



POPULAR SCIENCE ARTICLE

Livestock 2.0: Harnessing the CRISPR-Cas9 Toolbox to Secure Global Food Systems

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Abstract

To address the rising demand for animal protein, the FAO projects that global meat and milk production must increase by 76% and 63%, respectively. Traditional livestock breeding, cloning, and artificial embryo transfers face severe structural constraints, including prolonged generation intervals, low selection efficiency, and a lack of control over specific traits. Furthermore, conventional disease management relying on antibiotics has led to environmental contamination and the dangerous spread of antimicrobial resistance. In light of these challenges, CRISPR-Cas9 has emerged as the premier genome-editing platform, surpassing older tools like Zinc-Finger Nucleases (ZFNs) and TALENs by being cheaper, simpler to design, faster to develop, and uniquely capable of targeting multiple genes simultaneously (multiplexing). Operating as programmable "molecular scissors" that combine guide RNA with Cas9 nucleases to introduce site-specific double-strand breaks, this technology is actively transforming agricultural and biomedical traits. While the potential of CRISPR-Cas9 is virtually limitless, the industry faces severe challenges. These include complex intellectual property patent landscapes, public uncertainty regarding the safety and consumption of genetically edited agricultural products, and regulatory constraints. Because precisely edited animals contain no foreign DNA footprints, they are virtually indistinguishable from natural variants, making market detection highly difficult. Moving forward, to secure a global market, developers must prioritize rigorous safety testing using Whole-Genome Sequencing (WGS) to identify unintended off-target mutations, establish science-based regulatory frameworks, and lead transparent, open public dialogues to foster societal trust and acceptance.

Keywords: CRISPR-Cas9, Gene expression, Disease resistance, Animal welfare, Regulatory frameworks, Food security

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1. Introduction

Overpopulation, urbanisation and lifestyle changes have increased the global demand for animal protein. The conventional rearing livestock in intensive farms presents significant disease risks. Traditional disease management relies upon vaccines and antibiotics, but the prolonged use of antibiotics has potential problems, including environmental contamination and antimicrobial resistance. In addition to this, traditional livestock breeding systems including cloning and artificial embryo transfer are characterised by lengthy generation intervals, relatively low selection efficiency and limited control over specific genetic traits. Thus, the field of genetic engineering is a promising technology that solves these traditional

problems thus improving livestock productivity, disease resilience and sustainability by enabling precise and heritable genetic modifications.

2. The Evolution of Genome Editing Platforms and CRISPR-Cas9

Genome editing has evolved from Mega nucleases (MegNs), Zinc-Finger Nucleases (ZFNs), and TALENs to the more versatile CRISPR-Cas9 system. ZFNs and TALENs require complex, time-consuming protein engineering for each target. CRISPR-Cas9, derived from the natural adaptive immune system of bacteria and archaea, is simpler, cheaper and faster to design, while offering high editing efficiency and multiplexing, making it particularly valuable for improving complex, polygenic traits in livestock.

The molecular mechanism of CRISPR-Cas9 happens in three sequential stages: target recognition, DNA cleavage and cellular repair. First, the Cas9 nuclease forms a complex with a single-guide RNA (sgRNA), which directs the complex to a complementary DNA sequence adjacent to a Protospacer Adjacent Motif (PAM). Once the target is recognised, Cas9 undergoes conformational activation and its HNH and RuvC domains cleave the two DNA strands, producing a double-strand break approximately three base pairs upstream of the PAM. The cell then repairs this break primarily through either Non-Homologous End Joining (NHEJ), which can introduce small insertions or deletions and is commonly used for gene disruption, or Homology-Directed Repair (HDR), which uses a homologous donor template to achieve precise gene correction or targeted gene insertion. Thus, CRISPR-Cas9 combines programmable DNA recognition, precise cleavage and cellular repair mechanisms to enable targeted genome modification.

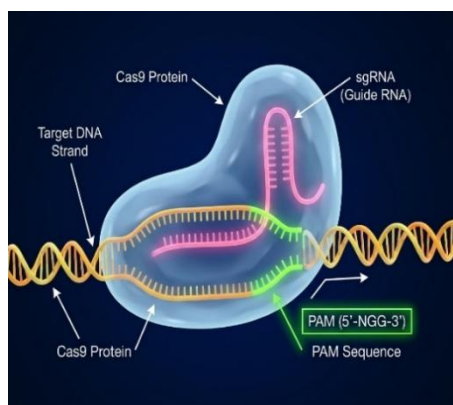


Fig. 1. CRISPR-Cas9 assembly and PAM recognition

3.Application in livestock productivity and trait improvement

The practical value of CRISPR-Cas9 lies in its capacity to enhance production traits, reproduction and welfare across species.

3.1 Muscle Development and Meat Yield

The most widely used application is the myostatin gene (*MSTN*, also designated *GDF8*). Myostatin acts as a negative regulator of skeletal muscle development, and knocking out the gene in cattle, sheep, goats and pigs blocks this inhibition of muscle growth. The result is a double-musled phenotype that yields significantly more meat and greater lean body mass. The outcome across ruminant and porcine species makes *MSTN* the archetypal demonstration of the technology in livestock.

3.2 Milk Composition and Hypoallergenic Dairy Products

Gene editing has been applied to remove the principal allergenic protein from milk. Knocking out the β -lactoglobulin gene — variously designated *BLG* or *LGB* (beta-globulin gene) eliminates common milk allergens and reduces the allergic potential of the product. The application has been pursued in dairy cattle as well as in goats and sheep.

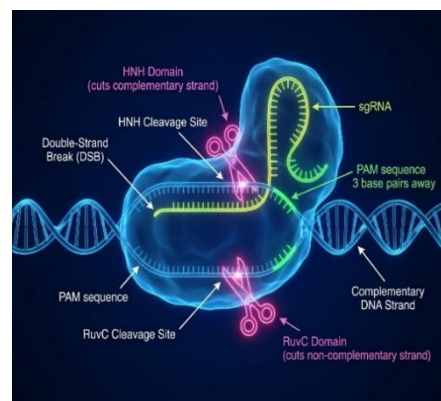


Fig. 2. Double-stranded cleavage

3.3 Cold Tolerance and Carcass Leanness in Pigs

Knocking the mouse adiponectin-*UCP1* construct into pigs restores a thermoregulatory capacity that domestic swine naturally lack. Edited animals preserve body heat in cold environments, which drastically reduces newborn piglet mortality under cold conditions, and simultaneously exhibit decreased fat accumulation of 4.89 per cent, producing leaner meat. This is notable because a single edit delivers a welfare benefit and a carcass-quality benefit concurrently.

3.4 Fibre Production in Goats and Sheep

Genome editing strategies have been demonstrated for increasing cashmere and wool yield. Knocking out fibroblast growth factor 5 (*FGF5*) removes the natural inhibitor of fibre growth, resulting in significantly increased secondary hair follicle density and longer cashmere fibres. Independently, knocking the thymosin beta 4 (*Tβ4*) gene into the *CCR5* locus of cashmere goats accelerates follicle stem cell differentiation and further increases cashmere yield, notably without reducing the fineness or quality of the fibre, since fibre value is determined as much by diameter as by mass.

3.5 Reproductive Efficiency and Fecundity

In sheep and goats, introducing point mutations at the *FecB* mutation site of the *BMPR-1B* gene, or editing *GDF9*, significantly increases ovulation rates, lambing rates and litter sizes. In cattle and buffalo, knock-out of the *OCT4* gene has been studied as a means of analysing early

blastocyst maturation. In buffalo specifically, knocking out the *TSP1* gene in cells *in vitro* improves the viability of progesterone-producing luteal cells, which may in turn allow scientists to regulate and extend the female reproductive cycle.

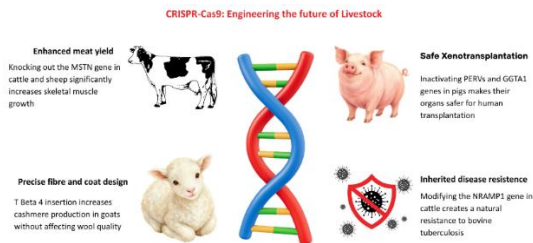


Fig. 3. Different genome editing in livestock species

3.6 Sex Pre-Determination and Embryo Sexing

Control over offspring sex carries direct economic value. In pigs, suppression of the *SRY* gene on the Y chromosome has been used to pre-determine the sex of offspring in order to maximise economic gain. In cattle and water buffalo, knocking an enhanced green fluorescent protein (*eGFP*) reporter into the Y chromosome of fetal fibroblasts enables the sexing of pre-implantation embryos, since male (XY) embryos can be readily separated under a fluorescence microscope by their green glow.

3.7 Animal Welfare: The Polled Phenotype

CRISPR has been used to breed hornless, or polled, cattle in order to improve animal welfare and handler safety. The approach introduces the 202 base-pair Celtic polled variant (*Pc*) into the fibroblasts of horned cattle, including Holstein dairy cattle, using either Cas9 or Cas12a. Animals carrying the introduced variant do not require the painful physical dehorning procedures that are otherwise routine in dairy husbandry.



Fig. 4. potential impacts of genome editing on livestock products

3.8. Genome Editing for Disease Resistance and Antiviral Breeding

Beyond productivity, the editing of specific loci permits the generation of livestock that are

constitutively resilient to devastating infections. Precise knock-in of the natural resistance-associated macrophage protein-1 (*NRAMP1*) gene into Holstein cattle, including integration at safe-harbour loci such as *Rosa26* or *FSCN1-ACTB*, significantly increases resistance to *Mycobacterium bovis* and thus protects against bovine tuberculosis. For brucellosis, CRISPR has been used to target and restrict bacterial replication genes such as *virB10* and *RpoA*, inhibiting intracellular replication of *Brucella*. In the case of John's disease, knock-out of the *IL10RA* gene has been employed to analyse immune and anti-inflammatory responses and to modulate pro-inflammatory cytokines. Knock-out of the prion protein gene (*PRNP*) in bovine cells and embryos, achieved by precise targeting of coding exon 3, confers protection against Bovine Spongiform Encephalopathy, commonly known as mad cow disease.

3.9 Xenotransplantation and Large-Animal Models of Human Disease

Pigs can serve as organ donors for human recipients. CRISPR-Cas9 is used to deactivate Porcine Endogenous Retroviruses (PERVs) in pig cells through multiplex inactivation of all active copies, thereby preventing cross-species viral transmission to human transplant recipients. It also knock-out of genes including *GGTA1* (alpha-1,3-galactosyltransferase) and components of the MHC system drastically reduces transplant rejection. Knock-out of the *CFTR* gene in sheep successfully models human cystic fibrosis. Introduction of precise single-point mutations into the non-specific alkaline phosphatase (*TNSALP*) gene in lambs creates a large-animal model of the rare human metabolic bone disease hypophosphatasia. In goats, knock-out of *PRP* and *NUP155* models heart disease, while knock-outs of interferon alpha (*IFNA*) provide models for studying fetal resistance to Zika virus infection. Thus, CRISPR Cas-9 offers wide scope of linking livestock to human therapeutics.

Gene	Effect on animal	Reference
Myostatin (<i>MSTN</i>)	Suppresses the negative regulator of muscle growth, producing a double-muscling phenotype that yields significantly more meat and greater lean body mass.	Zhou <i>et al.</i> (2022)
Celtic Polled Variant (<i>Pc</i>)	Produces physically hornless (polled) dairy cattle, completely avoiding the need for painful manual dehorning procedures.	Gu <i>et al.</i> (2020)
Scavenger Receptor (<i>CD163</i>)	Renders pigs fully immune to Porcine Reproductive	Whitworth <i>et al.</i>

	and Respiratory Syndrome Virus (PRRSV), protecting against both European and North American genotypes.	(2015)
Macrophage Protein 1 (<i>NRAMP1</i>)	Significantly increases resistance to bovine tuberculosis (<i>Mycobacterium bovis</i>), reducing herd mortality and zoonotic transmission to humans.	Gao <i>et al.</i> (2017)
Beta-lactoglobulin (<i>BLG</i> / <i>LGB</i>)	Removes the primary milk allergen, yielding hypoallergenic milk and dairy products for consumers.	Zhou <i>et al.</i> (2017)
Fibroblast Growth Factor 5 (<i>FGF5</i>)	Increases secondary hair follicle density and fiber length, dramatically boosting cashmere wool yield.	Wang <i>et al.</i> (2016)
Alpha-1,3-galactosyltransferase (<i>GGTA1</i>)	Eliminates the alpha-gal cell-surface antigen, which drastically reduces transplant rejection and human anti-pig cytotoxicity in xenotransplantation.	Petersen <i>et al.</i> (2016)

4. Bioethical, Legal, Economic and Regulatory Considerations

The application of livestock genome editing raises important ethical, legal, economic and regulatory considerations. Ethically, while applications such as the polled phenotype and genetically mediated disease resistance may reduce animal suffering, increased efficiency could also encourage industrial farming. Public acceptance remains uncertain, particularly regarding off-target effects, animal welfare and the adequacy of regulatory oversight, highlighting the need for transparent governance, sustained public dialogue and robust safety assessment. The intellectual property and patent landscape surrounding CRISPR-Cas systems is also complex and may influence researchers' and commercial developers' freedom to operate, making balanced licensing and regulatory frameworks important for continued innovation. Economically, the global CRISPR gene-editing market is projected to reach US\$10.82 billion by 2030, reflecting the substantial commercial potential of the technology. Regulation presents an additional challenge because precisely edited animals may contain no readily detectable foreign DNA footprint, making them potentially indistinguishable at the sequence level from animals carrying naturally occurring variants. Consequently, regulatory authorities must establish appropriate, science-based frameworks for assessing genome-edited livestock, while developers should employ

comprehensive genomic analyses, including whole-genome sequencing, to identify unintended genetic alterations and ensure the safety, stability and consistency of edited animals before their commercial application.

5. Conclusion

CRISPR-Cas9 is an economical, rapid and highly versatile system, unequalled among current genome-editing platforms in efficiency and cost-effectiveness, and it holds effectively limitless potential to transform both crop and livestock breeding. The evidence surveyed in this chapter shows the technology operating simultaneously across four registers: raising productivity through targets such as *MSTN*, *UCP1*, *FGF5* and *Tβ4*; improving product quality through *BLG* and related loci; conferring resistance to bacterial, prion and viral disease through *NRAMP1*, *PRNP*, *CD46*, *CD163*, *chNHE1* and *chANP32A*; and advancing human biomedicine through xenotransplantation and precise large-animal disease models. Continued research and the broader circulation of this technology are advocated as means of securing global food systems in an era of declining natural resources, shaping the future of global agriculture, animal health and human well-being alike.

References

- Gao, Y., Wu, H., Wang, Y., Liu, X., Chen, L., Li, Q., Cui, C., Liu, X., Zhang, J., & Zhang, Y. (2017). Single Cas9 nickase induced generation of NRAMP1 knockin cattle with reduced off-target effects. *Genome Biology*, 18(1), Article 13.
- Gu, M. J., Gao, L., Zhou, X. Y., Wu, D., Wei, Z. Y., Li, G. P., & Bai, C. L. (2020). Fixed-point editing of POLLED sites in Mongolian cattle without horns. *Journal of Agricultural Biotechnology*, 28, 242–250.
- Petersen, B., Frenzel, A., Lucas-Hahn, A., Herrmann, D., Hassel, P., Klein, S., Ziegler, M., Hader, K. G., & Niemann, H. (2016). Efficient production of biallelic GGTA1 knockout pigs by cytoplasmic microinjection of CRISPR/Cas9 into zygotes. *Xenotransplantation*, 23, 338–346.
- Wang, X., Cai, B., Zhou, J., Zhu, H., Niu, Y., Ma, B., Yu, H., Lei, A., Yan, H., Shen, Q., & Shi, L. (2016). Disruption of FGF5 in cashmere goats using CRISPR/Cas9 results in more secondary hair follicles and longer fibers. *PLOS ONE*, 11(10), Article e0164640.
- Whitworth, K. M., Rowland, R. R., Ewen, C. L., Tribble, B. R., Kerrigan, M. A., Cino-Ozuna, A. G., Samuel, M. S., Lightner, J. E., McLaren, D. G., & Mileham, A. J. (2016). Gene-edited pigs are protected from porcine reproductive and respiratory syndrome virus. *Nature Biotechnology*, 34(1), 20–21.
- Zhou, S., Kalds, P., Luo, Q., Sun, K., Zhao, X., Gao, Y., Cai, B., Huang, S., Kou, Q., Petersen, B., & Chen, Y. (2022). Optimized Cas9:sgRNA delivery efficiently generates biallelic MSTN knockout

sheep without affecting meat quality. BMC Genomics, 23(1), Article 348.
Zhou, W., Wan, Y., Guo, R., Deng, M., Deng, K., Wang, Z., Zhang, Y., & Wang, F. (2017). Generation of

beta-lactoglobulin knock-out goats using CRISPR/Cas9. PLOS ONE, 12(10), Article e0186056.