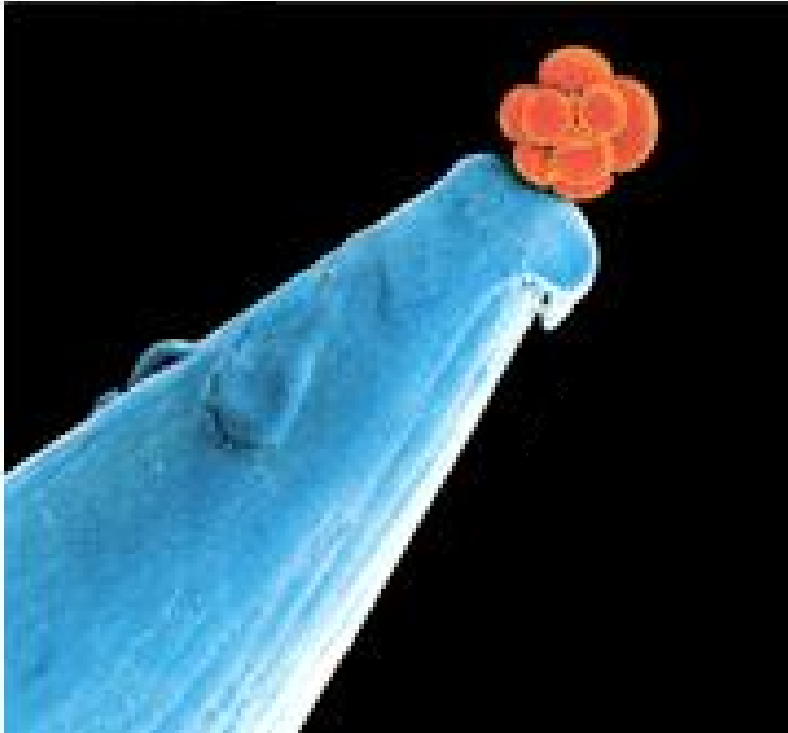
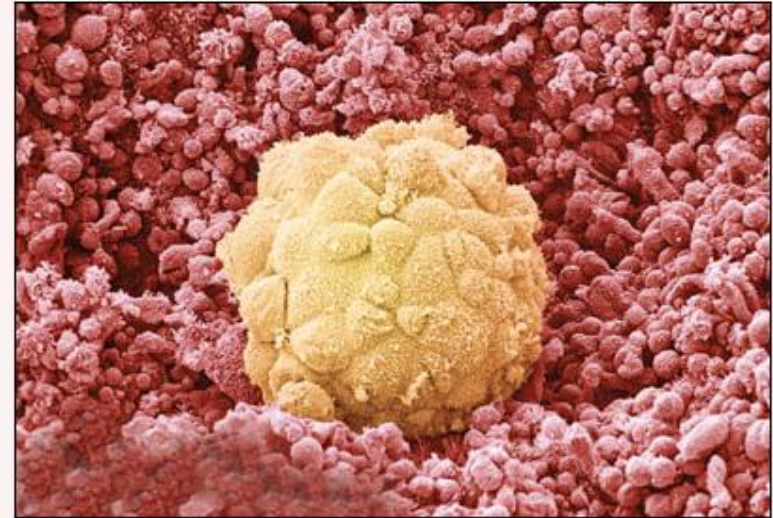


Emerging Issues in Human Embryonic Stem Cell Research



**A morula-stage embryo
on the head of a pin**

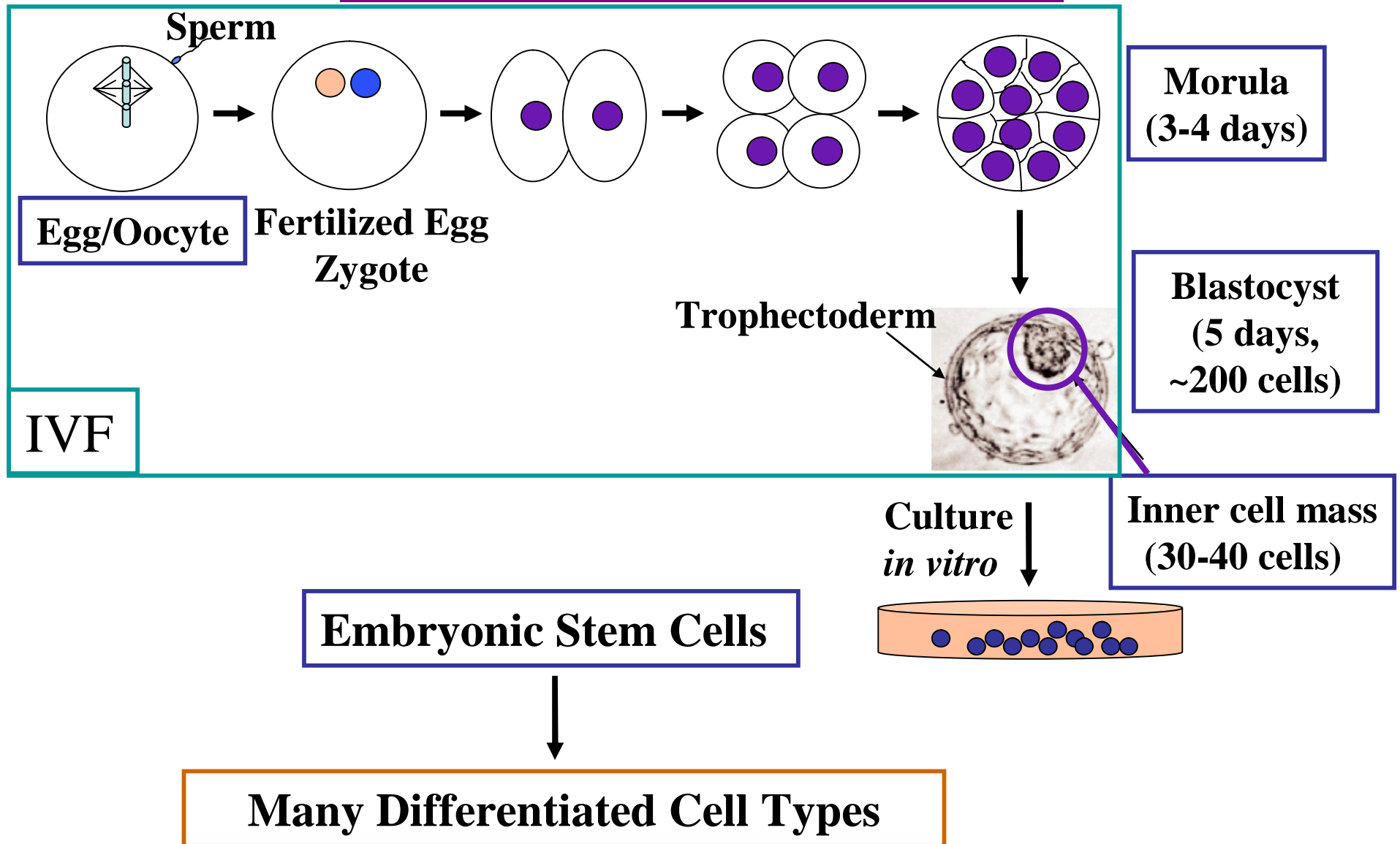


Y. NIKAS/WELLCOME PHOTO LIBRARY

A six-day-old embryo nestles in the womb, but which of its features mean it is alive?

**A 6-day-old embryo
implanting**

Early Embryonic Development & Generation of hES Cells



Steps in the Production and Use of hES Cells

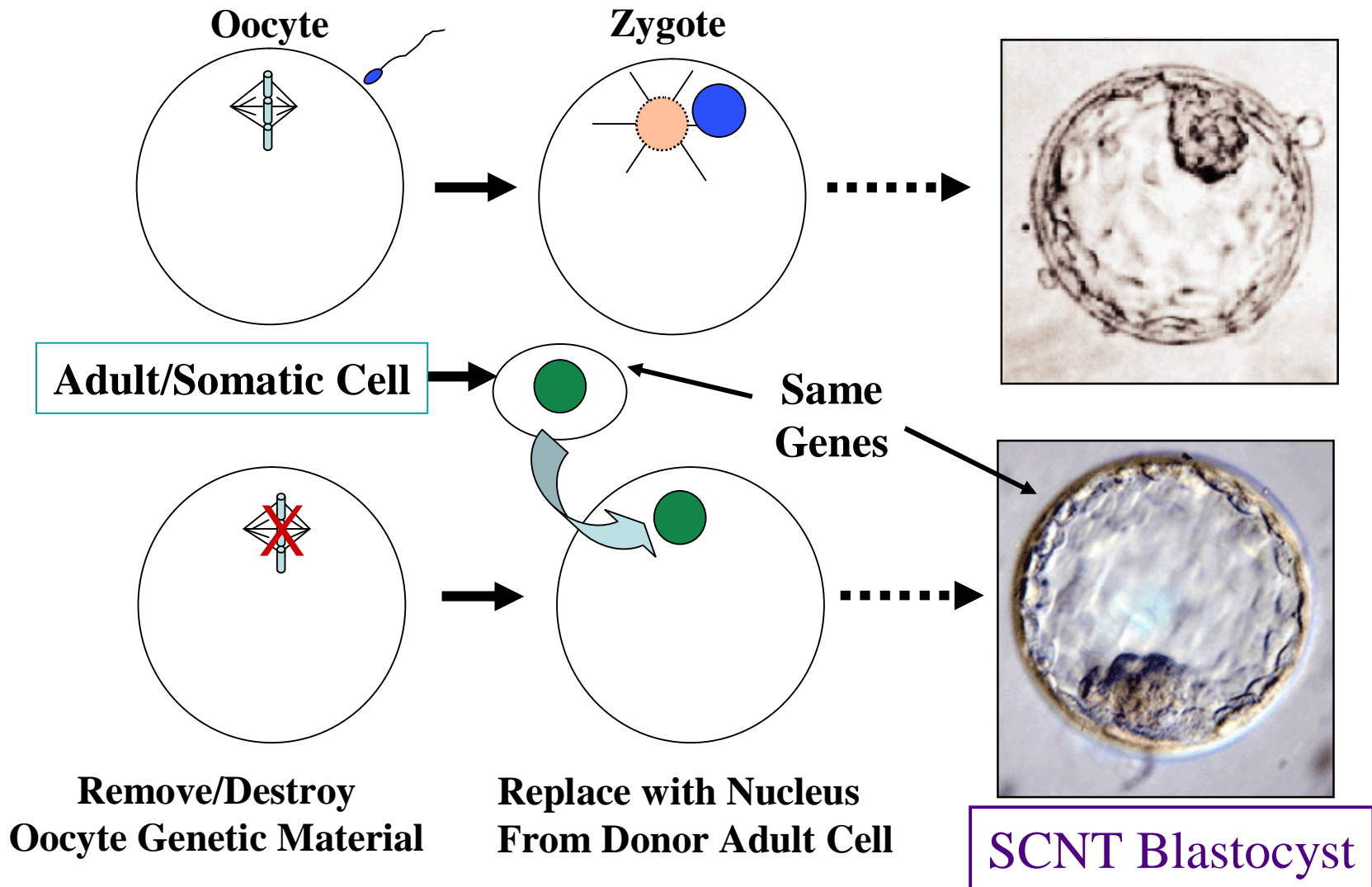
- **Derivation of hES Cells**
- **Transfer and Importation of hES Cells**
- **Differentiation of hES Cells *in vitro***
- **Testing of Potential of Differentiated Products**
 - *in vitro*
 - *in vivo*
- **Clinical Trials**
- **Intellectual Property Issues**

Derivation of hES Cells

- **Excess Blastocysts from *In vitro* Fertilisation (IVF) Clinics**
- **Additional Surplus Materials from IVF Clinics**
- **IVF specifically for hES Cell Generation ★**
- **Nuclear Transfer (NT) for hES Cell Generation**
 - **Disease-specific hES Cells ★**
 - **Patient-specific hES Cells ★**

Several of these methods require human oocytes

Comparison of Normal Preimplantation Development with Nuclear Transfer (NT)



Oocyte Procurement

- **Availability of Donors**
- **Potential Medical Risks**
- **Reimbursement/Compensation**
- **Inducements/Incentives**
- **Justice - payment for donations for reproductive IVF is routine**
 - **Should all oocyte donations be altruistic?**
 - **Should payment be allowed?**

Alternative Sources of Oocytes

- **Failed-to-Fertilise Oocytes from IVF Procedures**
 - **Not an unlimited source, may be of poor quality**
 - **IVF clinical practice should not be altered to generate excess oocytes even with informed consent**
- **Maturation of Immature Oocytes (e.g. ovariectomies)**
 - **Maturation of oocytes is not yet reliable, needs more research**
- **Animal Oocytes**
 - **All plausible but yet to be proven for human material**
 - **Experiments are underway to validate**
 - **Use of animal oocytes raises some issues**

Avoiding the Need for either Oocytes or Viable Embryos

- **Extraction of Single Cells from Morulae or Blastocysts**
 - adjunct of Preimplantation Genetic Diagnosis-PGD
 - need to ensure that the embryo is undamaged
- **hES Cells from Arrested Embryos from IVF Procedures (normally discarded)**
 - what criteria will establish that the embryos are truly non-viable?
 - will such hES cells be compromised?

Attempts at Alleviating Ethical Concerns

- **Altered Nuclear Transfer (ANT)**

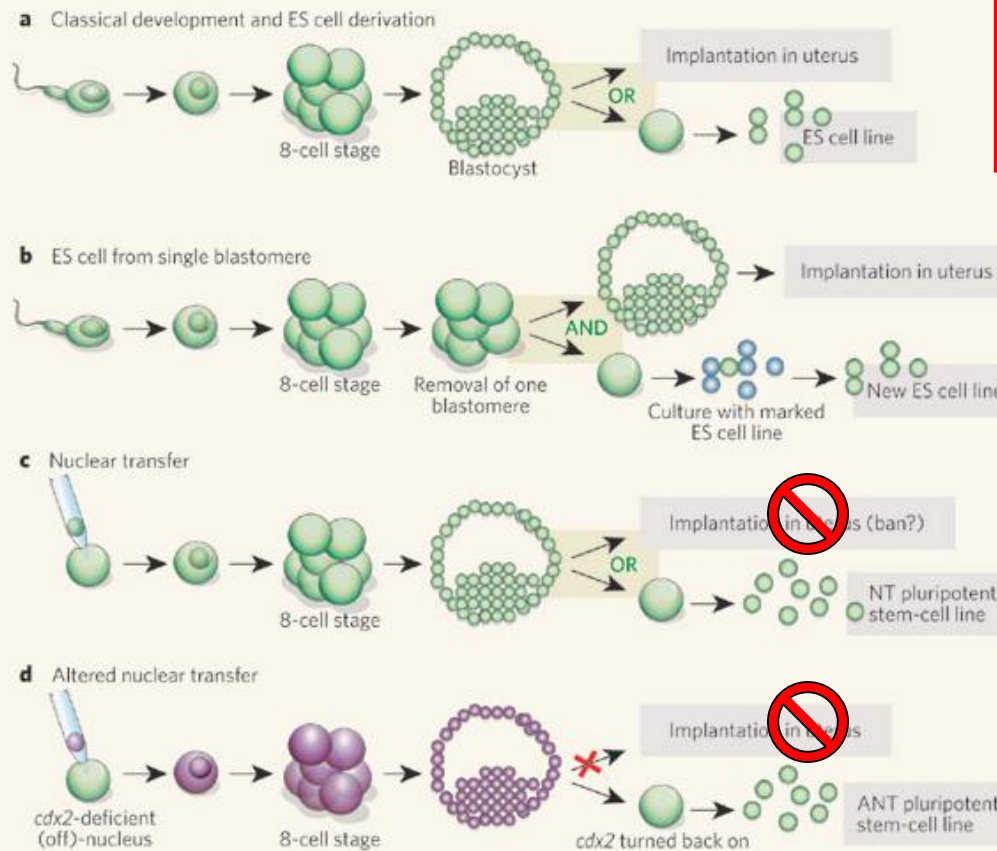
Incapacitate the somatic nucleus prior to transfer

- **Parthenogenesis - activating an oocyte without sperm**

Still needs oocytes

**There are both technical/scientific and ethical issues
with these methods**

Summary - Methods for Generating hES Cells



Standard method -
from blastocysts (IVF)

From single
blastomeres (PGD)

Nuclear
Transfer (NT)

Altered Nuclear
Transfer (ANT)

a, The classical derivation of embryonic stem (ES) cells destroys the embryo from which they are derived. **b**, Lanza and colleagues¹ have used a modified method that does not compromise the embryo, but is not donor-specific. **c**, Donor-specific pluripotent stem cells can be made using nuclear transfer (NT) techniques. **d**, An altered nuclear transfer (ANT) method developed by Meissner and Jaenisch² blocks expression of the *cdx2* gene until the blastocyst stage, making it unable to implant.

Other Potential Sources of hES Cells

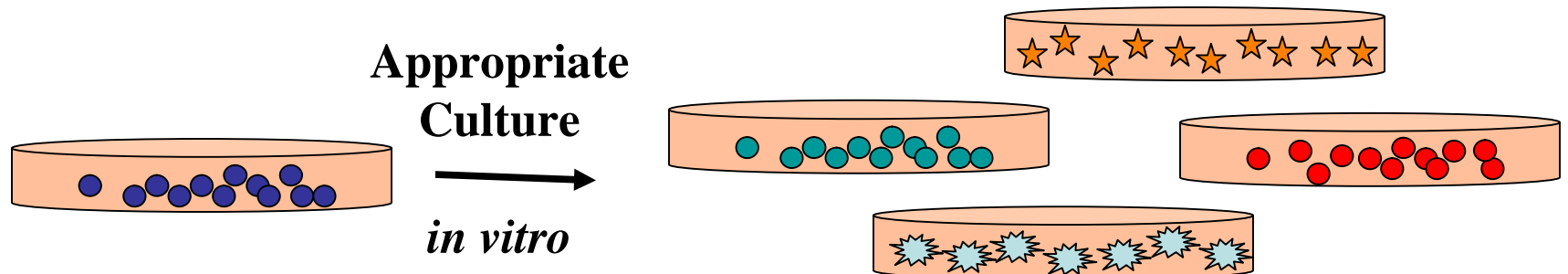
- **hES Cells from Male Reproductive Tissue**
- **Sperm and/or Oocytes Derived from hES Cells**
- **Reprogramming of Somatic Nuclei to Pluripotency**

Transfer and Importation of hES Cells

- Interoperability of Guidelines/Regulations/Criteria
 - How to ensure quality/provenance of hES cell lines - for both ethical and scientific reasons

Differentiation (*in vitro*) of hES Cells

- Interfacing with NIH Regulations



Embryonic Stem Cells

Many Differentiated Cell Types

Testing Potential of Differentiated Cells

- *In vitro* tests
- *In vivo* tests - Chimeras

Use of chimeras raises some issues but will be required by the FDA before clinical use

These Issues Apply Also to Adult Stem Cells

Steps in the Production and Use of hES Cells

- **Derivation of hES Cells**
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