Institution: University of Edinburgh and SRUC, Scotland's Rural College

Unit of Assessment: 6

Title of case study: Promoting public and policy-maker understanding of the benefits of genetic modification (GM) technology in chickens; transgenic birds that do not transmit avian influenza.

1. Summary of the impact (indicative maximum 100 words)

Impact: Public policy and public engagement: public awareness towards GM animals.

Significance: The chicken industry is worth £2 billion per annum in the UK alone. GM technology offers increased productivity, biosecurity and welfare as well as biotechnology applications in production of protein therapeutics. Realization of this technology requires public acceptance.

Beneficiaries: general public, applied researchers, pharmaceutical industry, poultry breeding companies

Attribution: Work performed by Professor Sang, Dr. Clinton (Roslin Institute, now part of UoE)

Reach: International: The work has been used to advise on policy for the USA (FDA) and European Food Safety Agency. As a further example Professor Sang's "our changing world lecture" has been viewed 1054 times across multiple countries.

2. Underpinning research (indicative maximum 500 words)

The production of transgenic chickens is technically challenging because embryonic development occurs on the surface of the egg yolk and development to hatch requires incubation in a shelled egg. Professor Sang (Group leader, Roslin Institute and UoE, employed 1984-onwards), funded by three grants totalling £1,957K from Viragen Inc. (Florida, USA), overcame these barriers. Her team developed a host egg culture system that enabled hatching of embryos after genetic manipulation. She then constructed lentiviral vectors capable of delivering transgenes to early chick embryos, which were subsequently hatched as healthy chicks [3.1].

From 2004-2006 Sang optimised the expression vectors in order to direct synthesis of foreign proteins specifically to the oviduct of laying hens, resulting in incorporation of the protein in egg white. This advance paved the way for expression of biologically active, therapeutic proteins that could be expressed exclusively in the oviduct and extracted from egg white [3.2].

Chick embryos are valuable models for investigating vertebrate development: they are accessible in the incubated egg and can be manipulated in functional experiments. From 2001-2007 Sang developed a transgenic chicken line ubiquitously expressing green fluorescent protein (GFP) and demonstrated that cells from GFP embryos could be transplanted to normal chick embryos to investigate the fate of transplanted cells, including identifying stem cell populations [3.3]. This technique was utilised further in collaboration with Dr. Clinton (Group leader, Roslin Institute and UoE, employed 1991-onwards) to demonstrate that somatic sex identity is cell autonomous in the chicken [3.4].

Genetic modification in the chicken has the potential to improve the productivity of domestic poultry. Sang and Dr Laurence Tiley (University of Cambridge) undertook a proof-of-principle study, describing generation of transgenic chickens that do not transmit avian influenza when infected with H5N1 virus [3.5].

3. References to the research (indicative maximum of six references)

3.1) McGrew, M., Sherman, A., Ellard, F., Sherman, A., Lillico, S., Gilhooley, H., Kingsman, A., Mitrophanous, K. & Sang, H. (2004) Efficient production of germline transgenic chickens using lentiviral vectors. EMBO Reports 5, 728-733. Recommended in Faculty of 1000. http://dx.doi.org/10.1038/sj.embor.7400171

3.2) Lillico, S.G., Sherman, A., McGrew, M.J., Robertson, C.D., Smith, J., Haslam, C., Barnard, P., Radcliffe, P.A., Mitrophanous, K.A., Elliot, E.A., Sang, H.M. (2007) Oviduct-specific

expression of two therapeutic proteins in transgenic hens. PNAS 104: 1771-1776 http://dx.doi.org/10.1073/pnas.0610401104

3.3) McGrew, M.J., Sherman, A., Lillico, S.G., Ellard, F.M., Radcliffe, P.A., Gilhooley, H.J., Mitrophanous, K.A., Cambray, N., Wilson, V. and Sang, H. (2008) Localised axial progenitor cell populations in the avian tail bud are not committed to a posterior Hox identity. Development 135, 2289-2299. Recommended by Faculty of 1000. http://dx.doi.org/10.1242/dev.022020

3.4) Zhao D, McBride D, Nandi S, McQueen H, McGrew M, Hocking P, Lewis P, Sang H & Clinton M (2010) Somatic sex identity is cell-autonomous in the chicken. Nature 464, 237-242. http://dx.doi.org/10.1038/nature08852

3.5) Lyall, J., Irvine, R.M., Sherman, A., McKinley, T.J., Nunez, A., Purdie, A., Outtrim, L., Brown, I., Rolleston-Smith, G., Sang, H., Tiley, L. (2011) Suppression of avian influenza transmission in genetically modified chickens. Science 331, 223-226. http://dx.doi.org/10.1126/science.1198020

4. Details of the impact (indicative maximum 750 words)

Public Policy and Awareness

Public policy and awareness represents the major realised impact of the research to date, and the primary focus of this case. The generation of birds that cannot transmit avian flu received national and international press coverage (e.g. http://www.bbc.co.uk/news/science-environment-12181382). The recognition of the potential of genetically modified birds encompassed both potential disease resistance and their potential use as bioreactors. A Google search (September 2013) on "Transgenic chicken and Roslin" generates >90,000 hits including such disparate web sites as medicalnewstoday.com, smartplanet.com, vetsonline.com, burrillreport.com, www.heraldscotland.com and theranger.co.uk. The increasing public acceptance was evident when the transgenic birds resistant to influenza were recently featured on the BBC1 show Countryfile (11.8.2013). This show was linked to a debate on the relative importance of genetic technologies in livestock improvement. The change in attitudes was evidenced in the positive stance taken by interviewees. The research not only demonstrated the feasibility of the technology, but also exemplified a major benefit to both animal welfare and human health.

The impact is evident in the explicit promotion of GM animals as well as plants, in the recently announced UK Agri-tech Strategy (2103) where the research at Roslin was directly cited. Sang and colleagues have used numerous other opportunities to explain and discuss GM technologies and issues including presentations and discussions with school children, public lectures, e.g. meetings of Edinburgh and Brighton Café Scientifique (~130 attendees) and University of Edinburgh public lecture series "Our Changing World" (~150 attendees, >1000 views).

In addressing the issues of safety, licensing and public acceptance that applications of genetic modification in poultry breeding and production raise, Sang has been an advisor to policy development, given a seminar on GM chickens to Centre for Veterinary Medicines, Federal Drug Administration (US regulatory body, October 2012) and been ad hoc advisor to the European Food Safety Authority GMO panel. The ethical issues of the use of transgenes have been widely debated, for example: http://bioethicsbytes.wordpress.com/2013/01/04/headline-bioethics-gm-chickens-offer-solution-to-bird-flu-problem/. Similarly, the technology sparked debate about whether it is possible to patent transgenic animals. http://www.slwip.com/services/ip_papers/transgenic_animals.html

Improved Animal Welfare, Health and Production

The investment in development of bird flu resistance is being advanced through collaboration with a world-leading poultry breeding company (EW-Group) (BBSRC Industrial Partnership Award BB/J017108/1; £432K). This investment is, of itself, a reflection of the awareness by the major breeding companies that the technology is likely to be effective and accepted. EW-Group will evaluate the potential of the GM approach to control avian influenza virus, while developing the business strategy and investigating the regulatory and public acceptance issues inherent in introducing genetic modification into their programme. Poultry meat is currently the second largest

(34%) meat market after pork, predicted to become the largest because of its broad appeal to people of different religious backgrounds. Industry experts believe that flu resistant birds would command a 10% premium price in markets in South East Asia where bird flu is endemic.

5. Sources to corroborate the impact (indicative maximum of 10 references)

5.1) "The incredible, edible therapeutic egg" J. Petitte and P. Modziak (2007) PNAS 104, 1739-1740. http://dx.doi.org/10.1073/pnas.0611652104

5.2) Wellcome Trust Strategic grant: A novel resource for vertebrate development biology: transgenic chick embryos expressing fluorescent reporter genes. (Available on request.)

5.3) National Avian Research Facility: http://www.narf.ac.uk/; Transgenic chicken facility: http://www.roslin.ed.ac.uk/transgenic-chicken-facility/

5.4) "Transgenic chickens curb bird flu transmission" Virginia Hughes. Nature. 2011. http://dx.doi.org/10.1038/news.2011.16

5.5) University of Edinburgh public lecture series "Our Changing World" Helen Sang lecture "Food for the future: the potential of GM animals" available on YouTube: http://tinyurl.com/pzpuevl

5.6) BBSRC publicity regarding The Roslin Institute's Doors Open Day events. http://tinyurl.com/q9rueus

5.7) BBC Radio 4 series: "Costing the earth: edition: GM update; broadcast May 21st 2013 http://tinyurl.com/odz66kd

5.8) Contributed to POST (Parliamentary Office of Science and Technology) Notes on "Livestock Disease" and "Improving Livestock" (2011) http://tinyurl.com/omxjgjw

5.9) Sang is *ad hoc* advisor to the European Food Safety Authority GMO Panel on "Guidance on the risk assessment of food and feed from genetically modified animals and on animal health and welfare aspects"