Stem Cell Ethics and IP: An Introduction

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Nomenclature

- CIRM: California Institute for Regenerative Medicine
- SCRO: Stem Cell Research Oversight Committee
- IRB: Institutional Review Board
  - Ethics oversight mechanism for enforcing federal regulations for the protection of human subjects in research

Prop. 71 & CIRM

- CIRM– policies posted for public comment at <http://www.cirm.ca.gov/>
  - Proposed medical and ethical standards regs
  - Intellectual property policy for non profit orgs
  - Proposed modification to COI policy

Research Ethics Overview

After Prop. 71

- Beyond the “moral status of the embryo”
- Protection of human participants in research
- Research animal protections
- Democratization in the governance of science

Beyond moral status questions

- WHICH EMBRYOS CAN BE USED IN RESEARCH?
  - Only those left over from IVF?
  - Is it morally permissible to make embryos purely for research purposes?
  - Is there a time limit beyond which in vitro embryos acquire properties that place limits on research?

Proposed Ethics Regulations

- not eligible for CIRM funding:
  - Culture of an intact human embryo or product of SCNT after the appearance of the primitive streak or 12 days, whichever is earlier
    - Implies that the point at which individuation occurs is morally significant and my impose limits
    - Easy political compromise
- CIRM-funded research will include derivation of stem cell lines, and the regulations include protections for oocyte donors
    - Implies that creation of embryos for research is ethically permissible

Human Participant Protections

- Some covered by existing federal regulations and institutional oversight mechanisms
  - People into whom stem cells might be injected
  - Under current interp of federal regulations: Oocyte donors when oocytes are being retrieved for research
  - CIRM proposed guidelines require IRB review when appropriate

- Some might fall through the cracks of existing regulations
  - DONORS OF OOCYTES, SPERM, EMBRYOS, CORD BLOOD, OR SOMATIC CELLS FOR SNCT

Protecting Donors

- May not have provider-pt relationship with health care professionals who retrieve gametes or with scientists who create embryos
- May not ever interact with CIRM-funded researchers and may not fit the regulatory definition of a “human subject”
- May have provided cells previously for banking or for a clinical intervention with a vague permission allowing undescribed future research
- Who has legal duties to protect and respect their interests???

Oocyte Donors

- Special concerns bcs of potential serious physical harms:
  - Procedure is burdensome, often extremely unpleasant and causes morbidity
  - Moderate probability ovarian hyperstimulation syndrome (medium and long-term risk)
    - Abdominal pain, occasionally leading to renal failure and hospitalization
    - Potential future infertility
    - Low probability of death
  - Long-term consequences not well known → uncertainty

Consent For Donation

- Help oocyte donors weigh risks against benefits and their motives/values

- Ensure that all donors who contribute to stem cell research are engaged in an activity that is consistent with their deeply held beliefs and their values.

CIRM proposed consent rules

- Donors of all cells have given VOLUNTARY AND INFORMED consent.
- Minimize conflicts of interest for those offering the opportunity to donate bio materials
    - generally, the donor's treating physician cannot be the CIRM-funded researcher
    - physician performing oocyte retrieval shall not have a financial interest in the outcom eof the CIRM-funded research.
- Donor's preferences re. the uses of their material must be documented and CIRM-funded research cannot violate these preferences

Special Rules for Oocyte Donors

- Enhance the standard consent PROCESS:
  - Must provide an adequate period of time for deliberation (adequate to be determined by the IRB)
  - The researcher shall take steps to ascertain that donors have understood the essential aspects of the proposed research
  - Other???

Informed Consent Summary

- Are the CIRM propsed regs repeating the mistakes of the federal regulations
  - Too much specificity about content
  - Not enough specificity about process
- Create a record-keeping emphasis but still do much research with less-than-adequate informed consent and less-than-adequate protection from real risks?

Animal Safety Concerns…

- Injecting human stem cells into animals could create a variety of chimeras
  - Yuck factor!!! But…
    - We already make a variety of human – non-human chimeras during research
    - Beyond the yuck factor: “What is actually wrong with making chimeras???”
  - One possible problem
    - Create an organism that has human-like cognitive or emotional qualities. It’s existence could constitute a harm, or we could inadvertantly harm it in research by failing to recognize its interests or rights

Democratization of Science

- Given that US science has been quite productive with governance largely left in expert hands, what could we or should we change?
  - Greater transparency and accountability
  - Priority setting that includes a broader range of interests and perspectives

- Trade-offs
  - Impede progress and create gridlock
  - Create disincentives that chase the best and brightest out of stem cell research or out of biomedical research altogether
  - Create disincentives for investors, diminish the number of treatments and products brought to market

"We're here to help with your stem cell research. I'm a philosopher and he's a politician."

IP and Licensing Policy

Why Worry About IP and Licensing

- Getting the most bang for Californian's bucks
  - Maximize knowledge production and diffusion
  - Maximize the number and rate of new products and treatments
    - Distributive justice: want tx to be affordable and available to those who need them

Patentable and Patented

- Human stem cells, and a method of making them, are patentable and already patented
  - James Thomson inventor, WiCel (U. of Wisconsin) assignee: US patent nos. 6,200,806 and 5,843,780 (the ‘806 & ‘780 patents)
  - Terms probably expire in 2015

- SNCT patented by Campbell & Wilmut
  - US patent no. 6, 147, 276
  - US patent only covers non-human mammals
  - Expires 2020

What is a Patent?

- RIGHT TO EXCLUDE others from making, using, selling, offering for sale, or importing the patented item or process
  - Not a positive right to make, do, etc.
  - A patent does not necessarily confer a monopoly
- Quid pro quo between the citizens and the inventor:
  - citizens obtain new, useful knowledge/products
  - inventor obtains exclusionary rights for a limited term of years.

Patentability

- Is it patentable subject matter?
- Is it useful as defined by law (utility)?
- Is it new as defined by law (novelty)?
- Is it non-obvious to one of ordinary skill in the art; is this enough of a contribution to knowledge to justify the patent right (non-obviousness)?
- Is the scope of the exclusionary right sought commensurate with the inventor’s contribution to knowledge (112 requirements)?

Patent “property” is defined by the patent’s claims

- Thomson patents claim:
  - Purified preparations of embryonic stem cells from humans and other primates
    - Pluripotent
    - Proliferate in vitro for over 1 yr while maintaining a stable, euploid karyotype
    - Have the potential to differentiate into “derivatives of” the three germ layers that represent the earliest developmental stages of an embryo (endoderm, mesoderm, ectoderm)
    - Defined by the presence and absence of certain cell surface proteins and enzyme activities

Scope of Thomson Patents

- What counts as “embryonic”?
  - Thomson recently filed a continuation in which claims do not use the term embryo or embryonic any more. Potentially, much wider claims.

- Others can still patent new stem cell inventions!
  - These new inventions must meet the requirements for patentability
  - New stem cell patents may or may not require cross-licensing with Thomson patents

Power of Owning Patent Rights

- Can exclude others from using something covered by a claim, even when their use is not commercial
    - Can prevent others from doing research without the patent holder's authorization (license)
- Patent rights are enforceable even if the owner is not making or using anything covered by the patent claims
- Need not enforce the right to keep it
- RIGHT COVERS INDEPENDENT INVENTION OF THINGS COVERED BY A CLAIM, AND AFTER-DEVELOPED TECHNOLOGY
    - WiCel can exert rights over new stem cell lines derived by CIRM-funded scientists
    - Recent MOU between WiCel and NIH

Patent Licensing

- Patentees have wide leeway in licensing:
  - Can license exclusively or non-exclusively
  - Can license only some of the rights
    - for instance, can put restrictions on types and numbers of uses
  - Field of use restrictions are permissible
  - Geographic restrictions are permissible

Other relevant licensing considerations

- Data Use Agreements
  - Transfer of data among non-profit researchers or between non-profit researcher and for-profit institutions (biotech or pharma)
- Material Transfer Agreements (MTAs)
  - Transfer among researchers of stem cells and other reagents
- Patent licenses, data use agreements and MTAs concern different rights
  - Authorization for research or product development can involve one, two or all three

Proposed CIRM Policy for Non-Profit Research Organizations

- Policy goals:
  - Achieve academic openness and bring scientific advances to the public via commercialization
    - May be some tension between these goals, need to figure out how to maximally advance both
  - A primary goal is to promote sharing of all types of IP
  - Promote collaboration between for-profit and non-profit entities so that basic science is translated into products efficiently
  - Provide financial benefit for the State of CA

Some Highlights

- CIRM-funded grantees must share materials described in publications
  - Within 60 days of receipt of a request and without bias as to the affiliation of the requester
  - Alternatively, authors may provide requestors with info re how to reconstruct or obtain the material
  - Sharing “without cost or at cost”

Highlights Continued…

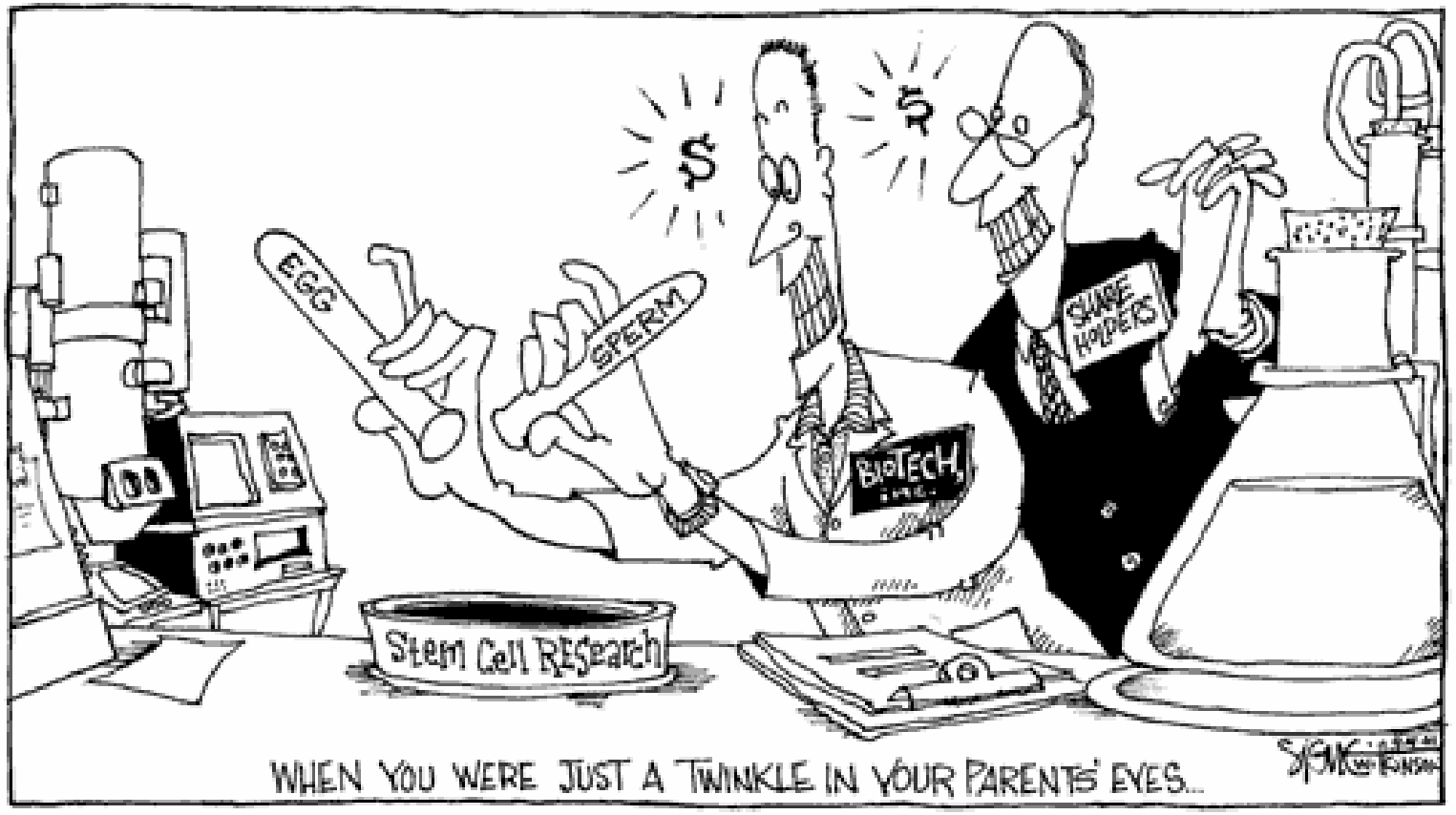
- Grantees can patent
  - Grantee institutions bear the costs of patenting
  - Grantee orgs shall report filing of patent apps on an annual basis
  - Must submit a patent licensing activity report annually
  - Grantees agree that CA research institutions have a no-cost, non-exclusive license for CIRM-funded, patented inventions

Highlights Continued…

- GRNATEES SHALL NEGOTIATE NON-EXCLUSIVE LICENSES WHENEVER POSSIBLE
  - Must document the commercialization capabilities of the intended licensee when granting an exclusive license
  - When exclusive licenses are granted the license will include benchmarks/milestones by which progress towards commercialization can be measured

Highlights Continued

- March-in Rights: CIRM can require licensing by a grantee or licensee, or CIRM can grant a license itself, if:
    - Grantee org has not made reasonable efforts, in reasonable time, to achieve practical application of a CIRM-funded patented invention
    - Bcs licensee has not adhered to an agreed upon plan to make therapies accessible
    - To alleviate public health and safety needs that are not reasonably satisfied by the grantee or its licensee and which needs constitute a public health emergency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EGG
SPERM
BIOTECH
SHARE HOLDERS
Stem Cell REsearch
WHEN YOU WERE JUST A TWINKLE IN YOUR PARENTS' EYES...