Ethical Dilemmas in Germline Editing: Focusing on Informed Consent

Second International Summit on Human Genome Editing

The University of Hong Kong

November 27-29, 2018

Judith Daar

Clinical Professor, UCI School of Medicine

Visiting Professor, UCI School of Law

Chair, ASRM Ethics Committee

Informed Consent and U.S. National Policy on Germline Genome Editing

"NIH will not fund any use of gene-editing technologies in human embryos…Advances in technology have given us an elegant new way of carrying out genome editing, but the strong arguments against engaging in this activity remain. These include the serious and unquantifiable safety issues, ethical issues presented by altering the germline in a way that affects the next generation without their consent, and a current lack of compelling medical applications justifying the use of CRISPR/Cas9 in embryos."

Francis S. Collins, Director, National Institutes of Health
Statement on NIH funding of research using gene-editing technologies in human embryos, April 28, 2015.

Sources of Consent for Research Using Gametes and Embryos

- Patients undergoing IVF
  - Autologous v. Donated Gametes
- Gamete Donors
  - Directed Donation to IPs
  - Provision to Clinic or Gamete Bank
- Fertility Clinics
  - Abandoned gametes, embryos
  - Unselected donor gametes, embryos
- Guardian Ad Litem
  - Appointed to represent potential child

Is There a Role for Guardian Ad Litem in Germline Research?

- GAL common in probate and child welfare legal proceedings
- Represented minor can be born or unborn
- Standard is to act in the best interest of the child
- Recent controversy over GAL appointment in embryo disputes
  - Challenges notion that preimplantation embryos are not persons
  - Could result in prohibition on embryo discard and cryopreservation
- GAL could be instructed to balance risks and benefits of proposed research, taking donor preferences into account

Standards for Research Approval: Is There a Role for Existing Models?

- Federal regulations address research on pregnant women, fetuses, neonates in 45 CFR 46, Subpart B.
- Risk to fetus must hold out direct benefit to pregnant woman or fetus; if no prospect of benefit, "risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means…"
- Research not otherwise approvable may move forward if further understanding of serious health problem affecting pregnant women, fetuses or neonates.

When Should Consent for Research Be Obtained?

"It is important that patients decide to donate embryo for research only after they have decided not to continue storing their embryos."

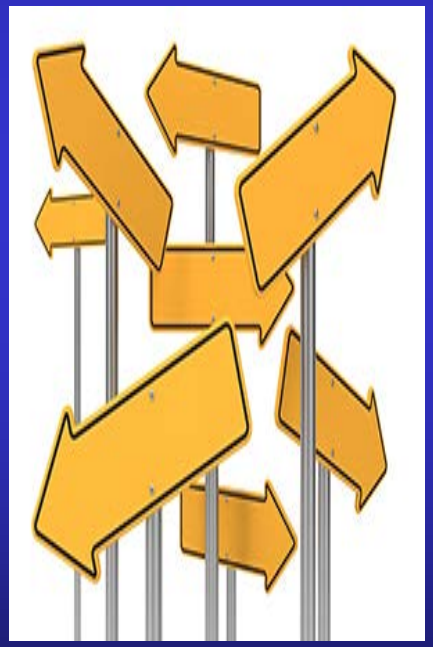
"[E]mbryos created through the use of a third-party gamete donor should be used for hESC research only if specific consent for such use was provided by the gamete donor in advance of the creation of the embryos."

Donating Embryos for Human Embryonic Stem Cell Research, Ethics Committee, American Society for Reproductive Medicine (2013)

Timing of Consent for Using Embryos or Gametes in Research

Prior to Retrieval

- IVF patients using their own gametes
- Directed/known gamete donors
- Donors supplying to banks w/o IPs
- Research setting



Following Retrieval

- IVF patients post-completion family or Tx
- 3rd party donors not previously queried
- 3rd party give broad consent for disposition
- Previous consent outdated or limited

Perspectives on Contemporaneous Consent for Research

Should always be required?

- In direct donation to research
- By embryo donors after IVF completion
- By all gamete providers via tracing

Should sometimes be required?

- By gamete/embryo donors who did not previously give consent to research

Should never be required?

- By gamete/embryo donors who assign full decisional authority to recipients

Judging the Substance: Broad, Roll-Down or Specific Consent?

- Broad Consent

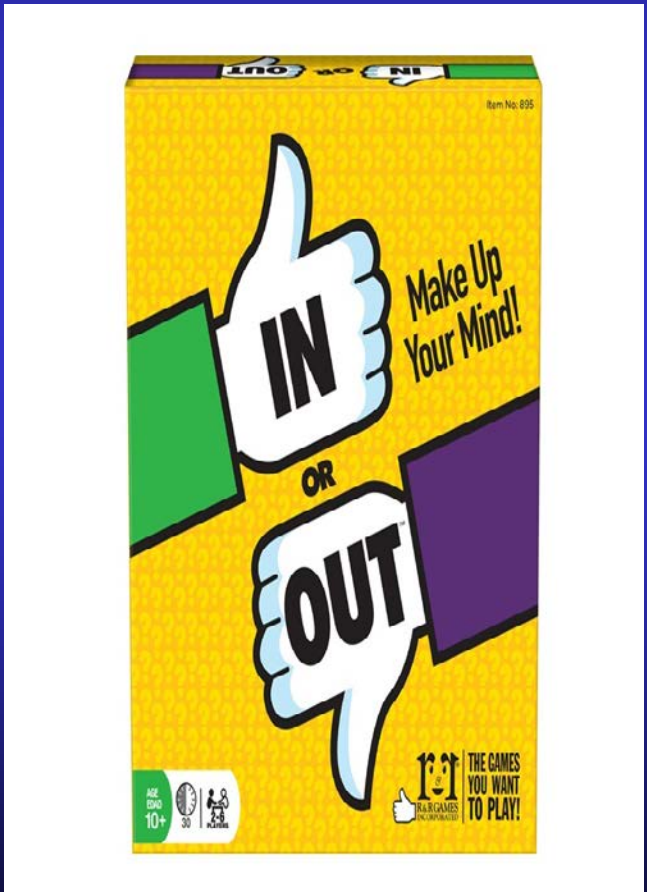
  General language granting consent to TBD research at some future point

- Roll-Down Consent

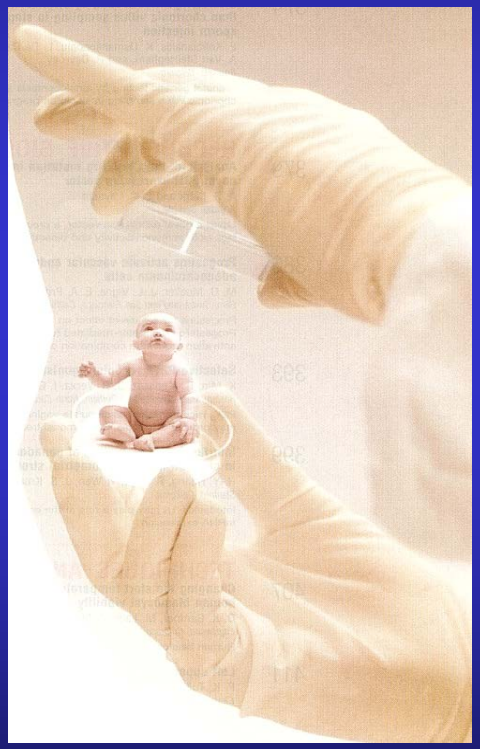
  Presents subject with list of rule-out or rule-in options

- Specific Consent

  Form must include project description, source of funding, policy on downstream disclosures, etc.



Final Thoughts…



- Global aspects of germline gene editing will impact consent process in each jurisdiction, best to plan for inclusion
- Researchers might consider intermediaries to secure informed consent to avoid (appearance of) conflict of interest
- Best practices account for change of mind, proxy decision-makers, risks of identification, impact on consanguineous relatives

Thanks So Much