

# Neural Chimeras: Welfare and Regulatory Considerations

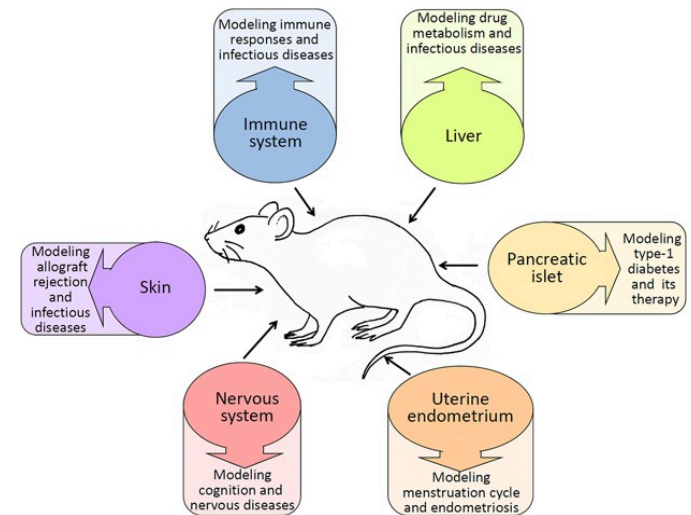
Megan Albertelli, DVM, PhD, DACLAM

Associate Professor, Comparative Medicine, Stanford University

NASEM Committee on Ethical, Legal, and Regulatory Issues Associated with Neural Chimeras and Organoids, 8/10 – 8/11/2020

# Similar Models

- PHS Policy: covers all vertebrates
  - AAALAC International: institutional oversight of cephalopods in research recommended
  - Professional team trained in maintaining welfare for a wide variety of species
- Animal models engrafted with human tissues
- Neural transgenic models
  - Huntington's Disease (Yang 2008)
  - MeCP2 overexpression (Liu 2016)



(Fujiwara 2017)

# Process of Review

- IACUC
  - Evaluation of proposed animal studies
    - Considerations of alternatives and justifications of species/animal numbers
    - Methods to minimize pain/distress
    - Nonstandard animal care needs
    - Experimental endpoints
    - Plan for removal from study if pain/distress cannot be relieved
  - Detecting and responding to unanticipated effects
    - Post approval monitoring
    - Pilot studies
    - Veterinary evaluations
    - Genetically modified animals- established guidelines for unanticipated phenotypes (Dennis 2000)

# Welfare

- Can we provide an environment that provides for physical and psychological well being, allowing an animal to maintain good health, exhibit species-specific normal behaviors, and adapt to a changing environment with minimal maladaptive behaviors, while meeting scientific study aims?
- Species-specific enclosures, diets, social housing, enrichment plans
  - Previous experience with domesticated species, behaviors in wild populations, needs of similar species, preference testing
- Specific research models or individual animal characteristics may require changes from standard practices to maintain welfare
  - Physical welfare: health monitoring, growth and development, breeding success
  - Psychological welfare: behavior (normal or maladaptive), physiological parameters, cortisol levels

(Weed 2005, Brown 2015)

# Pain Detection and Management

- Pain: an unpleasant sensory and emotional experience associated with actual or potential tissue damage
  - Should be expected in an animal subjected to any procedure or disease model that would be likely to cause pain in a human (Kohn 2007)
- Cageside assessments of behavior and clinical condition, may be difficult in prey species that typically hide signs of pain

- Scoring systems
- Grimace scales
- Analgesic self administration



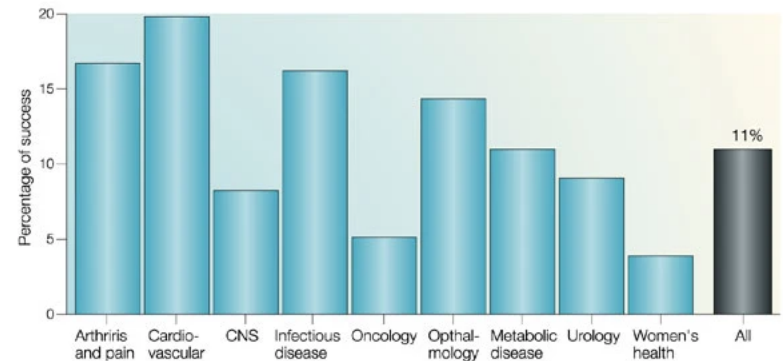
(Sotocinal 2011)

- For potentially painful procedures (as based on human perception), establish baseline anesthetic and analgesic plans

# Changes in Awareness and Abilities

- Focus on behavioral differences from wild type animals rather than determining if human like awareness is present
- Standardized behavioral assays to examine memory, learning, anxiety, personality traits, social interactions
- Observation of interactions with environment, social groups, human caretakers may provide insight for areas of further study

# Ethical Considerations



(Kola 2004)

- Ability to provide animal welfare is a key component of ethical animal research
- Translation of animal model CNS disease to approved human therapies is low
  - Alzheimer's Disease new drug therapies: 0.4% success rate (Cummings 2014)
  - NHPs most relevant model but maintaining welfare is more difficult, labor intensive, and expensive than other species
  - Rodents with more human-like CNS may provide relevant models with welfare that is easier to achieve

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