

# Contemporary Issues Facing Mouse Repositories

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# Outline

- Services and capacities
- Outside the freezer
  - biosecurity & quality control
  - education & information
- Apply best practices
- Transportation
- CRISPR/Cas9 revolution



# Repositories – More than just freezers

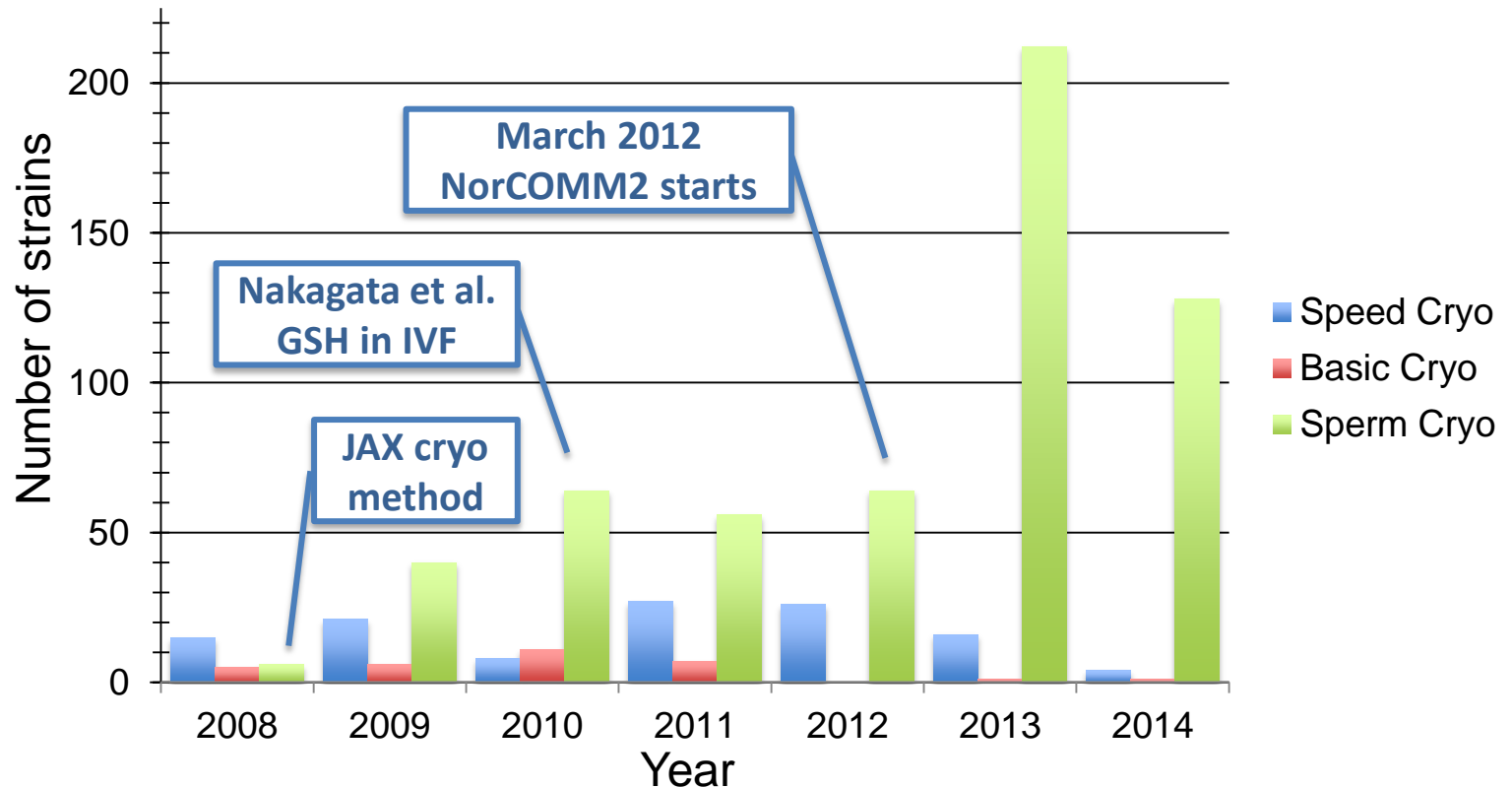
## **Cryo Services**

- Cryopreservation
  - embryos from natural mating or IVF (speed cryo)
  - sperm
- Cryorecovery
  - embryos
  - sperm
- ES cell distribution
  - gene trap & gene targeted ES cells
- Mouse line distribution

## **Added value**

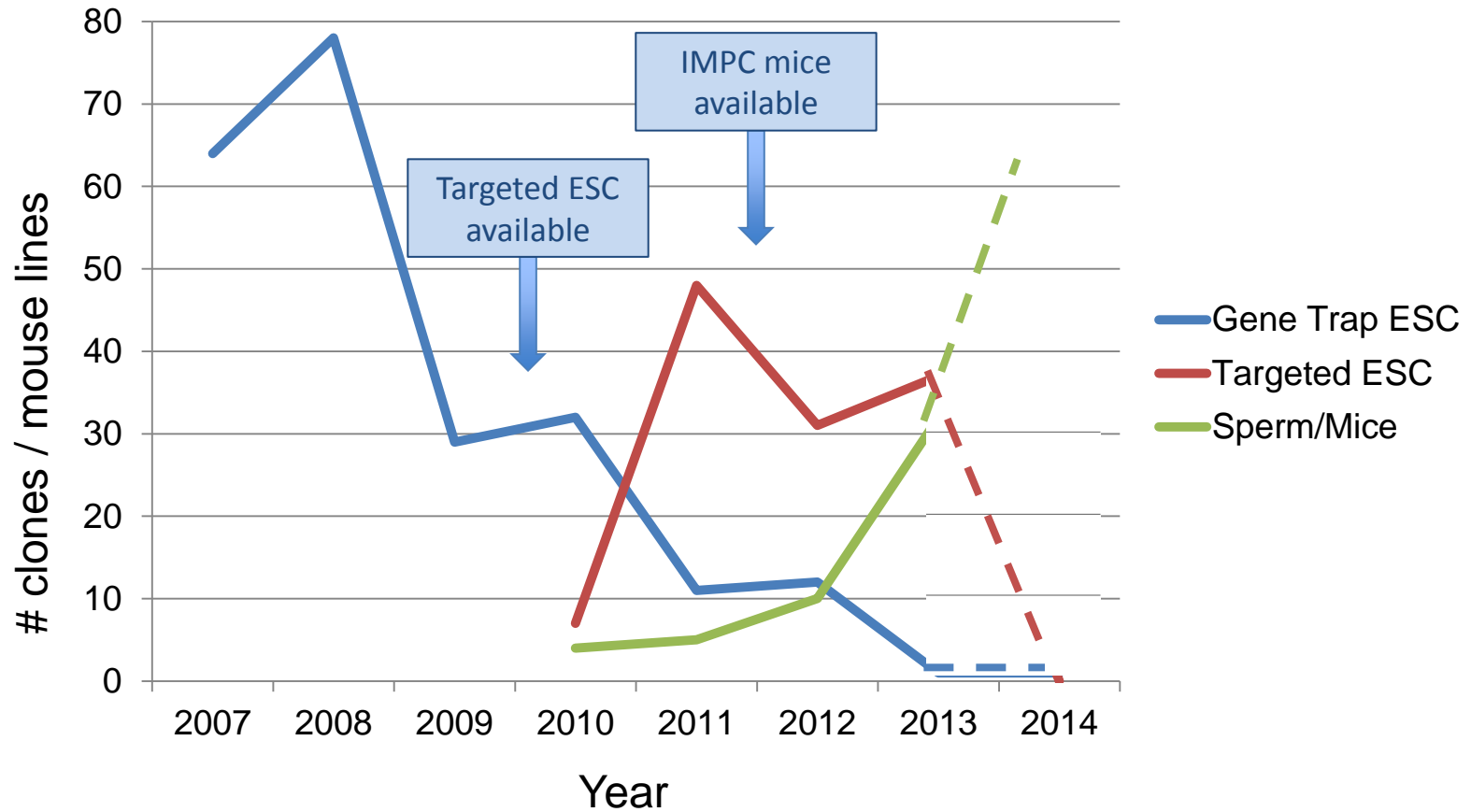
- Biosecurity for research colonies
  - majority of non-IMPC requests for “back-up”
- Quality control
  - genetic background
  - mutation-specific
- Reagent selection
  - education
- Line rescue
  - non-breeding chimeras
  - non-breeding/infected established strains

# Cryopreservation Service Stats



*Number of deposited strains by service type at CMMR*

# Distribution Service Trends



*Number of requests by resource type from CMMR*

# Biosecurity & Quality Control

- Sustainability
  - fee-for-service & repository funding
- Recoverability
  - biosecurity →  $\geq 2$  independent sites
  - best practices for cryopreservation & recovery
- Genetic verification
  - documentation of genetic background and mutations
  - clear and validated genotyping protocols
- Communication
  - mouse line passports “frozen” with deposit
  - encourage deposit of data, e.g. MGI, IMSR, data sites

# Education & Information

- Understand the resource
  - work with end-users to understand extant quality control results
  - educate users on best practices for validating imported resources
- Assist in decision making
  - selection of resources
  - methods of deposit back to repository

# The 3Rs for Archiving & Distribution

## TOTAL MICE / STRAIN WITH ONE RECOVERY

Speed Cryo → 35-36 mice

Sperm Cryo → 20-33 mice



### *Animal Use*

Lines for distribution → embryos

Lines for archiving → sperm

### *Financial Considerations*

Where is majority of cost to be borne, archiving or recovery?





# Accessibility

- Facilitate transfer
  - reduce costs associated with recovery
    - more efficient IVF
  - reduce costs associated with shipping
    - fresh embryos/gametes/tissues
    - ship frozen embryos/gametes on dry ice
  - work to simplify transfers, including simplifying/eliminating MTAs

# Transportation

- single-issue groups working to block the sharing of mouse models
  - British Airways and Lufthansa have stopped transporting animals
  - global issue as other airlines are subject to action
- increasing public concern *vis a vis* genetic engineering
- outreach and education

# Impact of CRISPR/Cas9

- Step change in mouse model production
  - era of the home-made mouse?
- Expertise
  - molecular biology skills wide-spread
  - microinjection & embryo transfer skills and infrastructure limited → Tg cores & repositories
- Scientific considerations
  - reproducibility → access to published line
- Ethical considerations
  - animals needed to re-make and quality control

# Acknowledgements



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Institut de recherche en santé du Canada

**SickKids**<sup>®</sup>



# Numbers for Cryo

## Embryo Cryo

- want 200-300 carrier embryos
- 20-25 embryos/straw
- 2 M & 20 F / IVF session
- 34 mice/cryopreserved strain, including QC

## Sperm Cryo

- 2-3 carrier males
- >10 straws/male
- 3 M & 5 F for QC / strain
- 8 mice/cryopreserved strain, including QC

## Embryo Recovery

- 20-40 embryos in 1-2 recipients per strain
- 0-20 pups/recovery (mean=5, 23% born)
- 33 lines recovered; 6 failed (~85%)

## Sperm Recovery

- 1 straw, 10-20 oocyte donors
- 4-178 (mean=73) embryos, 1-5 recipients
- 1-65 pups/recovery (mean=28, 35% live born)
- 11 lines recovered; 1 failed (~92%)