CENTRE FOR
INVASIVE SPECIES SOLUTIONS

Future of nationally coordinated rabbit biocontrol R&D

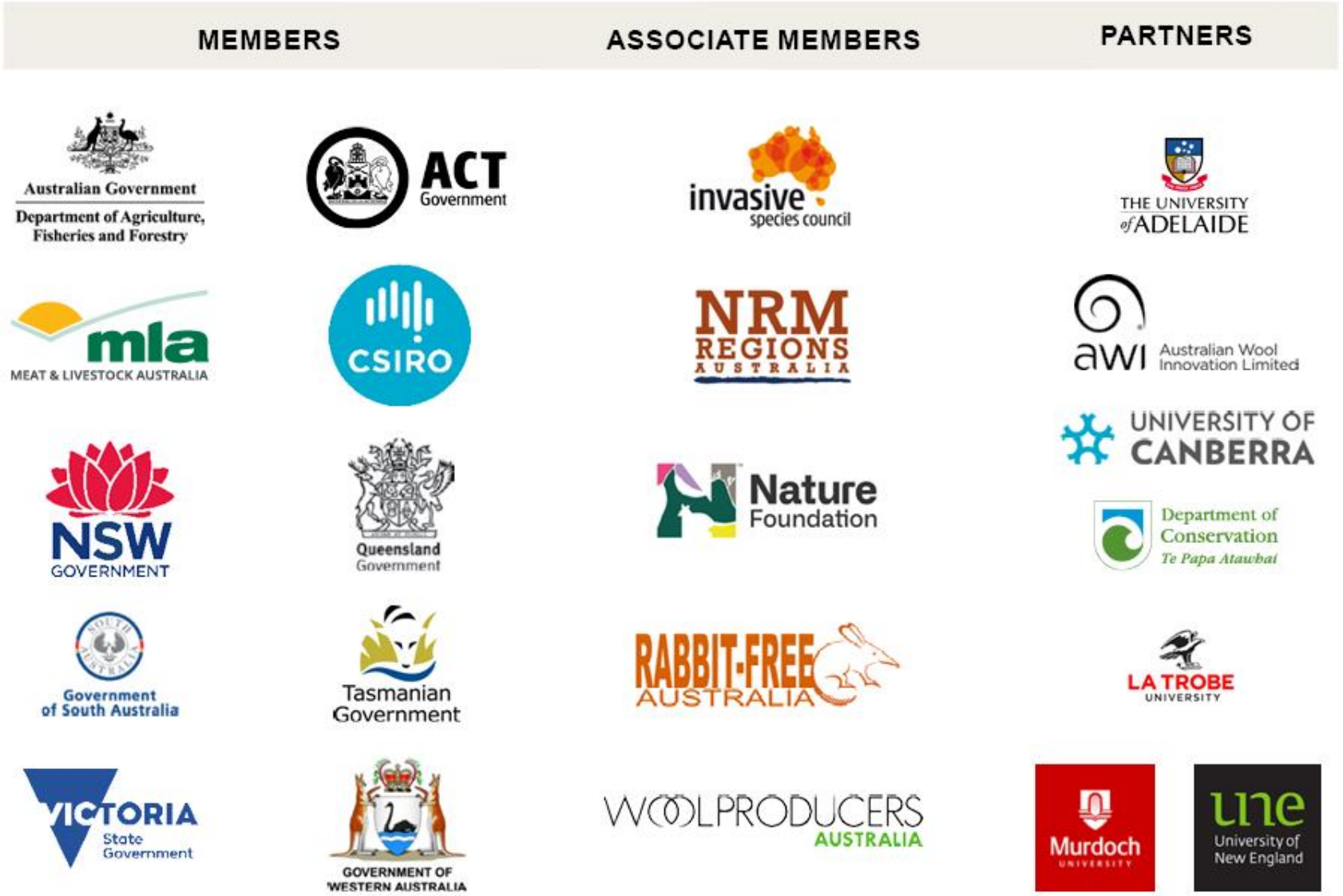
ANDREAS GLANZNIG, CEO

RABBIT R&D WEBINAR

7 MARCH 2023

Centre collaboration: members & portfolio partners

+ 62 additional R&D bodies



Rabbit Biocontrol Pipeline R&D Strategy

> Release of a new biocontrol agent every 10-15 years to counteract inevitable genetic resistance and/or waning biocontrol effectiveness

Short term:

1. **Optimise**: Better use of existing viruses

Explore RHDV2 as additional registered biocide (CISS, 2017-2022)

Optimise existing BCs and better integration with conventional control (proposed)

Medium term:

2. Discover new viruses/pathogens

3. Select for better strains of existing viruses

Long term:

4. Develop novel genetic biocontrol approaches

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CISS Innovation Pipelines:

4 streams of rabbit biocontrol R&D

	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029
1 Optimise	RHD Boost			Boost Rollout			Boost Rollout Plus (K5 release & impact assessment)			RHDV2 as a registered biocontrol agent/ National optimisation of rabbit biocontrol ?			*National biocontrol integration, monitoring and optimisation program* — *Optimise existing biocontrols and their integration with conventional management and monitoring systems: Determine distribution, impacts and interactions of circulating pathogens, detect possible evidence for genetic resistance, better detection (diagnostic) and monitoring methods, better use of biocides, possible registration of RHDV2 as addition al biocide*								
2				Bioprospecting (desktop analysis)			Eimeria intestinalis and E. flavescens distribution in Australia					MLA: Off-shore and on-shore bioprospecting				*New leads for additional biocontrol agents? Continued bioprospecting watching brief*				
3				RHD-Accelerator Platform technology			RHD Accelerator Plus					MLA: Rabbit organoids for the in vitro cultivation of RHDV				*Accelerator stage III: turbo charging the natural selection of superior virus strains for subsequent releases*				
4										Gene Drive Business case						*Transfer of successful genetic control strategies from model organisms to rabbits (GBC program)*				
												MLA: Population genomics modelling for genetic rabbit control								

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BIG THANK YOU TO CURRENT AND PAST PROJECT MEMBERS

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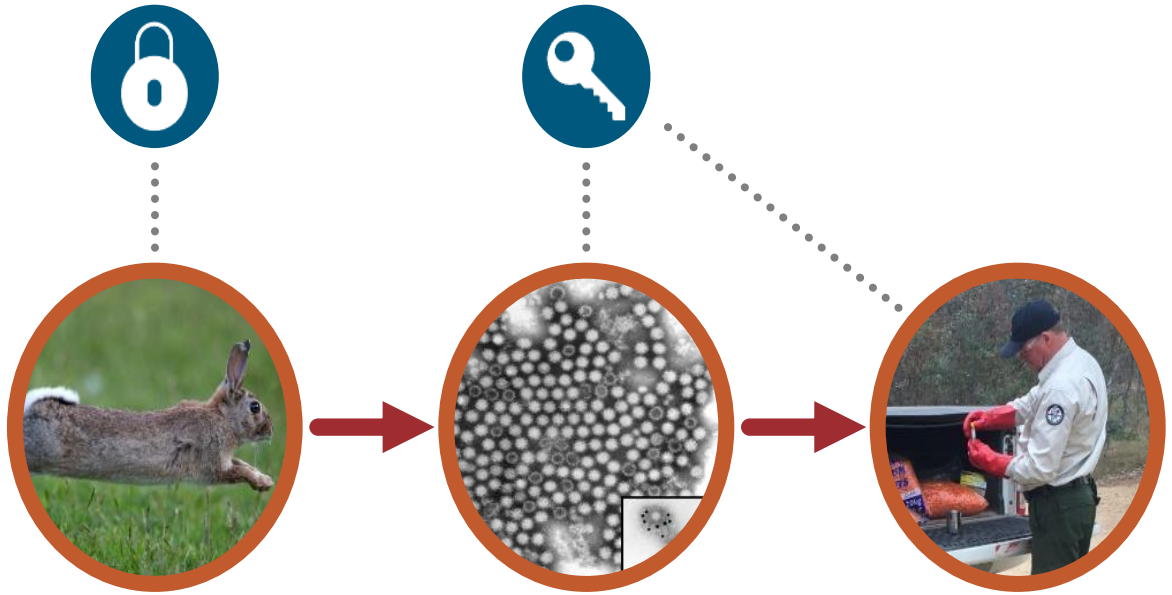
CISS Innovation Pipelines:

rabbit biocontrol

1. RHDV1 K5: first rabbit biocontrol agent in 20 years



Discovery of RCV-A1 — **Freeze-dried RHDV** — **RHDV1 K5 release**

2009 ····· 2015 ····· 2017

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The University of Adelaide · Queensland Government · Government of South Australia · Parks Victoria · Victoria State Government · Government of Western Australia · ACT Government

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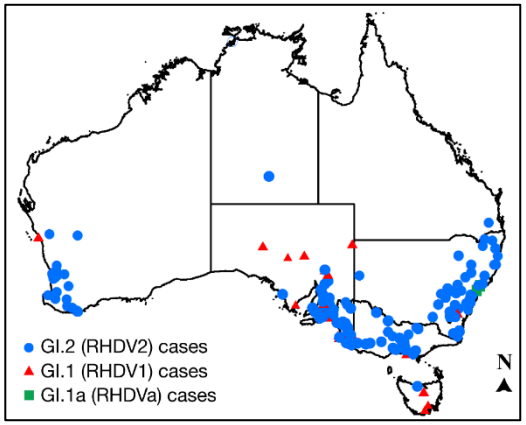
CISS Innovation Pipelines:
rabbit biocontrol

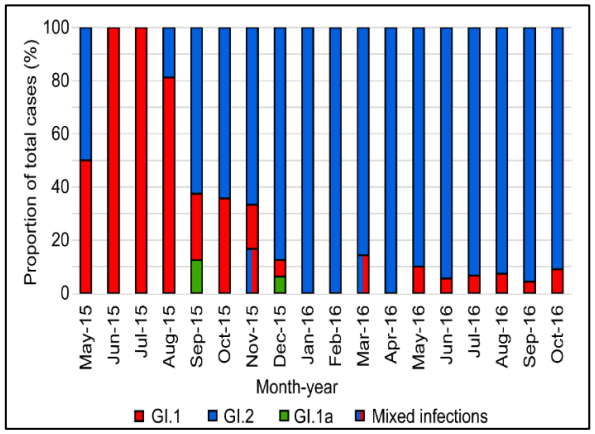
1. RHDV2: A new rabbit calicivirus

- Emerged in Europe in 2010
- Can overcome immunity to other strains
- Kills rabbits (including young) and European hares
- First reported in May 2015 (arrived in ~2014)
- Has become dominant strain in Australian environment
- Reduced rabbit populations by ~ 60% on average

Suitable as a year round registered biocontrol agent?

Science (2017-22) and economic impact assessment concluded that there is not a strong business case at this time





(Hall et al., 2015; Mahar et al., 2018; Hall et al., 2017+2018, Ramset et al., 2020)

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2. Discover new rabbit pathogens





What is killing rabbits?

Can we use it as the next biocontrol?

=> Exploratory NGS sequencing of unexplained lagomorph deaths

In Australia	Overseas North & South America
Hepatitis E in Australian rabbits	**Novel Hepaciviruses, others……?** **=> ongoing**

Centro UC
CAPES - Center of Applied Ecology & Sustainability

Jenckel et al., 2021a, Jenckel et al., 2021b, Jenckel et al., 2022

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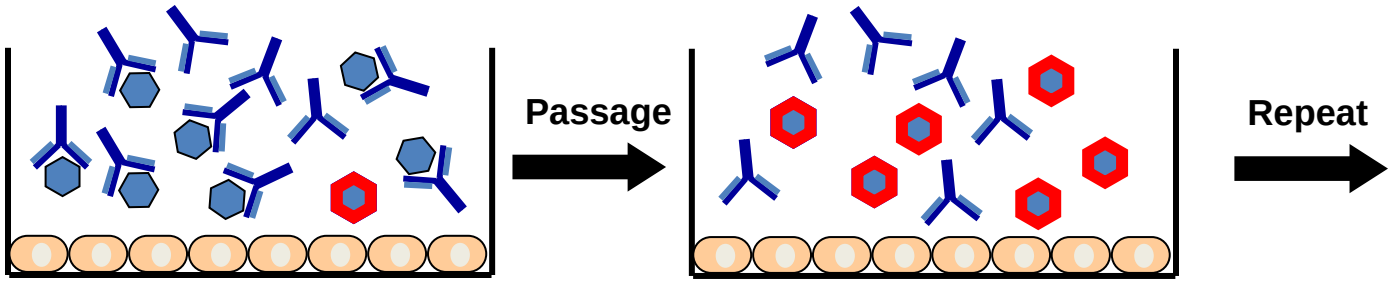
3. Select for better RHDV strains: RHD-Accelerator

=> Selection of immune escape mutants



- Next superior virus strain for release (overcomes immunity to existing strains)
- PLATFORM, repeated use, stay one step ahead
- Non-GM
- Needs a culture system!! -> lacking for >30 years for many caliciviruses

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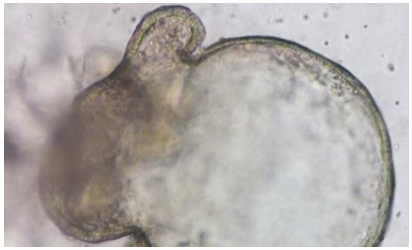
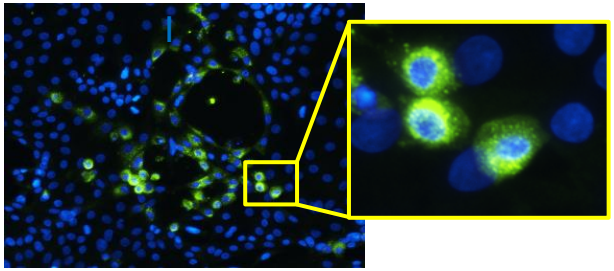
RHD-Accelerator- Development of an Organoid culture system for cultivation of virus



dsRNA/DAP



- First reproducible *ex-vivo* culture system for RHDV replication in > 30 years
- Optimisation and upscaling underway
- Liver organoids can also be used to study species specificity

Species	RHDV-1	RHDV-2
Rabbit	+++	+++
Hare	-	+++
Mouse	-	-
Cat	-	-
Fox	-	-

Hepatobiliary organoids derived from leporids support the replication of hepatotropic lagoviruses

Egi Kardia, Omid Fakhri, Megan Pavy, Hugh Mason, Nina Huang, Elena Smertina, Mary K. Estes, Tanja Strive, Michael Frese, Robyn N. Hall

doi: https://doi.org/10.1101/2022.04.07.487566

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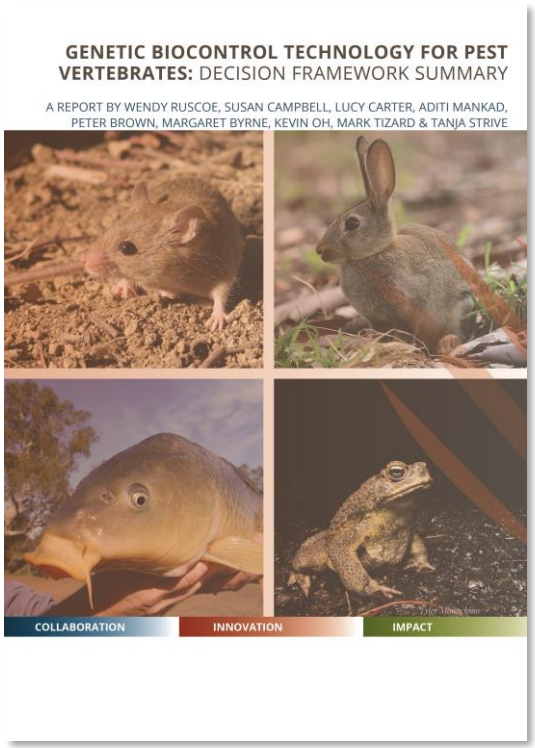
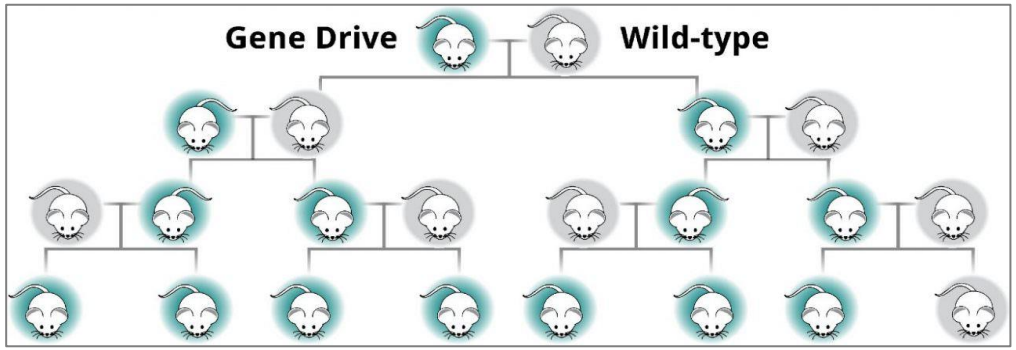
4. genetic biocontrol



National R&D program (Current)

- **Prioritisation and decision framework**
  > mice, rats, rabbits, carp, foxes, feral cats
- **Proof of concept research** on mammal (mice) and fish (zebrafish) models



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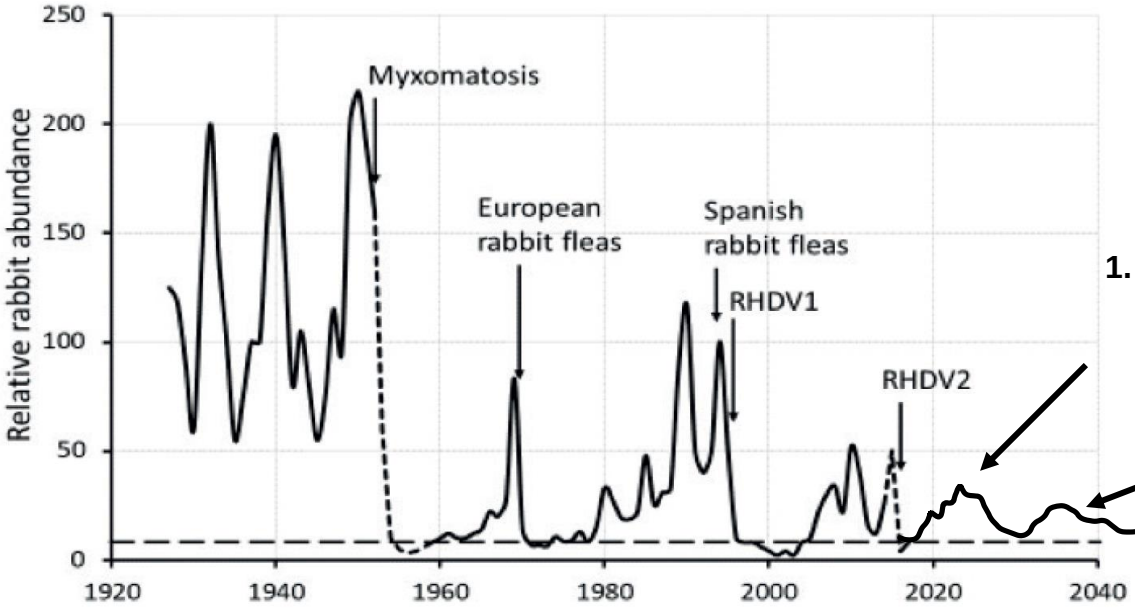
The show must go on…..



1. Optimised use of existing viruses

2. New pathogen??

3. RHD-Accelerator??

4. Genetic Biocontrol?????

The show must go on…..