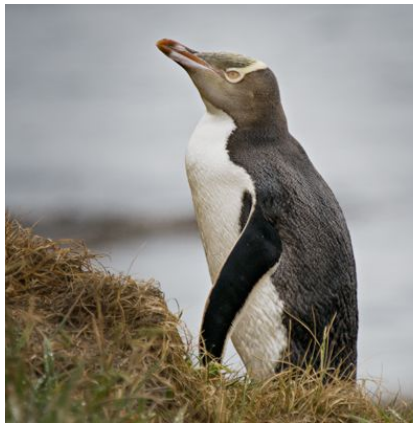






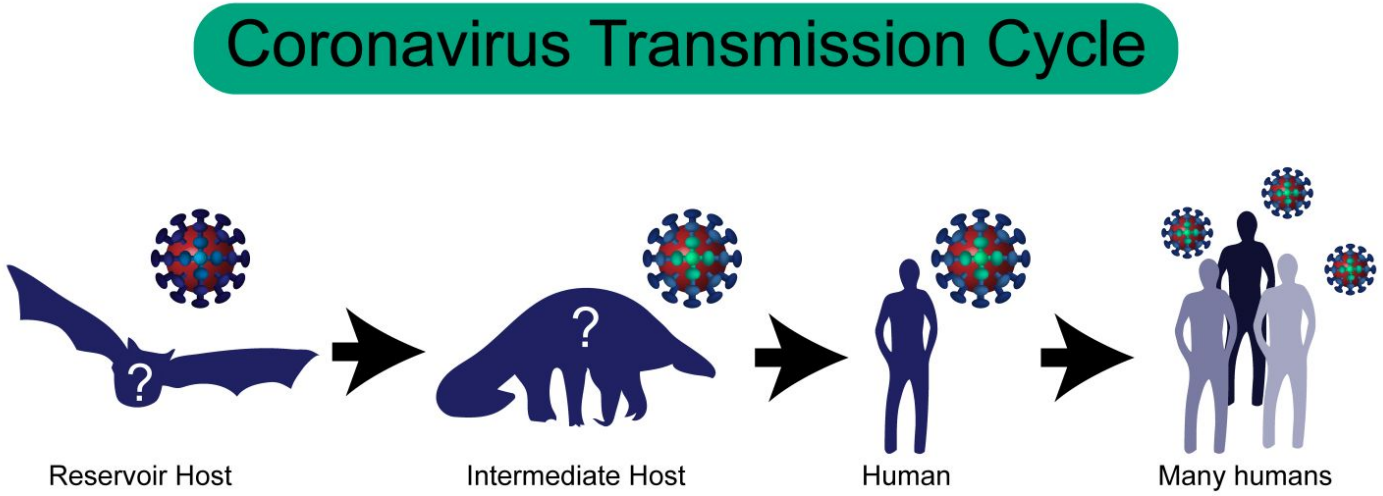
Oral delivery gone wild: Considerations for wildlife species

A/Prof. Arlene McDowell

75%

of emerging infectious diseases in humans originate in

animals



https://sitn.hms.harvard.edu/flash/2020/covid-19-emerging-viral-diseases-journey-animals-humans/

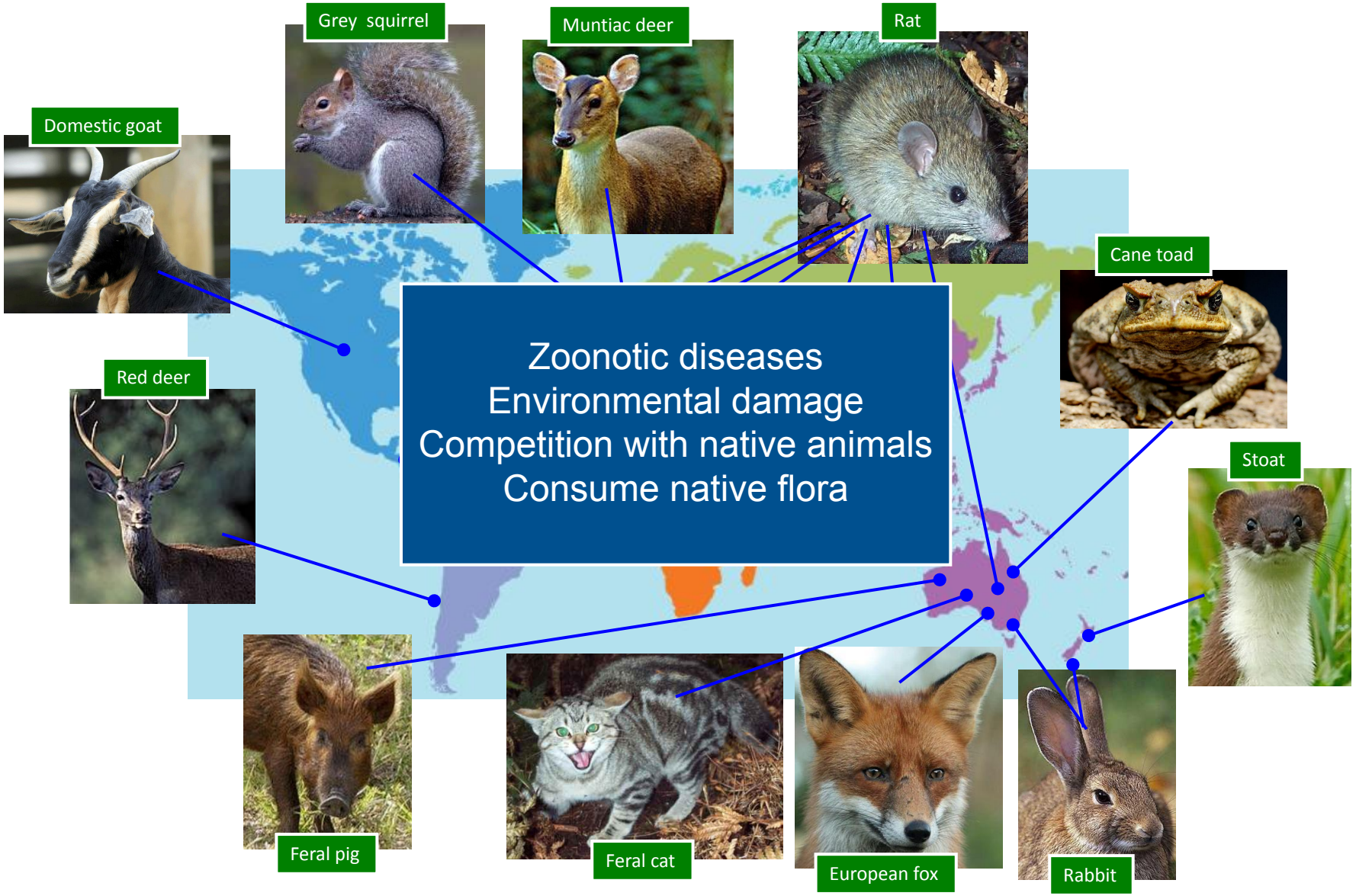
World Health Organization

Health Topics | Countries | Newsroom | Emergencies

Multi-country monkeypox outbreak in non-endemic countries

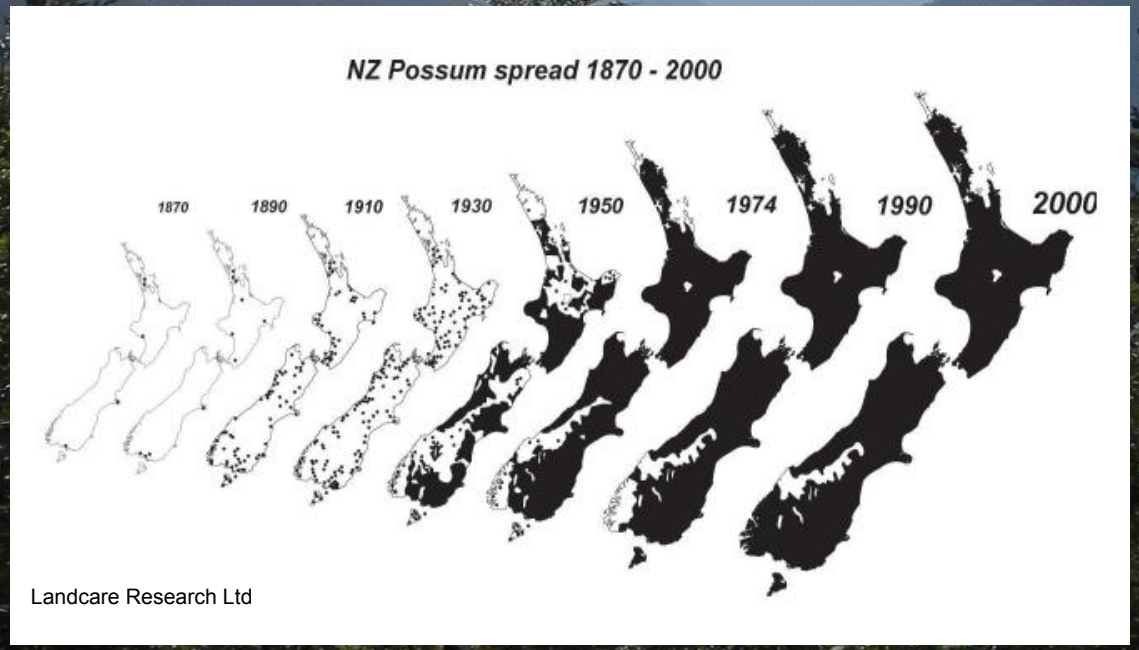
21 May 2022

Wildlife pests – a global problem



A. McDowell 2013. Delivery systems for wildlife. *In* Rathbone and McDowell. *Long acting animal health drug products: Fundamentals and Applications*. Advances in Delivery Science and Technology © Controlled Release Society 2013

Wilmont Pass, Fiordland, New Zealand



- Spread Tb
- Destroy forests
- Kill native birds

Warning 1080 Poison

Sodium fluoroacetate

will be present on the ground from: 20-8-09

The baits are 6 gram cylindrical cereal pellets. 16mm in diameter and 25mm in length. They are coloured mid to light green.

- DO NOT touch bait
- WATCH CHILDREN at all times
- DO NOT EAT animals from this area
- Poison baits or carcasses are

DEADLY to DOGS

Department of Conservation
Te Papa Atawhai

For more information contact:

Cheryl Pullar, Department of Conservation, Owaka Field Base,
20 Ryley Street, Owaka. Phone: 03 419 1000

Unauthorised removal of signs or baits is an offence

Aerial bait distribution

https://www.doc.govt.nz/nature/pests-and-threats/methods-of-control/1080

https://www.nzherald.co.nz/nz/1080-finding-the-facts-in-a-poisonous-issue

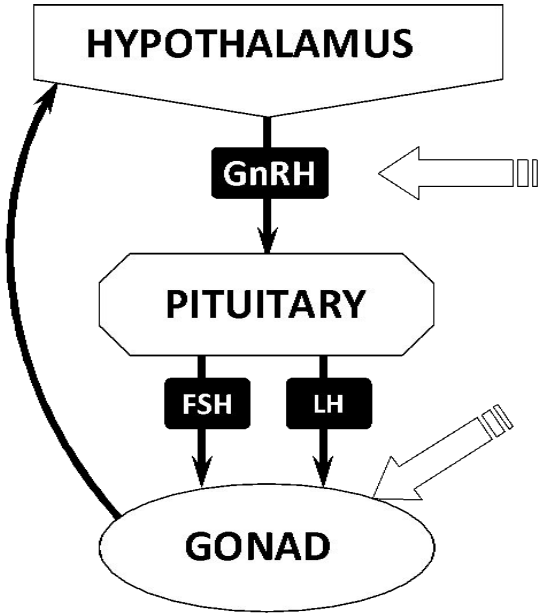
https://www.tv-wild.com/1080-poison

Fertility control: D-Lys^{6}-GnRH

- Water soluble analogue of GnRH (LHRH)
- Biological response is release of LH and FSH
- Chronic exposure suppresses gonadotrophins

- Degraded when delivered orally

- Ovuplant® (Deslorelin) wildlife contraceptive implant
  - reduced fertility in possums when administered as slow-release implant[1]



[1]Eymann J, Herbery CA, Thomson BP, Trigg TE, Cooper DW and Eckery DC (2007). Effects of deslorelin implants on reproduction in the common brushtail possum (*Trichosurus vulpecula*). *Reproduction Fertility and Development* 19: 899

Delivery

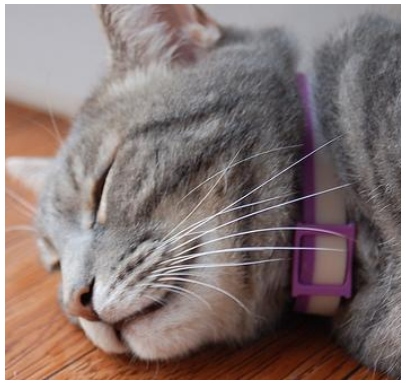
Humans ✓





Farm animals & pets ✓



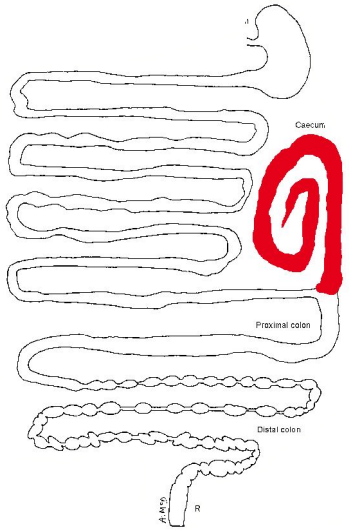



Wildlife ✓ / ?

McDowell *et al.* (2006). Application of pharmaceutical drug delivery for biological control of the common brushtail possum in New Zealand: A review. *Wildlife Research* 33: 679

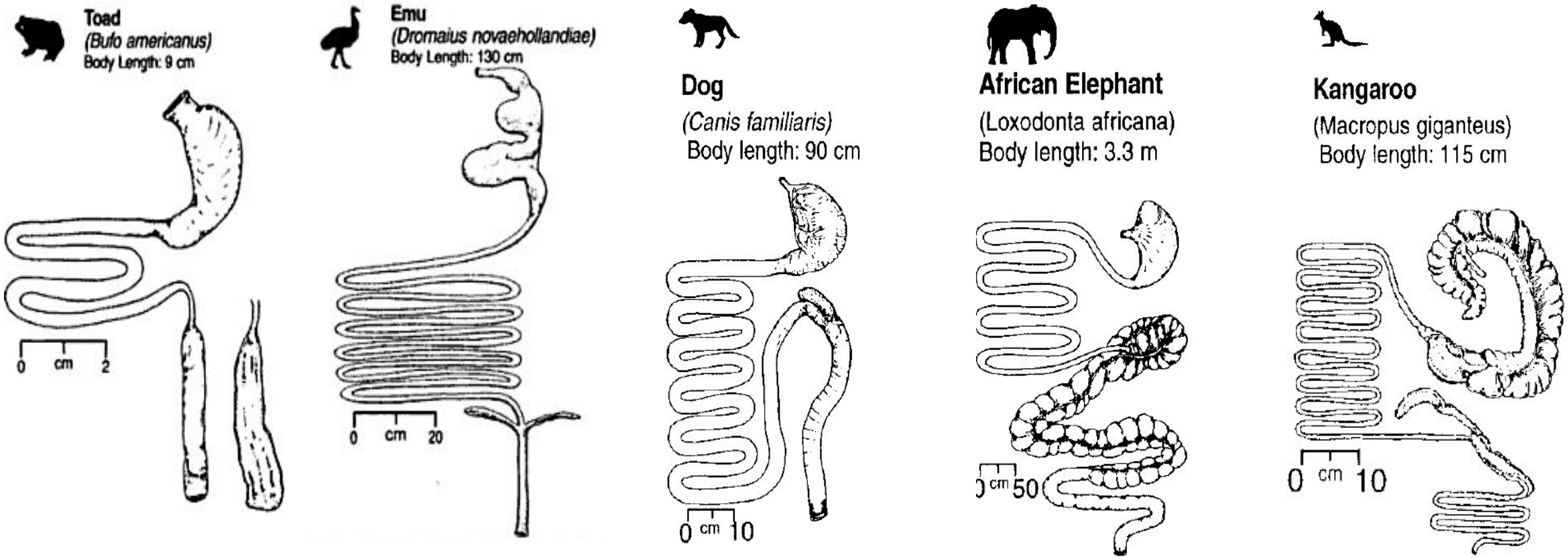
Remote delivery to a free-ranging, feral animal

(Nano)formulation → Oral delivery → Biological effect



A marsupial folivore

McDowell *et al.* (2006). Application of pharmaceutical drug delivery for biological control of the common brushtail possum in New Zealand: A review. *Wildlife Research* 33: 679



Amphibian | Bird | Mammal carnivore | Mammal herbivore | Marsupial herbivore

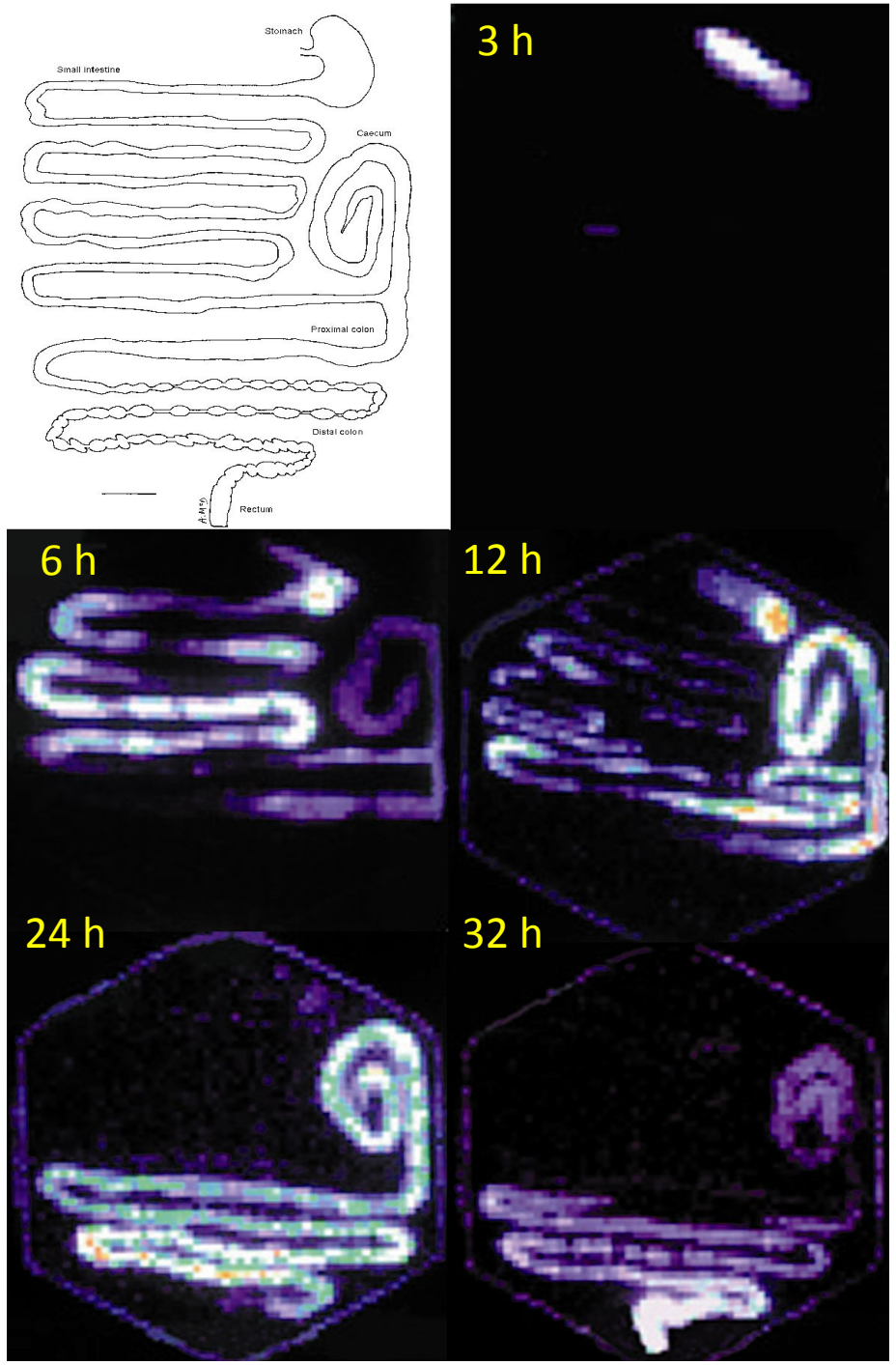
Stevens and Hume 1995

McDowell and McLeod (2007). Physiology and pharmacology of the brushtail possum gastrointestinal tract: Relationship to the human gastrointestinal tract. *Advanced Drug Delivery Reviews* 59: 1121-1132

Gastrointestinal transit

- Mouth to anus transit time (Foley and Hume 1997)
- Fed brushtail possums
  - males and females
- Administered by intubation
  - Fluid (Technetium-DTPA), *n* = 4
  - 75-125 µm Tc-particulates, *n* = 4
  - 500-700 µm Tc-particulates, *n* = 4

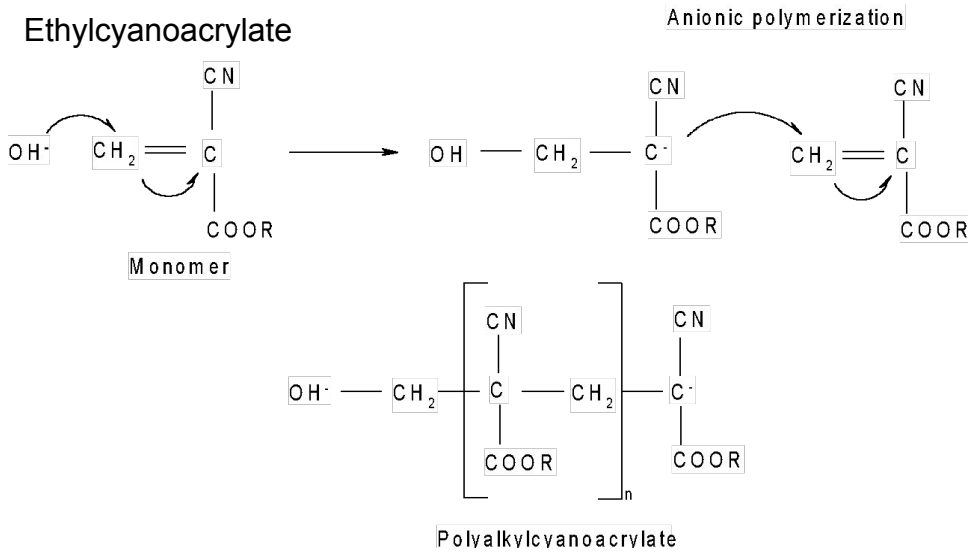
- 12 h to hindgut
- Transit is independent of
  - body mass
  - gender
  - time-of-day the dose is given



McDowell et al. (2005). International Journal of Pharmaceutics 302: 125
McDowell et al. (2004). Australian Mammalogy 27: 61

PECA nanoparticle formation

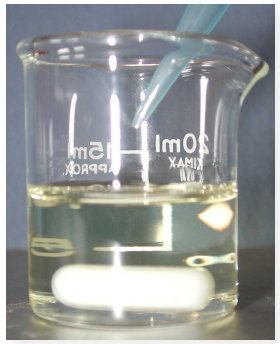
- Poly(ethyl cyanoacrylate), PECA nanoparticles
  - *In situ* interfacial polymerization of W/O microemulsion



Nanoparticle	Size ± SD (nm)	Polydispersity index ± SD	Zeta potential ± SD (mV)
Empty	191 ± 23.0	0.115 ± 0.039	-27.5 ± 1.1
D-Lys^6-GnRH	220 ± 32.0	0.092 ± 0.052	-3.0 ± 1.9

ECA monomer

W/O microemulsion:
10% water (active)
36% oil
54% surfactant



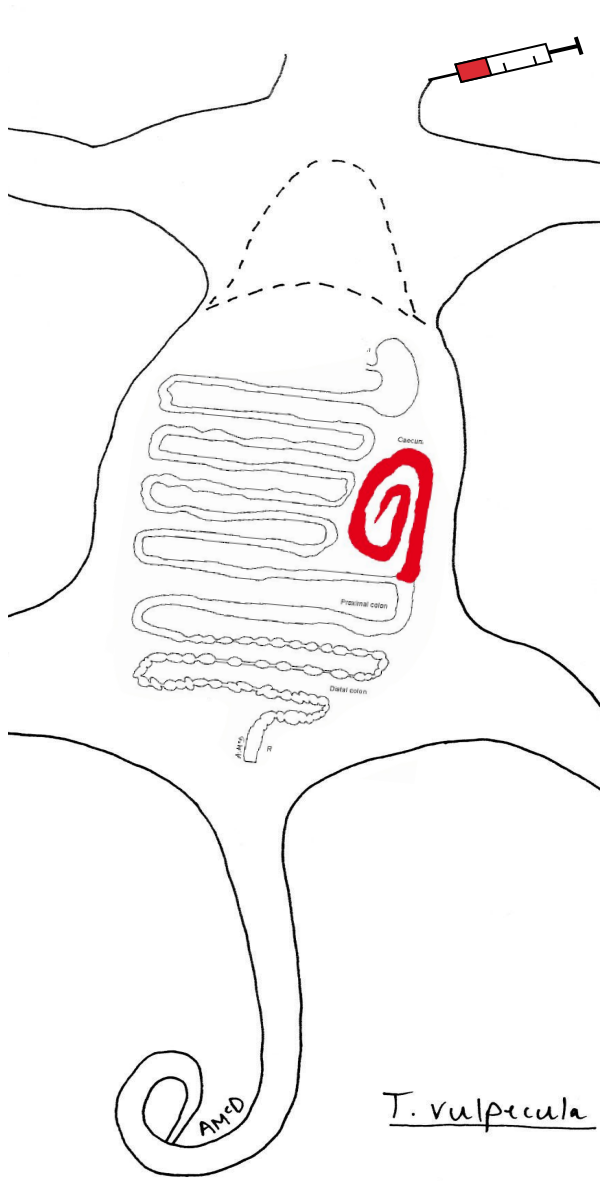
Stir
@ 4ºC

Entrapment efficiency
95 ± 4%

Nanoparticle suspension

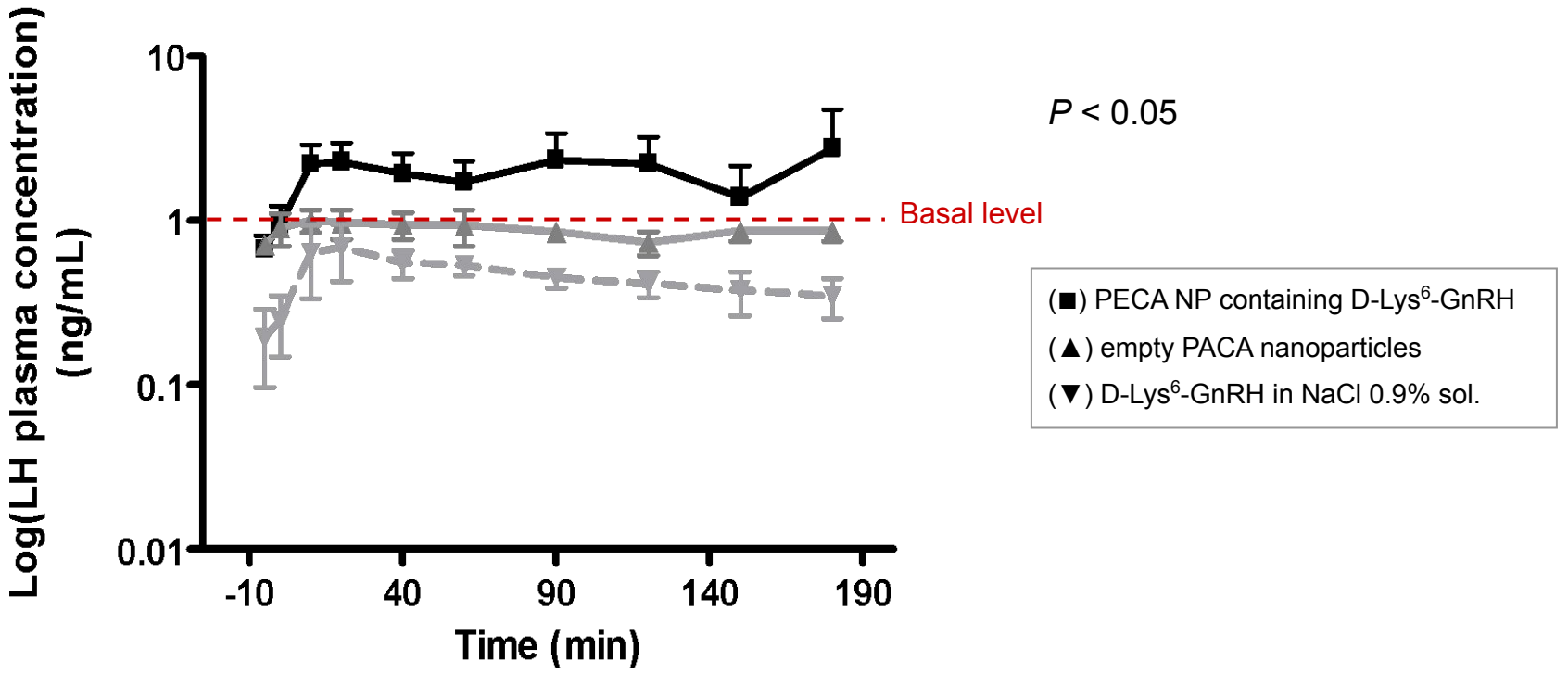
PECA nanoparticles *in vivo*

Formulation	Dose (mg)	Route of administration	*n*
D-Lys^6-GnRH NPs	2.0	i.c.	5
Empty nanoparticles	-	i.c.	5
D-Lys^6-GnRH solution	2.0	i.c.	5
D-Lys^6-GnRH solution	0.5	i.v.	3



Funding from FRST OBI National Centre for Possum Biocontrol

Biological response to D-Lys^6-GnRH formulations *in vivo*

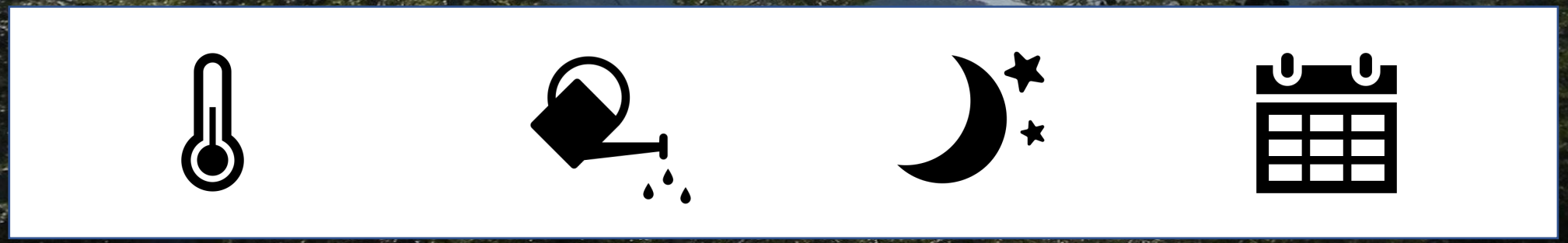


Kafka AP, McLeod BJ, Rades T, McDowell A (2011). Release and bioactivity of PACA nanoparticles containing D-Lys^6-GnRH for brushtail possum fertility control. *Journal of Controlled Release* 149: 307-313

Storage facility in NZ. A controlled environment?

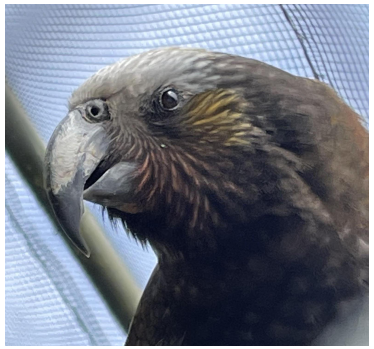
BJ McLeod

Environmental stability?




Compliance?
Size of dose?
BJ McLeod

New bioactive compounds






Sterilization of pests for conservation of native species using a cell-targeting approach

- Mammal-specific
- Contraceptive
- Oral bait

PREDATOR FREE NZ

MBIE Endeavor Fund Smart Idea ($1 M)

Caroline Decourt, Regan Anderson, Arlene McDowell, Greg Anderson

Concluding remarks

- Coronavirus highlights that wildlife health is important to human health
  - Control of overabundant, introduced species
- Sufficient intact D-Lys^{6}-GnRH can be delivered in nanoparticles to elicit a pharmacological response of infertility in the brushtail possum
- Challenges for remote oral delivery to wildlife that are beyond those of veterinary and human medicine and extends into environmental considerations
- Opportunities for nanomedicines and CR technologies to be utilized for wildlife applications

Acknowledgements

Collaborators

Assoc. Prof. Doug Eckery (Colorado State University)
Dr Bernie McLeod (formerly AgResearch, Invermay)
Euan Thompson (formerly AgResearch, Invermay)
Prof. Ian Tucker (formerly School of Pharmacy, University of Otago)
Dr Alex Kafka (Coriolis Pharma, Germany)
Prof. Thomas Rades (University of Copenhagen)

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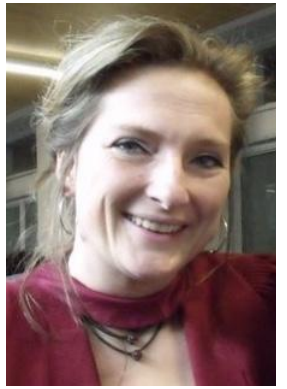
University of Otago Research Grant

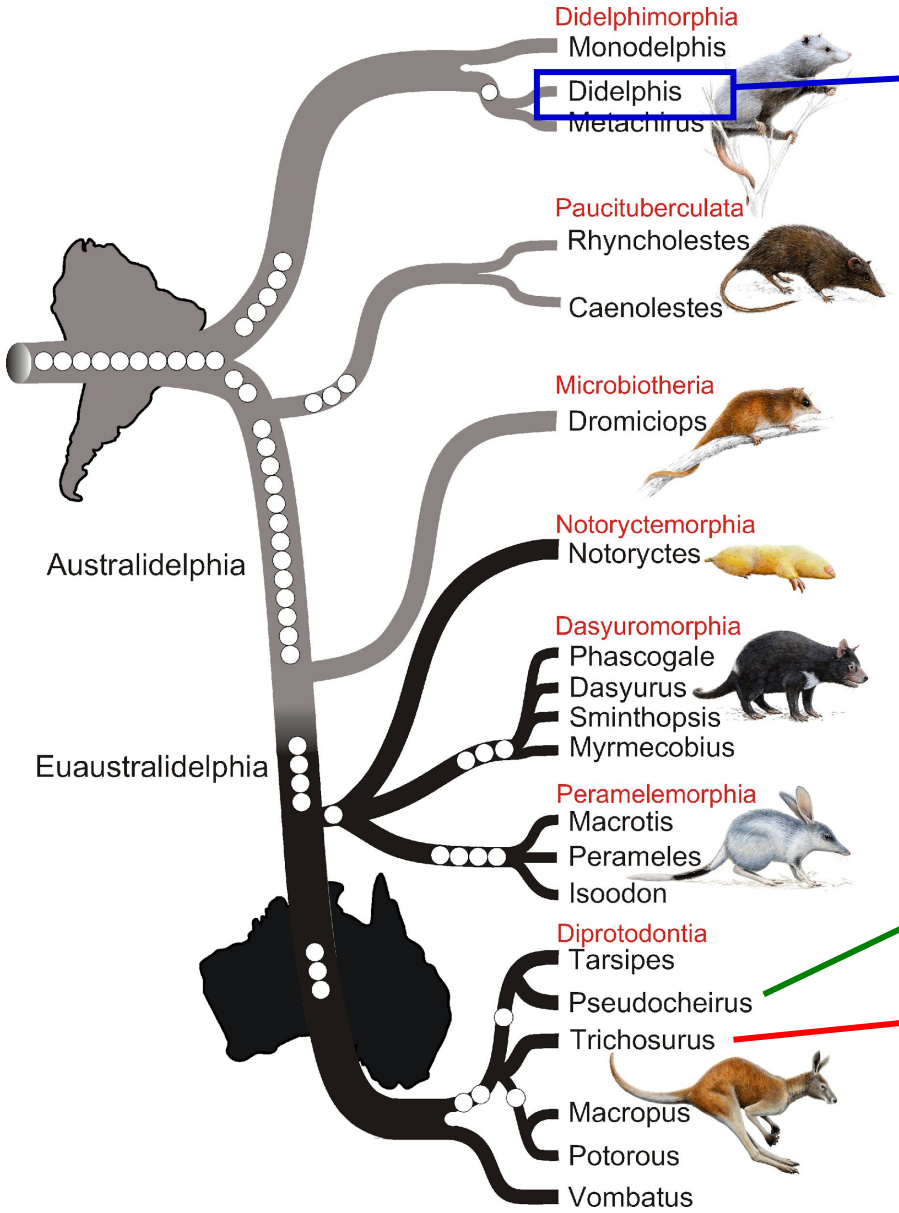







arlenemcdowell.com

@spunky_possum



Nilsson et al. PLoS Biology 8:e1000436

Opossum

Ringtail possum

Brushtail possum