Contributed paper

THE ANSTEE HUB FOR INHERITED DISEASES OF ANIMALS (AHIDA) – DEVELOPMENT OF A NEW ONLINE PLATFORM FOR SURVEILLANCE, REPORTING AND CONTROL OF INHERITED DISEASES IN ANIMALS

I. Tammen[1,4], C. Wade[2,4], B. Waud[1,4], M. Gimeno[1,4], B.D. Velie[2,4], B. O'Rourke[3,4] and F.W. Nicholas[1,4]

[1] Sydney School of Veterinary Science, Faculty of Science, The University of Sydney, Sydney, NSW, 2006, Australia
[2] School of Life and Environmental Sciences, Faculty of Science, The University of Sydney, Sydney, NSW, 2006, Australia
[3] Elizabeth Macarthur Agricultural Institute, Department of Primary Industries, Menangle, NSW, 2568, Australia
[4] Anstee Hub for Inherited Diseases of Animals (AHIDA)

SUMMARY

Inherited diseases are often rare but their cumulative impact is substantial. The published data about inherited conditions in animals, and particularly about monogenic disease with known likely causal variants, is steadily increasing. However, limited information is available about how frequently these conditions occur. Animal owners and veterinarians often don't know how to report emerging genetic conditions, how to find out about available information about existing conditions or how to connect with researchers who would be interested to investigate such conditions. This problem can be addressed by the provision of a curated portal for the reporting of potential inherited disorders by owners or veterinarians. This paper describes the initial planning of a centralised resource for surveillance, reporting and control of inherited diseases of animals in Australia.

INTRODUCTION

For humans, the global reference compendium Online Mendelian Inheritance in Man (OMIM, https://omim.org/) includes 5,762 monogenic inherited diseases and other traits for which causal variants have been reported (https://omim.org/statistics/geneMap). Most of these could also occur in any animal species. However, while the number of monogenic traits and diseases in animals for which causal variants are known is steadily increasing (Figure 1), to date these represent only a relatively small number of inherited monogenic diseases for any of the major domesticated animal species (Table 1).

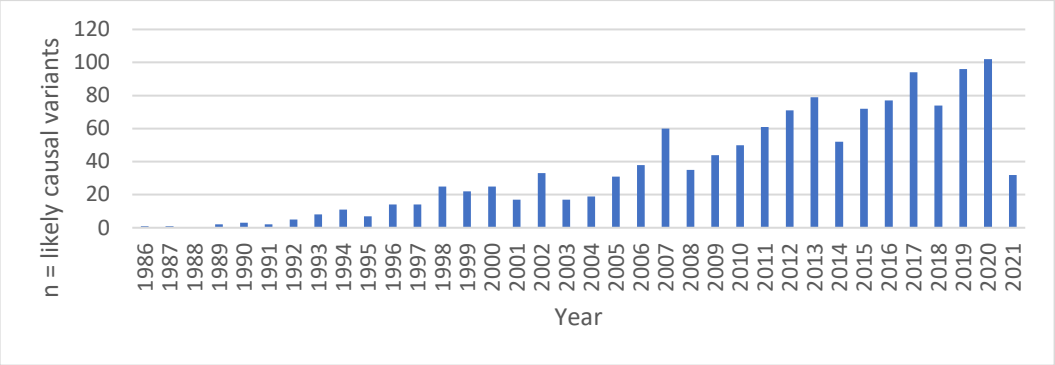

Figure 1. Likely causal variants for monogenic traits and diseases reported per year in Online Mendelian Inheritance in Animals (OMIA, https://omia.org/)

Table 1. Summary of information about inherited conditions (phenes) in major domestic species in Online Mendelian Inheritance in Animals (OMIA, https://omia.org/). Phenes include disorders as well as non-disorder traits such as blood systems and most pigmentation traits. The numbers for deleterious conditions for each category are listed in brackets

	Dog	Cattle	Cat	Pig	Sheep	Horse	Chicken	Goat
Total phenes (disorders)	787 (731)	555 (503)	363 (328)	286 (239)	258 (195)	242 (210)	223 (163)	90 (53)
Mendelian phenes (disorders)	364 (331)	261 (228)	117 (92)	92 (69)	112 (71)	49 (41)	132 (93)	20 (12)
Mendelian phenes (disorders) with likely known causal variant(s)	299 (269)	167 (146)	84 (68)	41 (28)	59 (32)	46 (29)	51 (29)	15 (8)

Population genetics modelling and whole genome sequence analyses suggest that all humans and animals are likely to be carriers of multiple deleterious alleles, further highlighting that inherited diseases pose a significant risk to health and welfare.

In animal populations, inbreeding and small effective population size increase the risk of recessive diseases: deleterious allele frequencies can amplify rapidly if particular sire lines are widely used. The result is that the risk of inherited diseases is greater in animals than in humans. Furthermore, inherited diseases in animals are often misdiagnosed, and are under-reported due to a lack of reporting structures, and concerns from many animal breeders that reporting suspected inherited conditions to their breed societies could cause reputational damage.

However, if an emerging disease is identified as inherited, effective mating plans can be implemented to reduce the risk of affected animals being born, either by predicting genotypes by pedigree analysis or by implementing DNA diagnostics once the disease-causing mutation(s) has been identified. Control of inherited diseases by these means has a direct effect on the betterment and welfare of animals.

Currently, Australia has no centralised resource for surveillance, reporting and control of inherited diseases in animals. Internationally, such resources are limited and often species-specific. Bequest funding has become available for the development of the Anstee Hub for Inherited Diseases of Animals (AHIDA) to provide a solution for preventing and controlling inherited diseases in animals throughout Australia, aiming at:

1. Establishing and maintaining an Australia-wide surveillance and reporting resource for inherited diseases in animals,
2. Prioritising emerging inherited diseases for research and control, based on published criteria that include incidence, welfare and (where relevant) financial impact
3. Facilitating undergrad/postgrad research projects on the highest-priority inherited diseases,
4. Disseminating information on emerging inherited diseases and, more generally, on the incidence/occurrence of inherited diseases and their management, to veterinarians, breed societies and the public, mainly via Online Mendelian Inheritance in Animals (OMIA)

This paper will outline the proposed structure of AHIDA, and the presentation will provide additional information on how stakeholder feedback from an online workshop held in August 2021 will be used to refine our vision.

PROPOSED STRUCTURE FOR AHIDA

AHIDA is a proposed online portal with designated entry points for researchers, veterinarians

and animal owners, for reporting and surveillance of inherited conditions in animals.

Veterinarians and animal owners will be prompted to submit to the database information about animals with suspected or confirmed inherited conditions.

Data submission will be guided using standardised nomenclature for species, breed (Universal Breed ontology, UBO) and disease phenotype (Universal Phenotype Ontology, UPO) using standardized nomenclature for diseases, clinical signs and pathology.

The breed and phenotype ontologies are currently being developed in collaboration with the leaders of the Monarch (ontology) Initiative (Shefchek et al. 2019), and aim to combine information from available resources such as DADIS (http://www.fao.org/dad-is/en/), LBO (https://www.animalgenome.org/bioinfo/projects/lbo/), SAVSNET (https://www.liverpool.ac.uk/savsnet/), SNOMED-CT (https://www.snomed.org/snomed-ct/why-snomed-ct) and VeNom (http://venomcoding.org/)..

Once fully integrated, AHIDA will directly link submitters with information about similar genetic conditions listed in animals (OMIA) or humans (OMIM), link to providers of DNA tests, provide generic information about management and control of inherited diseases in animals, and if requested, connect submitters with species expert panels for further advice.

Our aim is to develop species expert panels which include geneticists, clinicians and pathologists who can provide genetic counselling advice and link submitters with research teams that have expressed an interest in a specific disease, disease group or species.

AHIDA will report – in a format to be developed in collaboration with stakeholders – occurrence of genetic diseases, likely based on type of disease and species and breed. When fully operational, it is envisaged that additional information about occurrence of inherited diseases will be available via reciprocal links to VetCompass Australia (https://www.vetcompass.com.au/) and the soon-to-be-developed Veterinary and Animal Research Data Commons, and interested genotyping providers could report allele frequencies for monogenic diseases for which likely causal variants are tested. This will generate more accurate information about occurrence of inherited diseases in Australian animals and will inform research initiatives and management strategies.

We hope to be able to link OMIA and AHIDA to existing image repositories so that images or videos relating to the disease phenotype can be shared among submitters, species expert teams and researchers.

Limited funding will be available for research students at the University of Sydney to investigate emerging conditions that have been prioritised according to evidence-based criteria. Prioritisation is likely to consider incidence, welfare impact, population characteristics (e.g., effective population size, International Union for Conservation of Nature (IUCN) status), likelihood/costs to develop an efficient management approach, availability of research and (where relevant) financial impact of the genetic condition.

CONCLUSIONS

While generous bequest funding has been made available for the initial development of this initiative, ongoing support from key industry stakeholders and breed societies, the veterinary profession and the wider research community will be required for the vision to succeed. A workshop to collect stakeholder feedback will have been conducted by the time of the conference and we will report on the reshaped vision.

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REFERENCES

Shefchek K.A., Harris N.L., Gargano M., Matentzoglu N., Unni D., Brush M., Keith D., Conlin T., Vasilevsky N., Zhang X.A., Balhoff J.P., Babb L., Bello S.M., Blau H., Bradford Y., Carbon S., Carmody L., Chan L.E., Cipriani V., Cuzick A., Della Rocca M., Dunn N., Essaid S., Fey P., Grove C., Gourdine J.P., Hamosh A., Harris M., Helbig I., Hoatlin M., Joachimiak M., Jupp S., Lett K.B., Lewis S.E., McNamara C., Pendlington Z.M., Pilgrim C., Putman T., Ravanmehr V., Reese J., Riggs E., Robb S., Roncaglia P., Seager J., Segerdell E., Similuk M., Storm A.L., Thaxon C., Thessen A., Jacobsen J.O.B., McMurry J.A., Groza T., Köhler S., Smedley D., Robinson P.N., Mungall C.J., Haendel M.A., Munoz-Torres M.C. and Osumi-Sutherland D. (2020) *Nucleic Acids Res*. **48**: D704.