**YEAR: 2013/14**

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**INSTITUTION: ABERDEEN UNIVERSITY**

**PROJECT TITLE: DEVELOPMENT OF A NEW CHCKEN MODEL OF THE HUMAN LOWER LIMB ABNORMALITY, CLUBFOOT**

**Brief Resume of your Project’s outcomes for the Society’s Website**: **(no more than 200-250 words)**.

*The title of your project and a brief 200-250 word description of the proposed/completed project. The description should include sufficient detail to be of general interest to a broad readership including scientists and non-specialists. Please also try to include 1-2 graphical images (minimum 75dpi). NB: Authors should NOT include sensitive material or data that they do not want disclosed at this time.*

‘Clubfoot’ is a very common lower limb abnormality that affects 1 in 500 babies born in Western Europe. Why the condition occurs remains largely unclear. Previous studies have shown a strong genetic component, but environmental influences and stochastic bad luck also appear to contribute. There are two published genetic mouse models that exhibit a clubfoot phenotype and they both show increased activation of an enzyme, LIMK1, that is required for normal growth of nerves during development. In the clubfoot mice, the peroneal nerve, which innervates the calf muscles on the outer side of the legs, was missing. This was thought to cause muscle weakness that underlies the clubfoot. To show whether or not increased LIMK1 activity was sufficient to cause clubfoot, extra copies of the LIMK1 gene were directly introduced into spinal nerves of developing chickens in ovo. This genetic manipulation was found to cause stalling of the peroneal nerve and, with low frequency clubfoot in the chicken embryos. Jasplakinolide, a drug that mimics LIMK1 over-activation by stalling the growth of nerves, was shown to have a similar effect. The data suggest that mutations that affect expression of human LIMK1 may predispose babies to clubfoot. This could be tested by sequencing LIMK1 in human clubfoot patients.

*File: UGProjectOutcomes201314CollinsonRoss*