Maxim A. Vodyanik,² Kim Smuga-Otto,^{1,2} Jessica Antosiewicz-Bourget,^{1,2} Jennifer L. Frane,¹ Shulan Tian,³ Jeff Nie,³ Gudrun A. Jonsdottir,³ Victor Ruotti,³ Ron Stewart,³ Igor I. Slukvin,^{2,4} James A. Thomson^{1,2,5*}

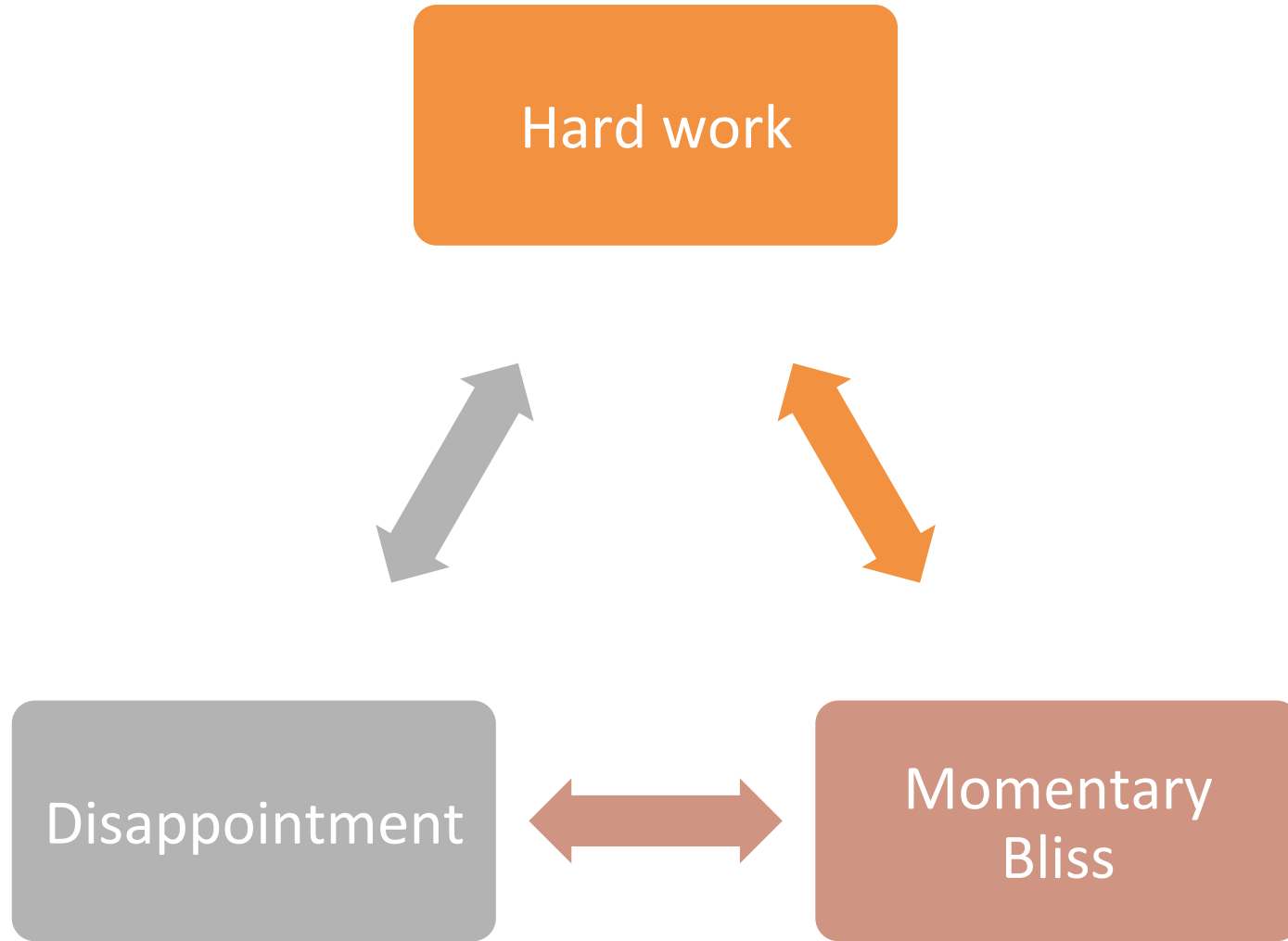
Science 318(5858): 1917-1920, 2007

PhD Personally

- Early success
- Increasingly problematic work environment



Why do
people
leave
academia?



“3 strike” culture of exclusion



Underrepresented group,
minority background



Setbacks: primary caregiver,
illness



Lack of support, resources

Life Happens

Dissertation committee, postdoc at Northwestern



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graph TD; A[Dissertation committee, postdoc at Northwestern] --> B[Car accident, medical withdrawal]; B --> C[Concurrent PhD in Alabama, eventual graduation]; C --> D[Loss of postdoc due to paternity leave]; D --> E[Primary caregiver for daughter];
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Car accident, medical withdrawal

Concurrent PhD in Alabama, eventual graduation

Loss of postdoc due to paternity leave

Primary caregiver for daughter

Encountering setbacks

- Negatives:
 - Personally distracting, upsetting
 - Effects on productivity, reputation
 - Underestimation of its effects
- Positives:
 - Juggling multiple tasks
 - Prioritization
 - Perspective
 - Resilience



Run your own race

- Be realistic
- Find ways to stand out
- Seek out support
- Ask what will make you happy

Thank You

Stem Cell Signaling Regulates GBM Phenotype

**T32 Training Program in Brain Tumor Biology (Graduate Student) and
T32 in Signal Transduction in Cancer Presentation (Postdoc)**

What is cancer?

seed vs soil

What is cancer?

seed vs soil

