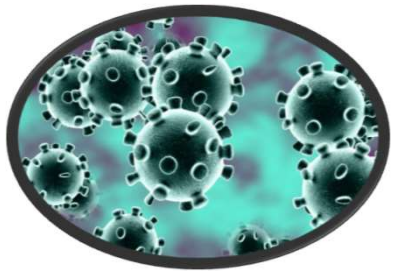

Animal Models to accelerate vaccines development

WHO Network experience during COVID

Simon Funnell
César Muñoz-Fontela
Bill Dowling
Lauren Schwartz
Ximena Riveros-Balta
Ana Maria Henao-Restrepo

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Powering research to prevent epidemics

To develop and standardize animal models to evaluate the potential for vaccine effectiveness and to understand the potential for enhanced disease after vaccination

+379 experts from **+20** countries and +**60** entities convened since Feb 2020

Live deliberations on **results**

Researchers collaborating on **protocols** and processes

Live state of the art **reviews** to guide developers and researchers

Info on **global capacity** to conduct animal studies

→

Facilitate access to global resources for **accelerated** evaluation

Enhanced **access** to animal laboratories for **ALL** developers

https://www.who.int/publications/m/item/global-animal-laboratories-capacities-to-support-vaccine-and-therapeutic-evaluation

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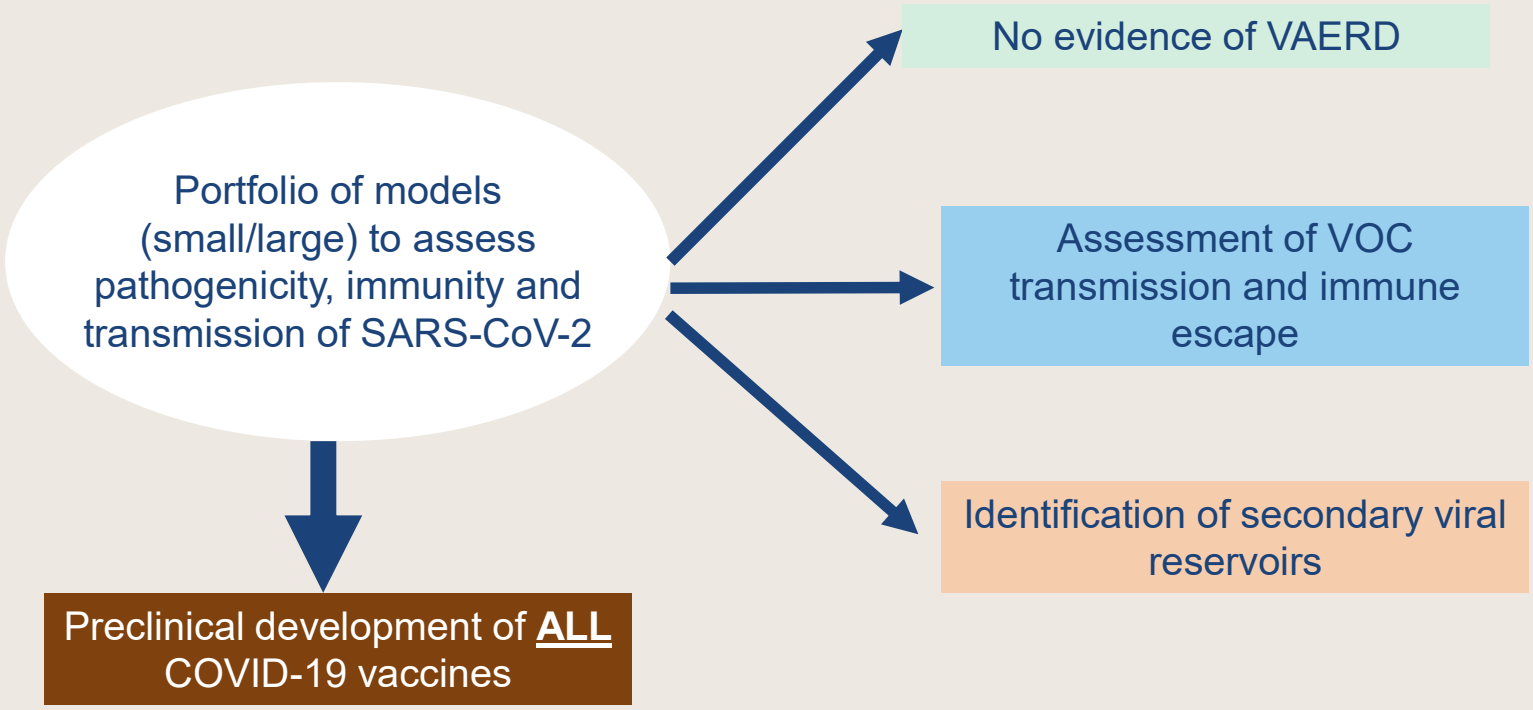
Achievements

(Muñoz-Fontela et al., Nature 2020 ; Funnell et al., Nat Commun. 2020 ; Muñoz-Fontela et al., PloS Pathog 2021 ; Funnell et al, NPJ Vaccines. 2021 Krause et al Vaccine. 2022)



Lessons learned

1) Unprecedented data sharing
2) Sharing failures and successes
3) Avoiding unnecessary repetition
4) Value of pre-prints
5) Standardization
6) ‘Proud to be WHO’

Challenges

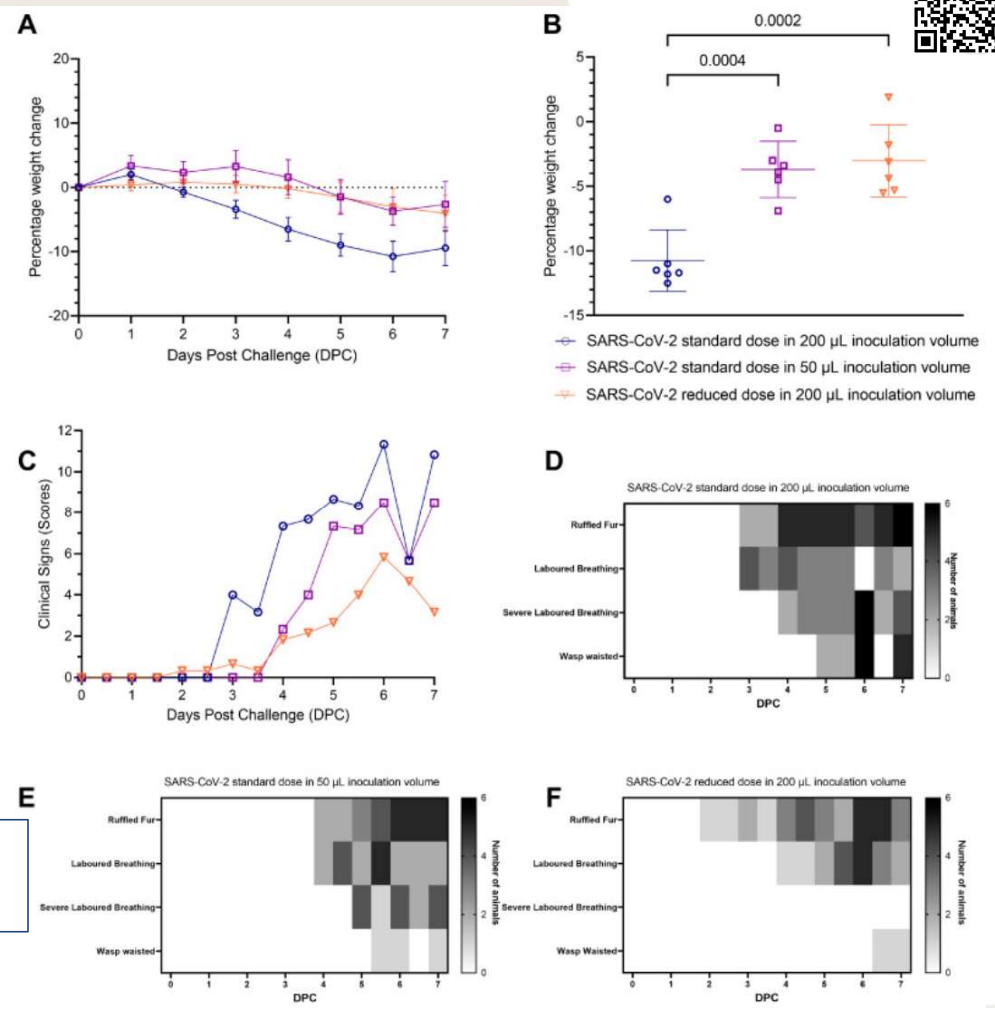
1) Animal model repositories
2) Standardization (e. g. hamsters)
3) Lack of immune reagents
4) Animal testing protocols and euthanasia endpoints
5) Moving targets need agility
6) Sharing, sharing, sharing…

SARS-CoV-2 Hamster Disease related to Volume of Intranasal Inoculum

Handley A, Ryan KA, Davies ER *et al.*, Viruses. 2023 Mar 14;15(3):748. doi: 10.3390/v15030748.

Publication	Volume of Intranasal Inoculation (µL)	Specifies per Nare?
Rosenke et al. [3]	50 total (25 per nare)	Yes
Abdelnabi et al. [10]	50 total (25 per nare)	Yes
Kawaoka et al. [9]	30 total	No
Osterrieder et al. [11]	60 total	No
Yuan et al. [12]	100 total	No
Yamasoba et al. [8]	100 total	No
Huo et al. [13]	200 total (100 per nare)	Yes
Ryan et al. [14]	200 total (100 per nare)	Yes
Song et al. [15]	200 total	No
Zhao et al. [16]	Only PFU provided—cites paper using 100 µL per nare	No
Sia et al. [17]	Only PFU provided	No

Protocols varied from the outset of the outbreak

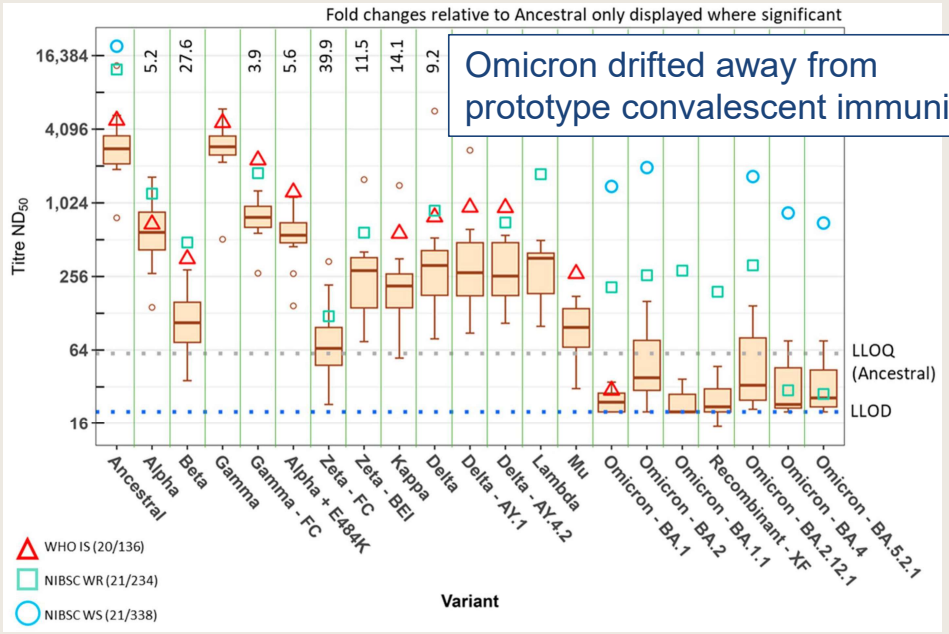


The IN volume of inoculum proportionally effects disease outcome in the hamster

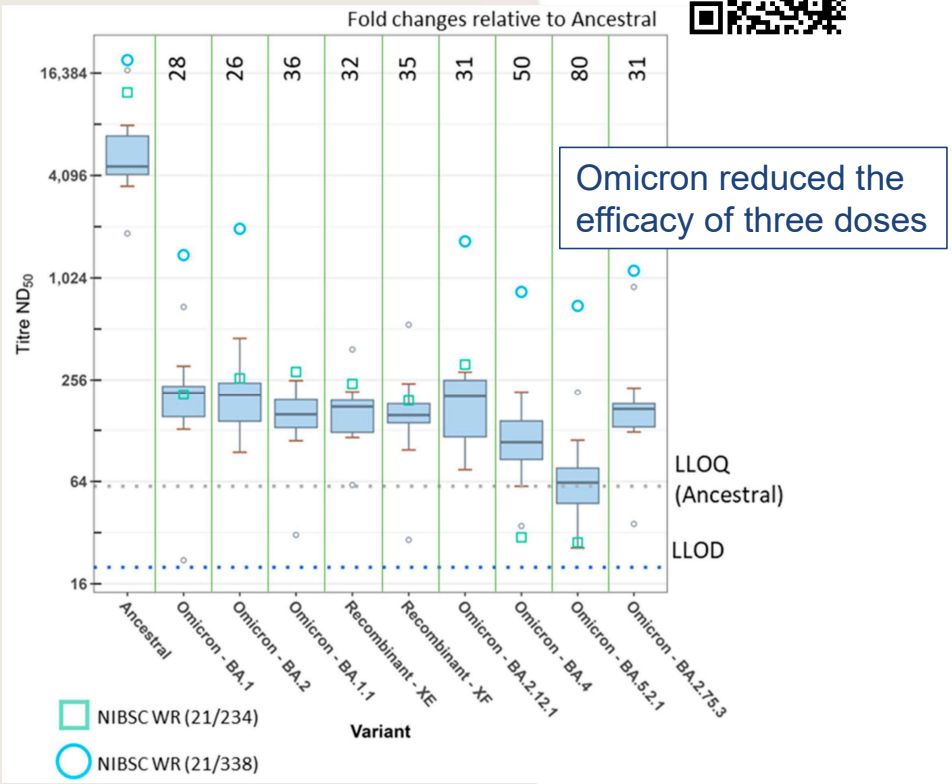
World H
Organization

A moving target needs “Agility”

Coombes *et al*, Viruses. 2023 Feb 25;15(3):633. doi: 10.3390/v15030633.



Omicron drifted away from prototype convalescent immunity



Omicron reduced the efficacy of three doses

Viral drift triggered new standards, boosters and reformulation

World Health Organization

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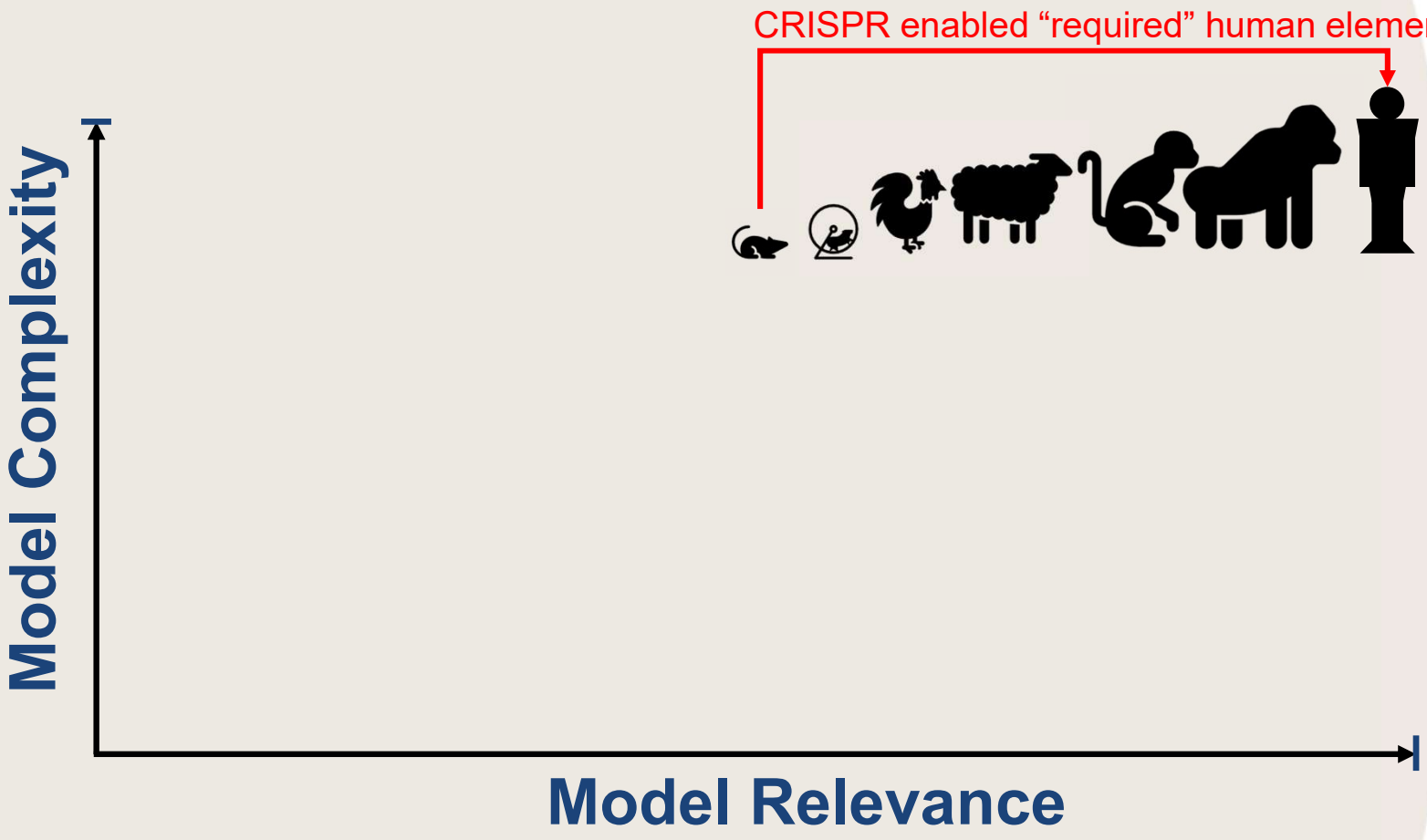
Looking at “Pathogen X”

1) Experience can save time and lives (SARS-1, MERS, MPx, Plague, CCHF)
2) Rapid sharing of data, ideas and models will reduce the time to develop vaccines and therapeutics
3) A good understanding of basic pathogenesis and immunology will speed vaccine testing (e. g. T cell epitopes in SARS-CoV-2 spike). Translational approach alone is not enough!
4) We should be prepared in case Disease X is human-specific



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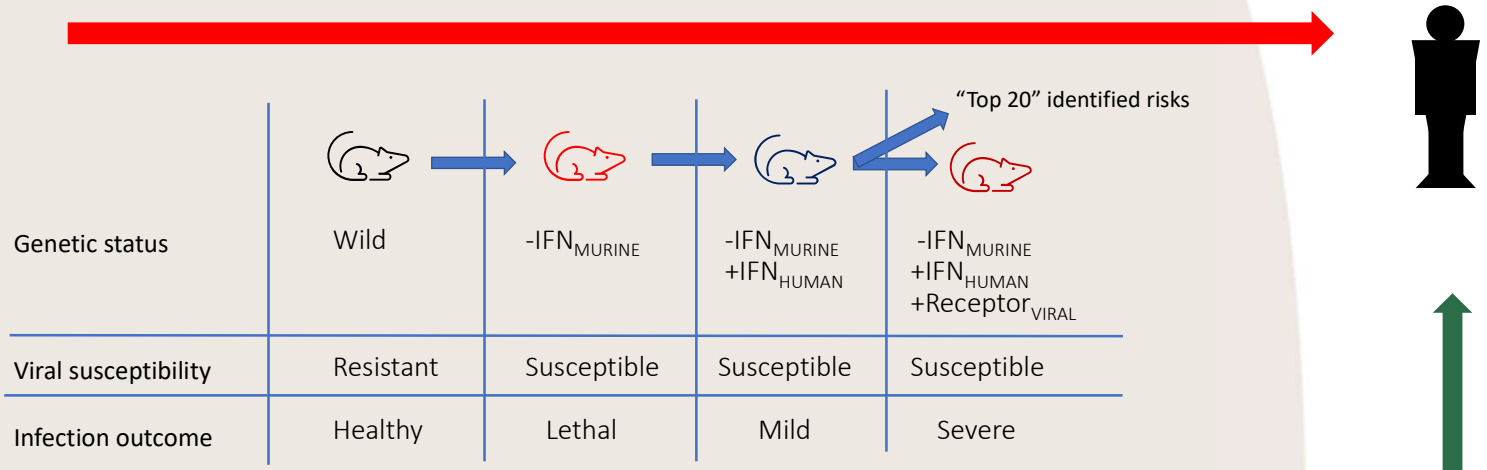
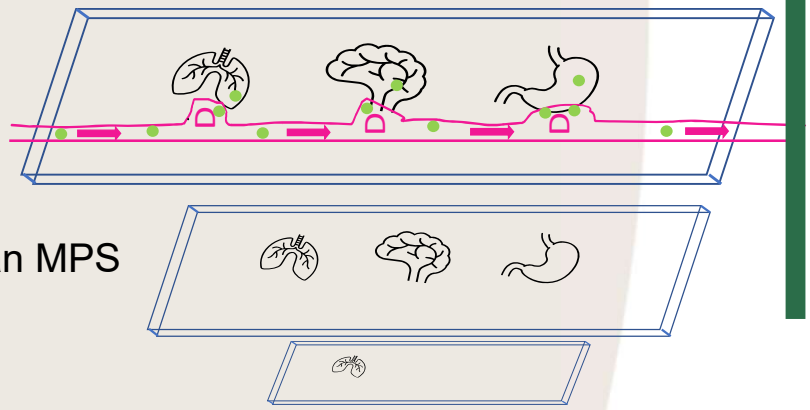
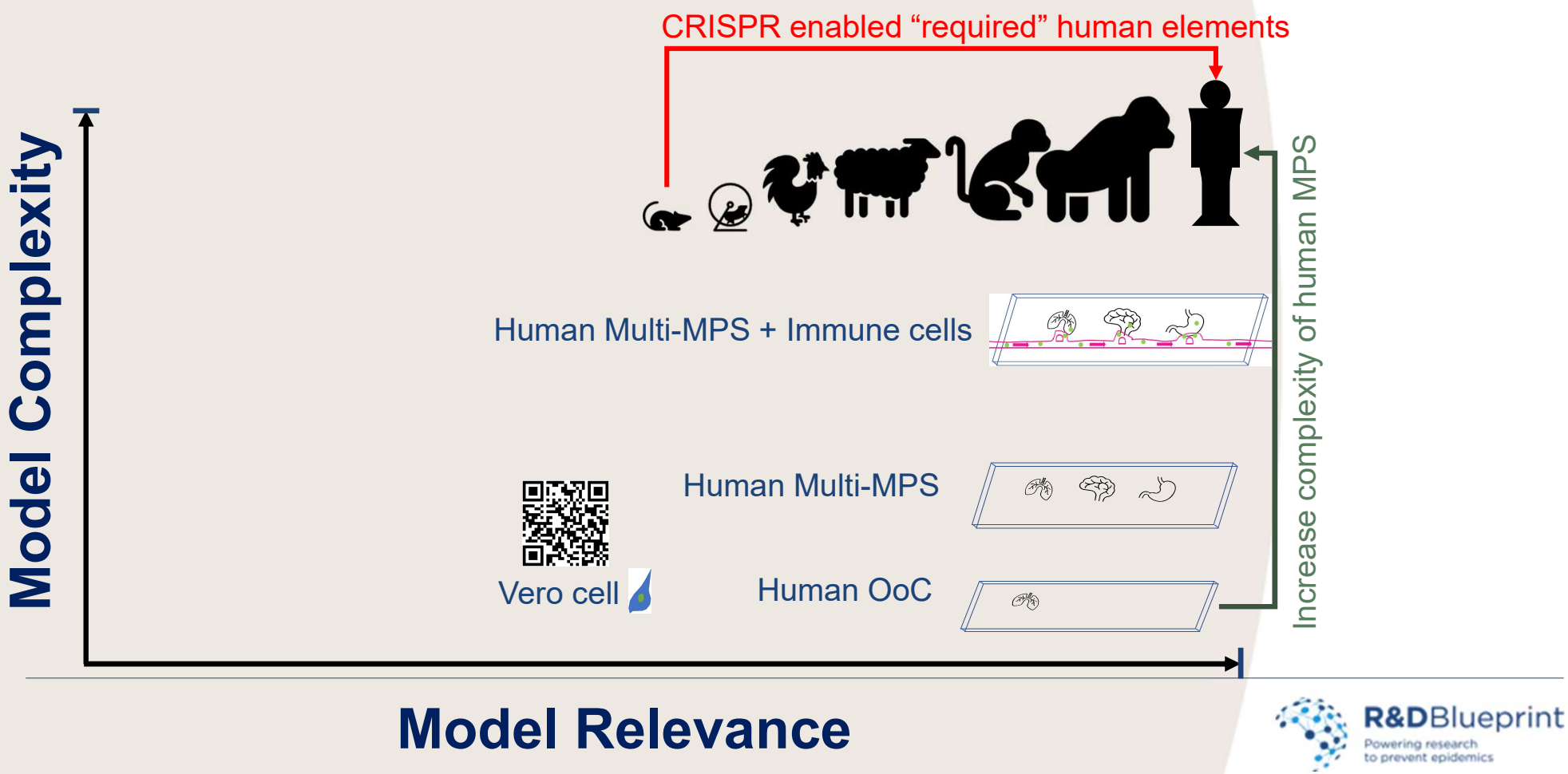


Add cellular immunity component



Set up multiple human organ MPS



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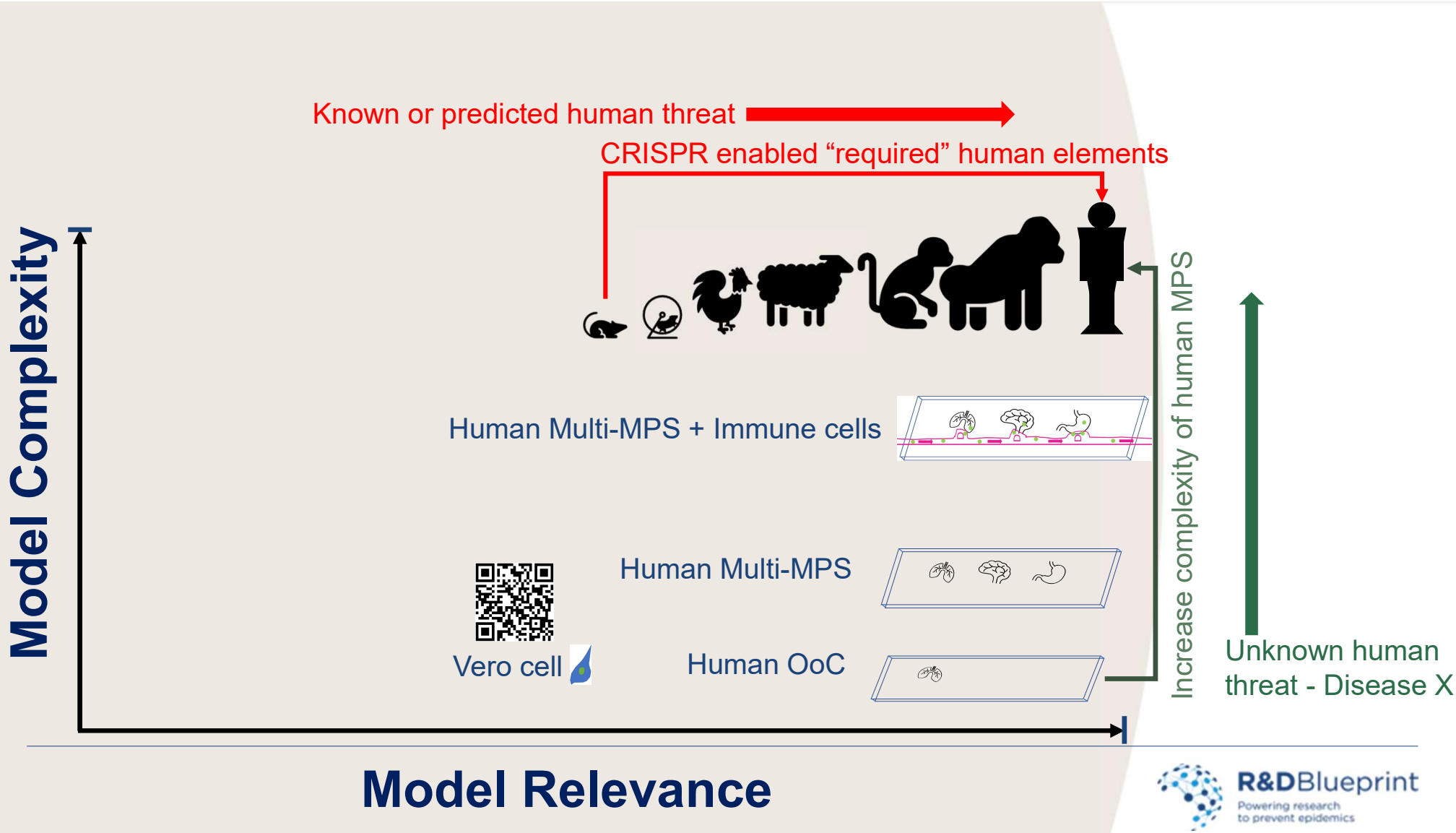
Known or predicted human threat
CRISPR enabled “required” human elements
Model Complexity
Human Multi-MPS + Immune cells
Human Multi-MPS
Vero cell
Human OoC
Increase complexity of human MPS
Unknown human threat - Disease X
Model Relevance
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Powering research to prevent epidemics

"What needs to be done?"

Sharing data and resources to accelerate development of drugs, therapeutics and vaccines especially standards, reagents, pathology data, clinical samples and methodology.

Simultaneous development of animal models refined for each of the known high-risk groups of pathogens along with simultaneous development of microphysiological systems which may complement or support *in vivo* approaches.

We should agree ahead of the next event to continue international data sharing