A chicken genomics resource for mapping myopia susceptibility genes: The Hong Kong UGC Chick Myopia Project

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Introduction
The rapid rise in the prevalence of myopia in recent decades implicates an important role for environmental (lifestyle) factors in the aetiology of the refractive errors, while high heritability implicates a strong genetic contribution. Gene-environment interactions may partly explain why both genetics and lifestyle factors have been shown to play important roles, e.g. responses to myopia-inducing cues from the visual environment may differ depending on an individual’s genetic background. In humans, well-powered studies capable of detecting such gene-environment interactions require larger sample sizes than those currently available, and thus few robust gene-environment interactions have been discovered to date. An alternative approach is to identify genes that confer a high susceptibility to myopia, or offer resistance against myopia, in an animal model. Animal studies have the advantage of providing a highly uniform environment, such as a carefully-controlled duration of exposure to visual form-deprivation or minus lens wear, which is expected to increase statistical power to detect gene-environment interactions. Indeed, it has previously been shown using this approach that more than 50% of the variation in susceptibility to form-deprivation myopia in chicks is determined by genetic factors.

Methods
In order to develop a resource for mapping myopia susceptibility genes in an animal model, we have launched The Hong Kong UGC Chick Myopia Project. Outbred chicks undergo high-resolution A-scan ultrasonography at age 7 days-old, followed by monocular form deprivation for 4 days. After the treatment period, the degree of induced myopia is quantified by retinoscopy and A-scan ultrasonography. A blood sample is taken for extraction of genomic DNA, and the neural retina from each eye is collected in RNAlater ready for RNA extraction. Sexing is carried out using an allele-specific PCR assay on the DNA sample. Chicks are treated in batches of approximately 25 (one batch per week).

Results
To date more than 300 chicks have been phenotyped using the protocol described above. Further work will bring the total to more than 1000, sufficient to map genes with significant effects on myopia susceptibility. The accuracy of the phenotypic assessment has been confirmed by validating previous findings: (1) greater pre-treatment and post-treatment anterior and vitreous chamber depths in males vs. females (P<0.001), (2) longer axial length in right vs. left eyes (P<0.001), (3) no correlation between change in body stature and susceptibility to myopia (r=0.1; P=0.16) and (4) a high correlation between the degree of induced myopia and induced axial elongation in treated eyes (r=0.79; P<0.001).

Conclusion
Genetic variants that cause increased susceptibility to, or resistance to, visually-induced myopia can be mapped by applying conventional genome-wide association study (GWAS) methods in this chick population. Fine mapping will be facilitated by analysis of gene expression levels of candidate genes in retinal samples from treated and control eyes. We aim to make the phenotypic data, DNA and RNA samples from this resource population available to the myopia research community, to maximise its impact for myopia research.