

## Session 6: Integrative application II

# Gene editing

Instructor: Guo Xu

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Setting the pace of progress – Innovation and the search for the good life



# Keeping us on track...

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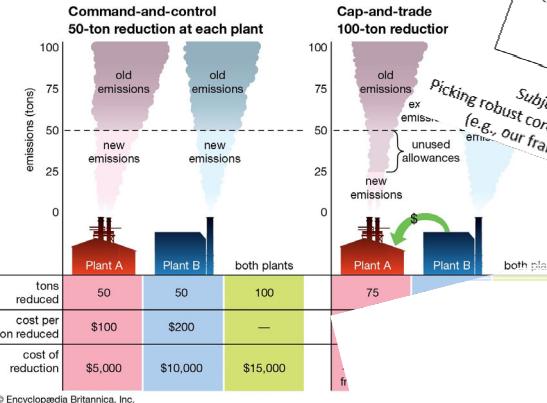
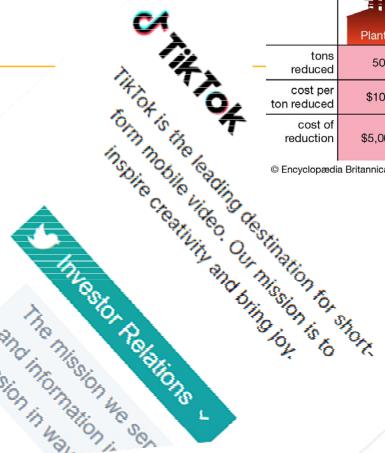
- **Assignment 4:** Great job!
  - Finalizing grades – will release them shortly
- **Ungraded assignment 5 (Just Supply Chains)**
  - To be covered in 4/26 GSI section tomorrow
- **Assignment 6 – graded and optional (bonus 5%)**
  - Individual assignment, due before next class
  - Groups who present get extension
- **Selected groups:** short presentation for next class

# Plan for today's session

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- Recap
- Case: Gene editing
  - General discussion
  - Group work
  - Share findings
- Closure – only for now...
- Course evaluation

# Part I: Recap



**theranos**



**Accountants Caught in E-mail Chain Rating Female Employees**

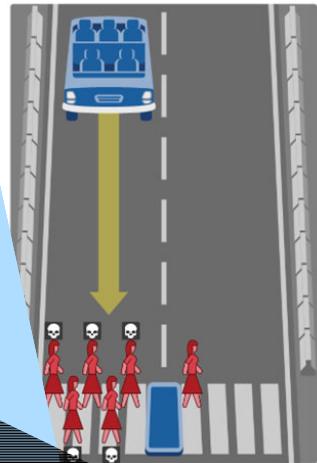
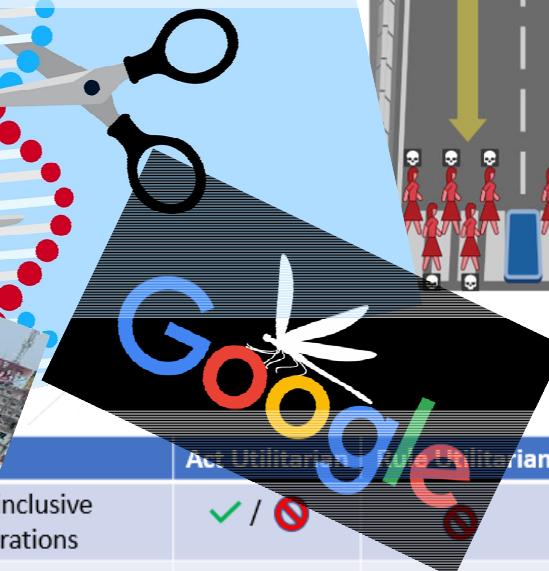
By MARY PLUMMER  
LONDON, NOV. 11, 2010

Ethical failures

Rationalization  
e.g., Moral disengagement, group pressure, slippery slope

Opportunity  
e.g., privileged relationships, opacity of new tech, private firm

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	Act Utilitarian	Duty Utilitarian	Duty Ethics
Non-inclusive celebrations	✓ / ✗		
Employer sponsored work-related celebrations		✓	✓
Employee sponsored work-related celebrations	✓	✓	✓

# Recap

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- **Limits to self-interest** as organizing principle
  - Bad leadership instills unethical culture & negative mutual expectations
  - Good leadership takes ownership of a collective problem and takes steps to resolve it
- We have **moral instincts** – these can be tricky
  - Shaped by traditions & emotions that vary with time and place
  - Instincts include self-serving bias, moral disengagement

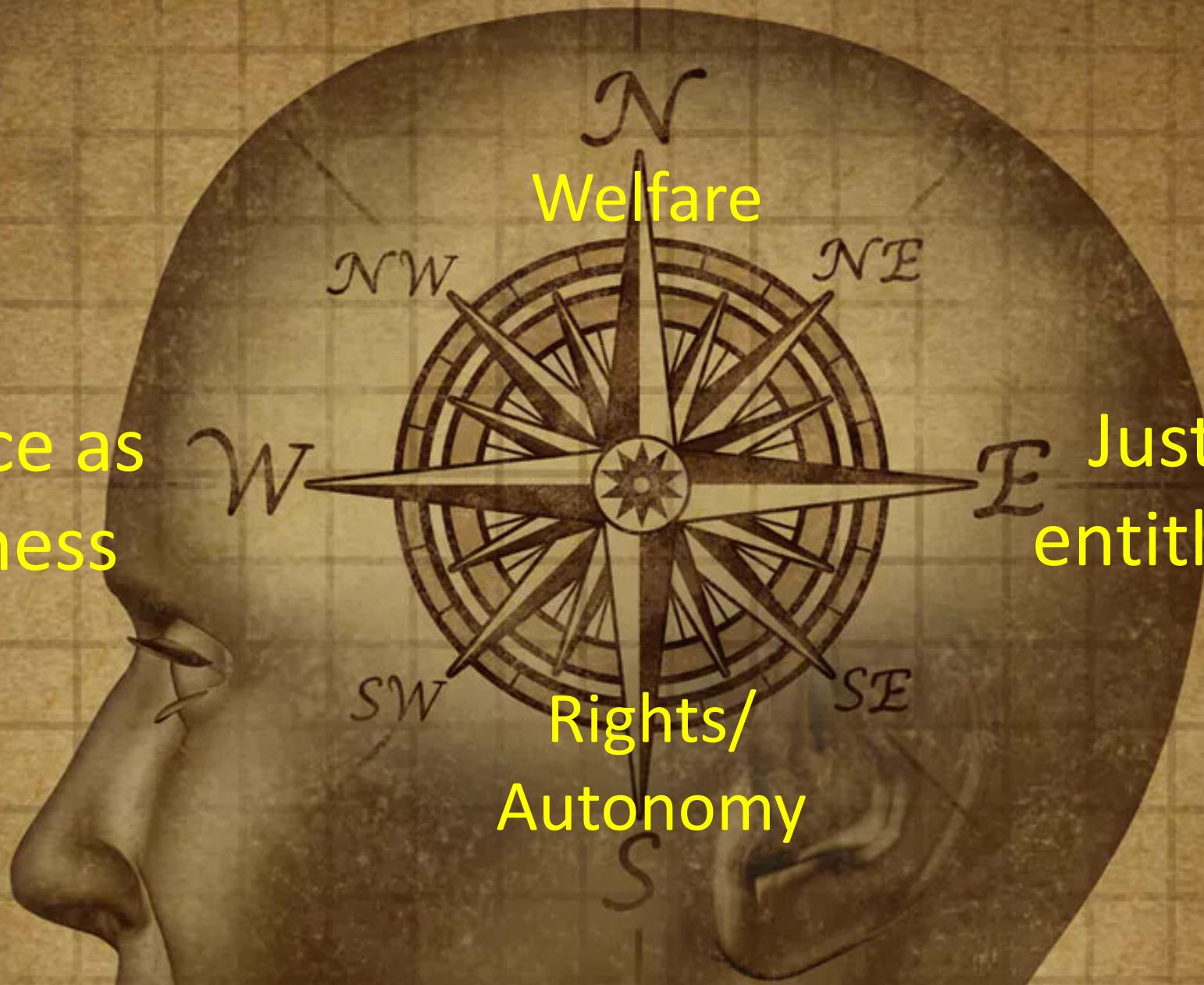
# Recap

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- Key hurdle in attaining satisfactory moral compass:
  - Absolute (one size fits all) vs relative values (anything goes)
- **Instead:** consider values that do well in a *tournament of moral ideas*
  - Ethical frameworks with core values of greater good, rights, dignity, justice
    - Ultimate reasons why we value more proximate traits such as transparency, honesty, loyalty
    - *Minimal assumptions, satisfy interchangeability of perspectives*  
- makes them good common ground to build agreements

Justice as  
fairness

Justice as  
entitlements



Frameworks to help develop a position on new challenges

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# Ethics – a portable toolkit

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1. Roadmap to ethical decisions
2. Values scorecard
3. Structure of ethics arguments
4. Guiding ethics discussion
5. Quick scorecard generator

# Recap



- Organizations, for profit or not, have a **specific purpose** linked to satisfying social needs
  - Purpose is value creation, not always equal to profit
  - Actions are justified by purpose, not profits
- A theory of CSR
  - Ethics-based profit restraint when markets and governments have failed
    - Not philanthropy, not PR

# Skill acquisition

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- Analytic **habits** from repeated use of frameworks
  - Identify relevant dimensions: welfare impacts, vulnerable parties, entitlements, instances of consent
- Identify **incentive structure**
  - Harmony game or prisoner's dilemma?
  - Ransom, coercive transactions, power dynamics
  - Coordination problems

# Skill acquisition

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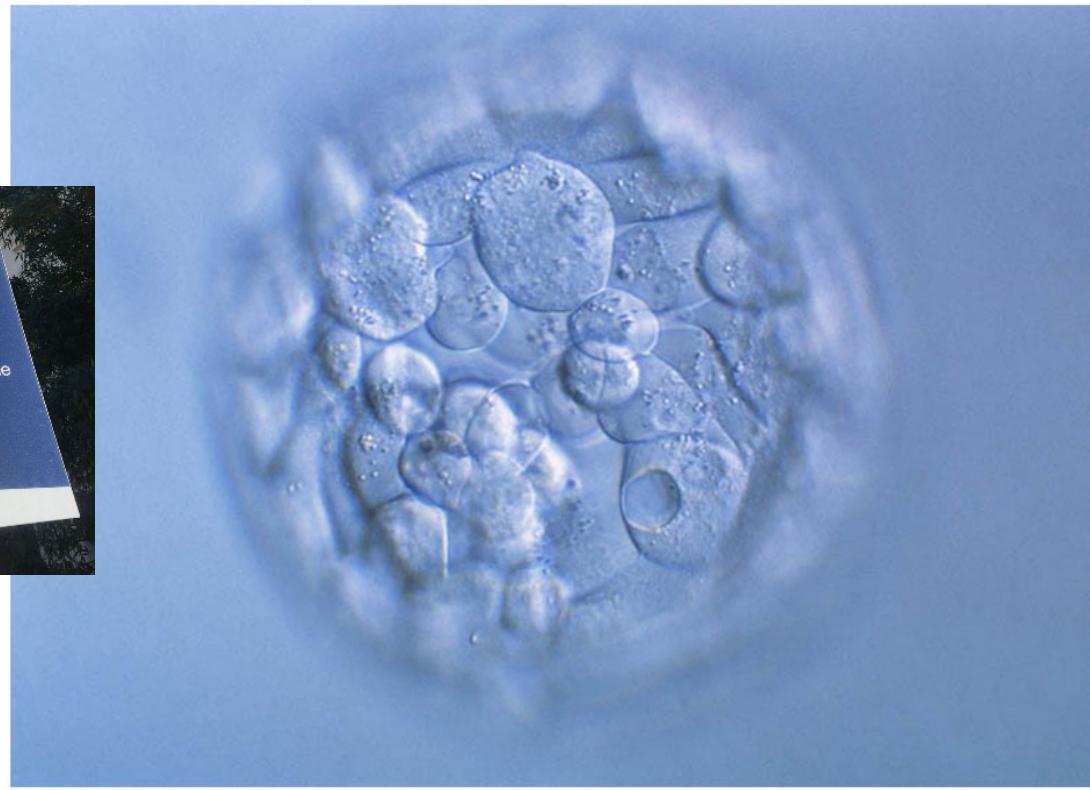
- Identify ways in which we morally disengage
- Check our *emotions*
- Check our *assumptions*
- Break down problems along relevant dimensions
  - Helps structuring good arguments, and
  - Facilitate otherwise difficult conversations

# Part II: Case



# Case: The (Selfish?) Gene Editor

- Key case facts



A Chinese scientist claims that twin girls have been born whose genomes were edited at the embryo stage. Credit: Pascal Goetgheluck/Science Photo Library

# Poll

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- “Editing human genes involves *manipulating nature*, is akin to ‘playing God’ and concerning.”
- A: Strongly agree
- B: Agree
- C: Neutral
- D: Disagree
- E: Strongly disagree

# Implications of Dr. He's CCR5 “surgery”

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- Replacing *CCR5* with existing *CCR5-Δ32* mutation
- Potential **positive** consequences (and business opportunity):
  - Immunity from HIV, faster recovery from stroke, enhanced cognition / memory, lower risk of metastatic breast cancer?
- Potential unintended **negative** consequences:
  - Higher risk of severe reaction to West Nile, Dengue Fever, Yellow Fever, Influenza, Multiple Sclerosis
  - Other “unknown unknowns”

# General risks of CRISPR gene edits

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- **Risk of mismatches:**
  - Cas9 targets sequence of 20 nucleobases, cuts if match
  - But sometimes also cuts with a match of only 1-17 (ignoring 18-20)
- **Risk of mutations at the site of cutting:**
  - After cutting, cell repairs DNA and can miss bases or “glue” back in the wrong place—so complete “cuts” can cause further problems
- **Risk of “mosaicism”:**
  - Only certain germ cells edited, others not
  - So future individual could be 40/60 edited/not-edited
- But researchers are gradually developing solutions:
  - Synthetic Cas9; “Dead Cas9”

# Case: The (Selfish?) Gene Editor

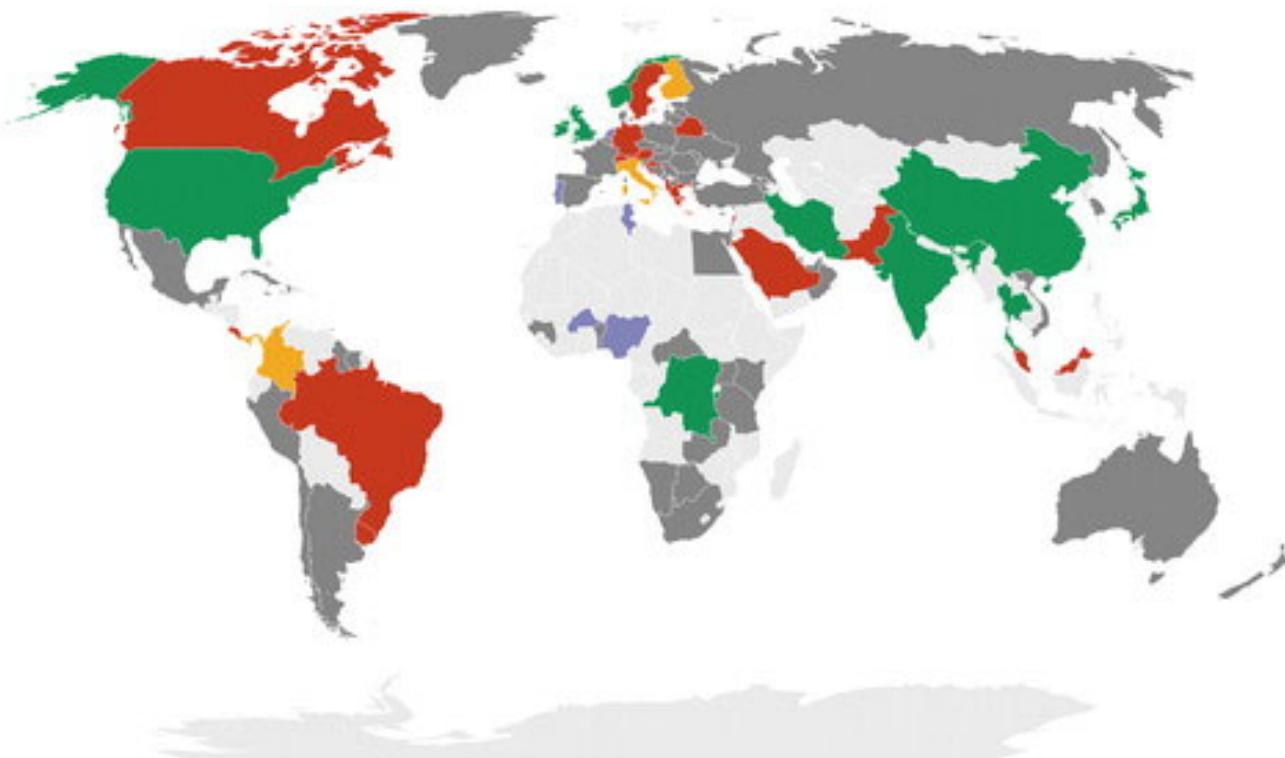
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- Key case facts
- Dr. He's possible paths?
  - What is the right policy approach?



A Chinese scientist claims that twin girls have been born whose genomes were edited at the embryo stage. Credit: Pascal Goetgheluck/Science Photo Library

# Gene editing – a regulatory gray zone



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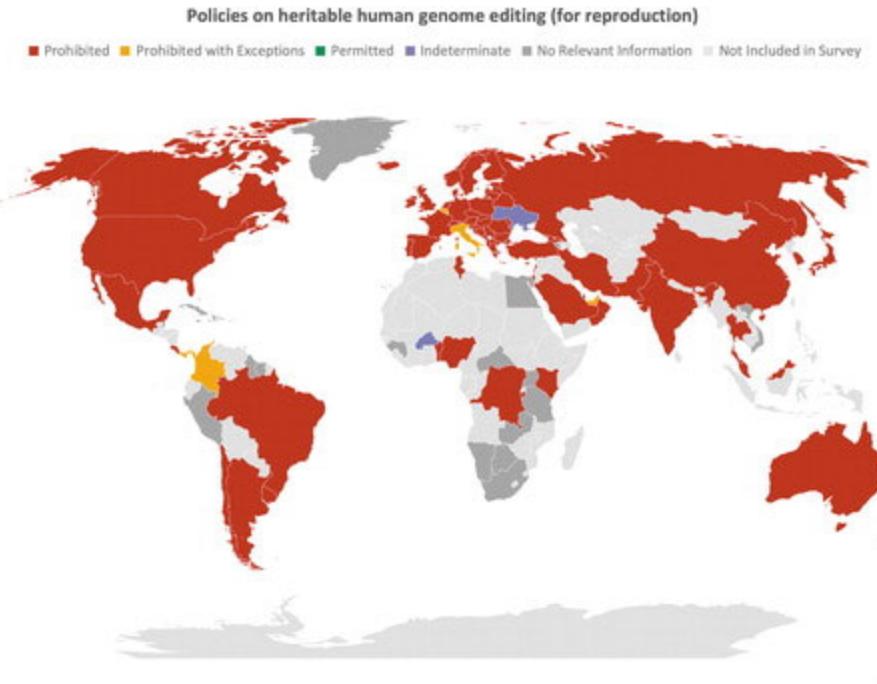
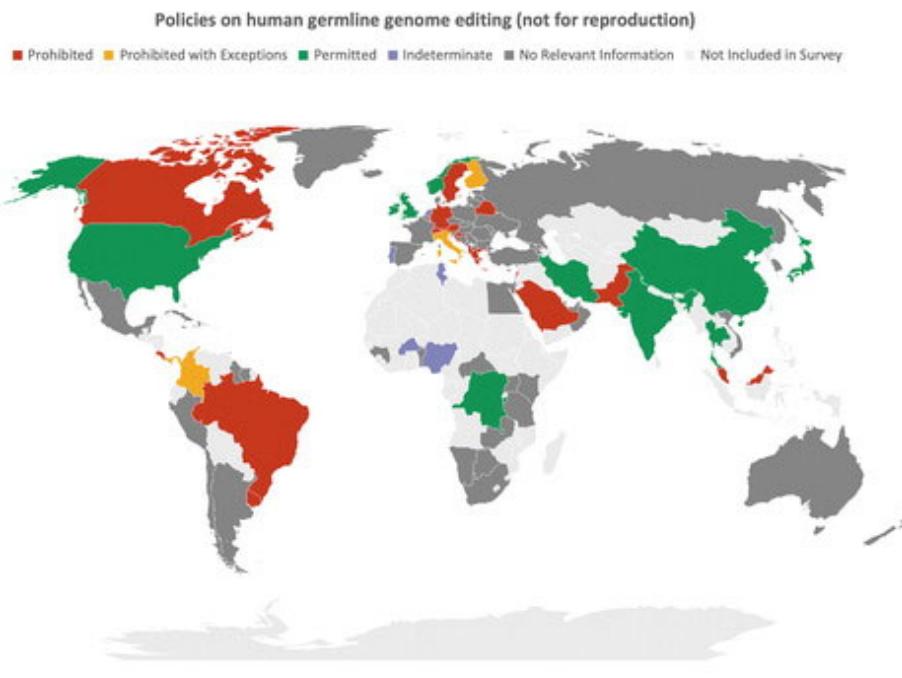
# Group discussion

- Dr. He thinks he can pull off twin babies experiment. Should he go ahead?
- A few possible “speeds”:
  1. No CRISPR research
  2. Somatic cell research only
  3. Germline research in animals + wait till risks in humans better understood, scientific consensus reached, regulation developed
  4. Germline research with nonviable embryos + wait as in 3
  5. “Full steam ahead”: gene editing with viable embryos

- Group assignment
  - Those on **my right**: Utilitarian
  - **Center**: duty ethics
  - **Left**: justice as fairness

# Ethics and law by “speed” of research

- Somatic gene editing (most permissible but highly regulated)
- Stricter (and lots of gray zones): Germline editing
  - Not for reproduction vs. for reproduction



# Epilogue (for now...)

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- **Nana**
  - One copy of *CCR5-Δ32* with 1 extra base pair
  - Other copy of *CCR5-Δ32* with 4 missing base pairs
  - May confer HIV immunity, but no one knows
- **Lulu**
  - One copy of *CCR5* (totally unedited)
  - Other copy of *CCR5-Δ32* with 15 missing base pairs
  - No HIV immunity
- **Both**
  - “Mosaicism” - some cells have edited DNA, others do not
  - Uncertainty about other potential unintended consequences
- **He Jiankui**
  - Released from prison April 2022 – seeking to relaunch career
  - Interview with the Guardian: “I did it too quickly”

# Part III: Closure



# Breathtaking innovation

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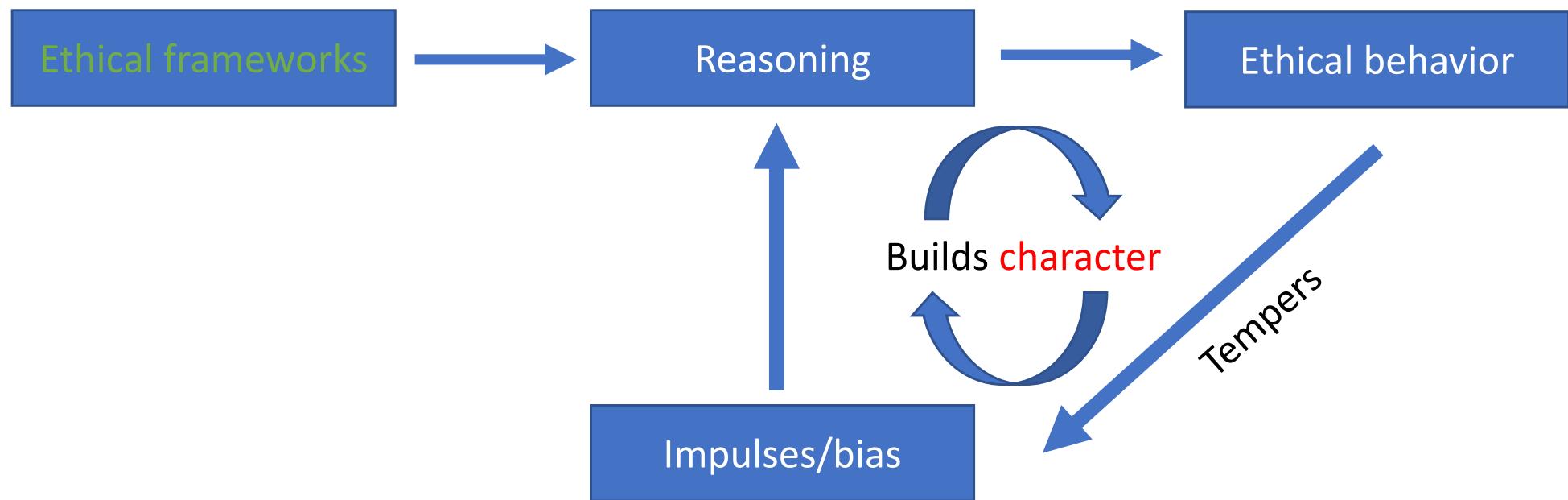
- New technologies now unlock possibilities unimaginable even a few decades ago...
- **Human gene editing**
  - Converged on emerging consensus in field of bioethics
- **Other domains:** AI, IoT, autonomous robots
  - *Ethical implications:* inequality, privacy, cybersecurity, digital addiction, non-human agency, fintech, etc
- Questions beyond strategy and legal compliance
  - We need **ethical leadership**

# Challenges to ethical leadership

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- Applying ethical frameworks is not easy
  - Psychological **biases** often cloud clarity in judgement
- Turning ethical judgements into action even harder
  - Need **courage** to speak up, manage emotions
- “**We are what we repeatedly do**” (Aristotle) – leadership requires practice and knowing...
  - ...who you want to become through your actions....
  - ...strategy for when to act (Detert)

# What is ethical leadership?



- *Ethical Leadership: ethical clarity + the character that can translate it into action*

# What Makes a Berkeley Leader?

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- Avoiding moral disengagement, taking ownership of a collective problem
- Identifying which moral failures will endanger key strategic assets and acting to avoid them
- Identifying firm's CSR, not as a luxury, but tied to organization's purpose
- Exemplifying shared values that yield successful coordination on the right goals

# What Makes a Berkeley Leader?

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- Avoiding moral disengagement, taking ownership of a collective problem
- *How do I know I must take responsibility?*
- Identifying which moral failures will endanger key strategic assets and acting to avoid them
- *How do I know which moral failures are serious?*
- Identifying firm's CSR, not as a luxury, but tied to organization's purpose
- *How do I know what is a good purpose?*
- Exemplifying shared values that yield successful coordination on the right goals
- *How do I know what are the right, inspiring, goals?*

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Ethics is how you know

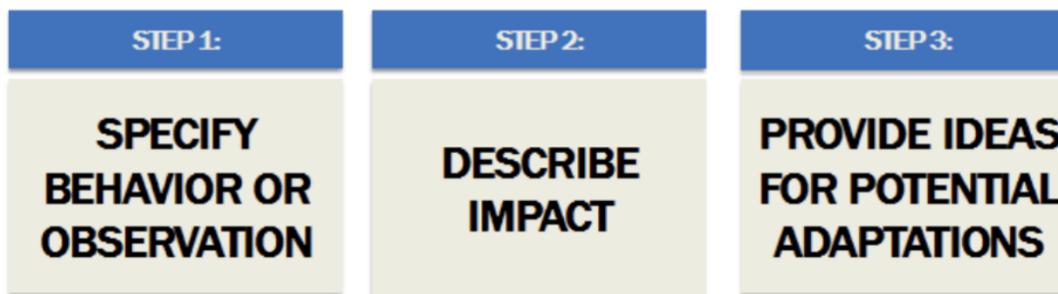
# Thank you for your feedback!

## ONLINE COURSE EVALUATION INSTRUCTIONS



- 1** Take out your mobile device and connect to the internet.
- 2** Go to the URL listed below and log in with your CalNet ID/password.  
[course-evaluations.berkeley.edu](http://course-evaluations.berkeley.edu)
- 3** If you are prompted to select a **Data Source**, please choose “**Haas-students**”, *even if you are not a Haas student and simply a student taking a Haas course*. Tap “Select” to start the survey for this course. If applicable, the GSI evaluation will follow.

### TIPS FOR PROVIDING COURSE FEEDBACK:



### Troubleshooting Tip!

*If you encounter a redirect error...*

*...switch browser to Incognito/Privacy Mode.*