

Using surrogate sires to disseminate high value genetics

Emily Clark¹, Simon Lillico¹, Jon Oatley²
and Mike Coffey³

¹The Roslin Institute, University of Edinburgh; ²Washington State University;
³Scotland's Rural College (SRUC)

Key Definitions

- **Genome editing** - Genome editing is the manipulation of the genetic material of an animal by deleting, replacing or inserting a DNA sequence.
- **New reproductive technologies** – technologies aimed at facilitating reproduction in breeding programs, including artificial insemination and embryo transfer.
- **Surrogate sires** – rams that are genetically infertile through genome editing of a single gene *NANOS2*.
- **Donor males** – ‘High value’ rams with ‘desirable’ genetics, who donate testicular tissue for stem cell culture and transplant into surrogate sires.
- **Spermatogonial stem cell transfer** – the process of harvesting stem cells from the testicular tissue of donor males and culturing them for transfer into recipient surrogate sires.

Harnessing the power of new breeding technologies

- The livestock sector in the UK has been effective in harnessing the potential of new breeding technologies.
- Artificial insemination is not routinely used in sheep breeding because of its invasive nature and expense.
- This limits the dissemination of genetics to what can be achieved through natural mating.
- As a consequence genetic improvement rates in sheep are low.
- The challenge is how to overcome this limitation.
- Surrogate sires can disseminate high value genetics by natural mating.

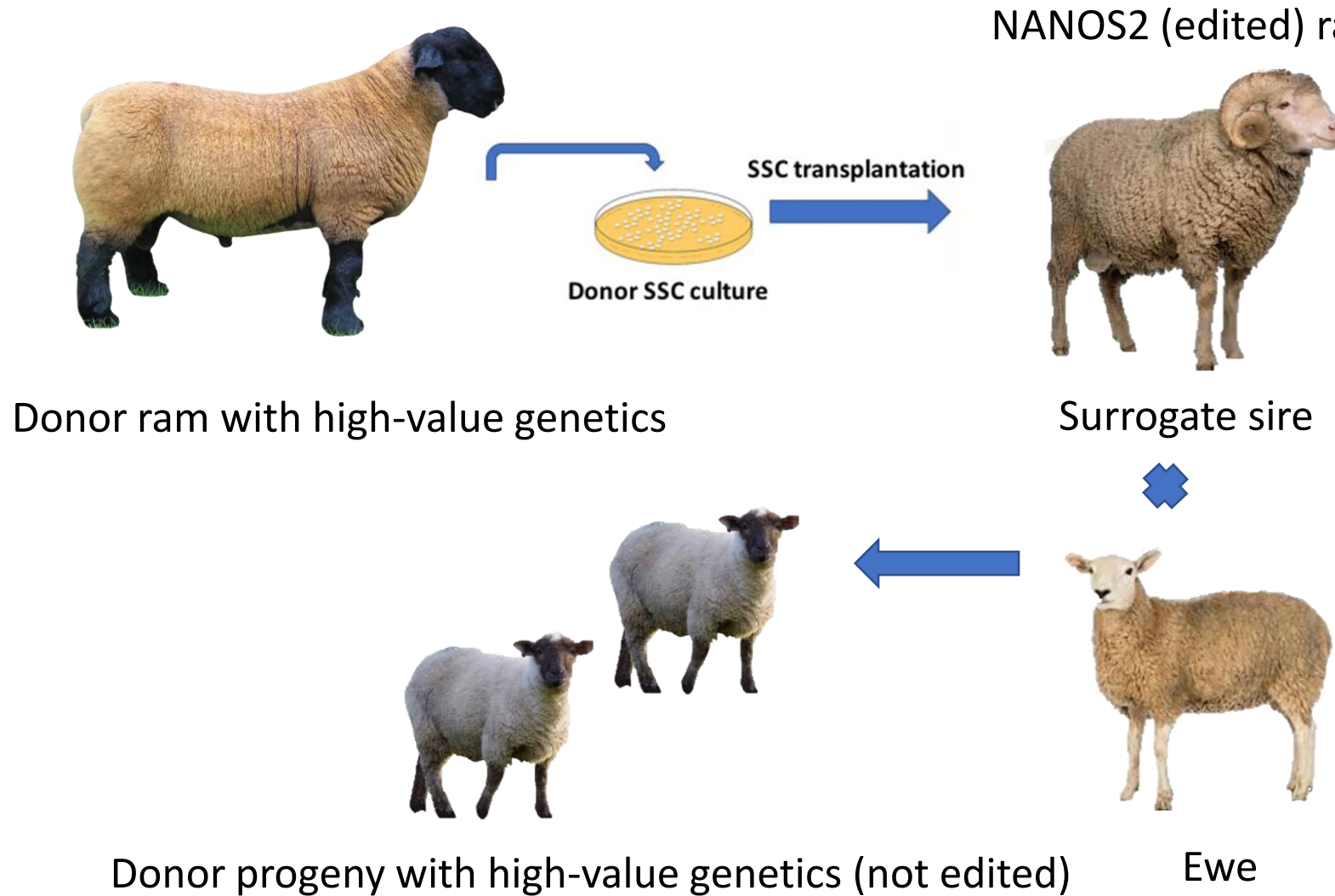


They operate essentially as mobile artificial insemination units



The Surrogate Sires Concept

Advantages



- **Surrogate sires are rams that are genetically infertile** as a result of editing the gene NANOS2.
- Through spermatogonial stem cell (SSC) transfer, **surrogate sires can propagate semen from donor rams**.
- Instead of having one ram **disseminating high-value genetics** we would have thousands.
- This would greatly accelerate how fast we can **achieve breeding goals** for a greener future.

Surrogate sires can accelerate genetic gain

- Gottardo et al. (2019) used simulations to model what using surrogate sires in a breeding could achieve.
 - ✓ Based on their models using surrogate sire technology in breeding programmes for livestock would significantly increase the genetic merit of commercial sires.
 - ✓ Achieving as much as 6.5 to 9.2 years-worth of genetic gain in comparison to a conventional commercial breeding program.

JOURNAL ARTICLE

A Strategy To Exploit Surrogate Sire Technology in Livestock Breeding Programs

Paolo Gottardo, Gregor Gorjanc, Mara Battagin, R Chris Gaynor, Janez Jenko, Roger Ros-Freixedes, C Bruce A. Whitelaw, Alan J Mileham, William O Herring, John M Hickey 

G3 Genes|Genomes|Genetics, Volume 9, Issue 1, 1 January 2019, Pages 203–215,
<https://doi.org/10.1534/g3.118.200890>

Published: 01 January 2019

Article history ▼

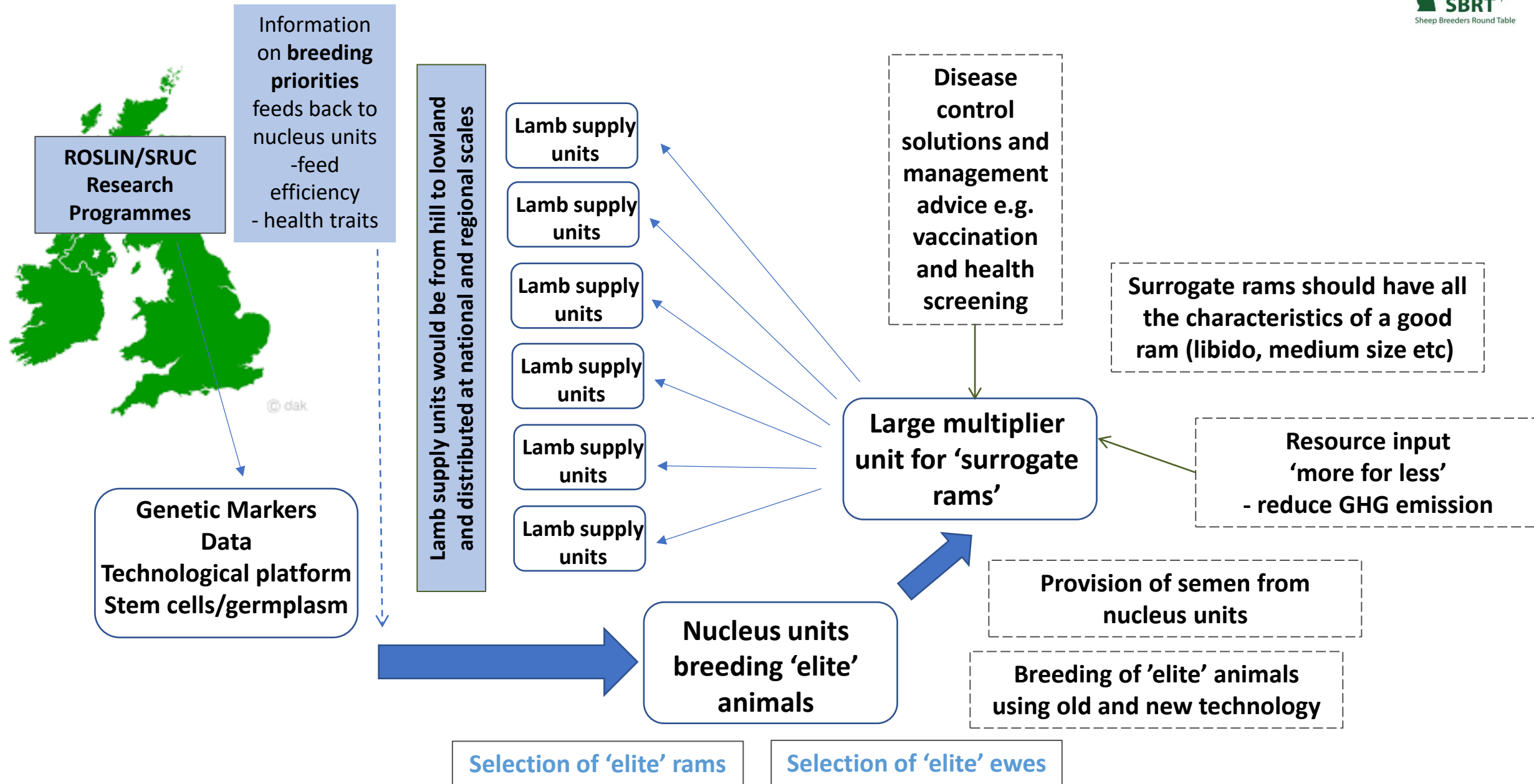
Reaching breeding goals quickly with surrogate sires

- **Surrogate sires provide a new breeding technology with the potential to overcome the limitations of artificial insemination.**
- **They could significantly enhance the efficiency and sustainability of sheep production in the UK.**
 - ✓ Surrogate sires provide an insurance policy disseminating genetics quickly that are likely to be important to the UK sheep sector in the future.
 - ✓ Reaching breeding goals fast and efficiently e.g. for a greener future this could be higher feed efficiency rates increasing profit and reducing environmental impact.

Relevance to the UK Sheep Sector

- There are approximately **33.3 million sheep** currently being raised in the UK, of which 16.2 million are breeding ewes, **and 400,000 are rams.**
Source: National Sheep Association <https://www.nationalsheep.org.uk>
- Capitalizing on **high-value genetics** in sheep **relies on** traditional approaches of in-house raising of breeding stock or the **purchase of sires from other producers.**
- **Surrogate sires** don't have to disrupt this – **they provide an alternative to AI**; the surrogate rams could still be purchased through the ram sales.
- Surrogate sires **can be context dependant** e.g. for hill or low-land and/or dual purpose.

A potential model for deployment of surrogate sires in the UK



Surrogate sires for a greener future

- UK sheep sector is a suitable sector to target for a proportional reduction in greenhouse gas (GHG) emissions as a contribution to a target of net zero by 2045.
- Mitigation strategies proposed include:
 - genetic/breeding programmes to select lower methane-emitting animals
 - dietary management to improve the digestibility of feed and fodder
 - better health and nutrition management to increase fertility and growth rates



Selection of donor rams for better feed efficiency may initially be of interest to sheep producers to decrease feed costs, lowering overall production costs and contributing to a greener future.



Incorporating shedding genetics would also reduce resource cost and increase sustainability.



NEWS

Home | InDepth | Israel-Gaza war | US election | Cost of Living | War in Ukraine | Climate | UK | World | Business

Science & Environment

Gene editing to produce 'super dad' livestock

15 September 2020



JON OATLEY

The genetically modified goats are a "proof in principle", say scientists

Where are we now with the technology?

- NANOS2 knock-out goats, mice, rats and cattle exist.
- In New Zealand there are DAZL knock-out sheep.
- We can isolate SSCs from sheep testes.
- SSC transfer from the donor to the surrogate hasn't yet been performed in sheep.
- To generate a recipient flock of NANOS2 knock-out rams would take 3-4 years.
- This is because sheep are seasonal breeders.



Considerations related to genome editing

- The technology of **gene editing is well established**, widely known and is currently going through regulatory processes in the UK.
- A key aspect of **surrogate sire rams** is that while they lack their own endogenous germline they **are otherwise physiologically normal**.
- **The offspring of surrogate sires are not edited or modified**, which may be more amenable to regulatory hurdles and help to alleviate consumer concern about genome edited products in the food chain.
- This is unique in that gene editing is being used to allow a natural mating process to take place and all subsequent offspring will be genetic descendants of non-gene edited animals.

Other Considerations

- Some infrastructure adjustment would be required to facilitate generation and distribution of surrogate sires, perform SSC transfer etc.
- The use of a relatively small number of donor rams would be very different to current practice.
- Care would need to be taken to minimise over-reliance on specific breeding lines.
- Equitable access to the technology would be essential.
- Practical implementation of surrogate sire technology would need to be carefully modelled and account for all potential risks, as well as the opportunities.

Summary

- Surrogate sires provide an effective new breeding tool to achieve genetic gain that is conducive for livestock production systems in which AI is difficult to implement.
 - ✓ Providing an insurance policy disseminating genetics quickly that are likely to be important to the UK sheep sector in the future.
 - ✓ Reaching breeding goals quickly and efficiently.
- Still at the proof-of-concept stage but the technology could be transformative.